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Programme

FARMACI INNOVATIVI E RADIOTERAPIA: COSA, COME E QUANDO INTEGRARLI CON I TRATTAMENTI RADIANTI NEL PAZIENTE ANZIANO

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The use of targeted therapy (TT) has favorably changed the outcome of various cancers. Elderly pts (>65 yy) are an heterogeneous group and represent the majority of cancer diagnoses. Tolerance and efficacy of TT in elderly pts seems to be similar to that in younger pts with an increase of specific AEs in elderly for selected TT.[1] Data on TT associated to radiation therapy (RT) are growing but in elderly population are extremely limited probably due to different issues as that are often under-represented in clinical trials.

TT come in two main forms: monoclonal antibodies and small molecules drugs. As regard the first, at date, evidence suggests as feasible a combination of primary RT with cetuximab in all pts with advanced HN cancer that are not eligible for CDDP based CT concomitant to RT (and elderly represents the majority of these pts) with specific toxicities as cutaneous rash and infusion reactions. InHER2 positive breast cancer there is a widespread use of trastuzumab associated to RT but limited study evaluated their combination, some data suggest a potential cardiac toxicity and others do not confirm it; at date pts age should not be limited this association.[2] As regards the second group, different drugs are tested. The proteasome inhibitor bortezomib may radiosensitize tumours blocking DNA repair, in a phase I trial looking bortezomib concurrent with palliative RT, in pts with metastatic solid tumour with age up to 80 yy, appears feasible with hematologic toxicity as the most common reported.[3] Histone deacetylase (HDAC) inhibitors may also radiosensitize tumours via DNA repair inhibition, in PRAVO trial (an escalated vorinostat dose trial with palliative pelvic RT for gastrointestinal carcinoma in pts with median age of 77 yy) the majority of AEs were G1/2 so the authors concluded that Vorinostat can be safely combined with short-term pelvic palliative RT.[4] Also inhibition of BRAF has been associated with radiosensitization and the introduction of small molecule BRAFV600 kinase inhibitors increase the overall and progression-free survival compared with conventional chemotherapy in metastatic melanoma pts; however some unexpected severe toxicity have been reported suggesting paying specific attention when RT and BRAFi are given even not concurrently but in shorter time, this datum should be further underline in elderly pts where seems to be also a slight decrease in efficacy in pts ≥ 75 years old.5

Conclusions. In elderly pts different aspects should be considered: 1-the numerous comorbidities exposed these pts to a combination of a large number of drugs with possible interactions and risk of increased toxicity or decreased efficacy of TT; 2-data concerning safety and toxicity of TT in these pts are limited; 3-data on TT + RT derived from trial in which the elderly pts were considered "fit" and not represent all geriatric cancer pts. Specific clinical trials for elderly pts would be useful.

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MANAGEMENT OF MENINGIOMAS: SURGERY OR RADIOTHERAPY?

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Meningiomas arise from arachnoidal cells in the meninges and represent about 14–20 % of intracranial adult tumors.[1] The majority of meningiomas are histological benign lesions that are slow growing, and without any symptoms for a long time. In that case the therapist may well suggest a wait-and-see strategy. The therapy of meningiomas focuses firstly on the surgical treatment. After surgical resection of benign meningiomas, progression-free survival rates at 5, 10, and 15 years are 93, 80, and 68 %, respectively.[2] Lesions close to critical structures, especially skull base meningiomas, are unlikely to be completely resected and are associated with an increased risk of recurrence, and/or surgery morbidity. Radiotherapy (RT) is an alternative treatment especially for inoperable, recurrent, or residual meningiomas and a local control (LC) is obtained in 68–100% of patients at 5–10 years.[3] The RT of meningiomas has evolved with the development of stereotactic techniques for the planning and RT delivery. Actually, meningiomas can be seen as a paradigm for the use of stereotactic RT because they are often clearly delineated. Almost all World Health Organization (WHO) grade I and II tumors never infiltrate the brain tissue, often have complex shapes, and are close to various radiosensitive structures. Radiosurgery (SRS) consent to deliver high RT single dose (12–15 Gy) and it is often adopted in the treatment of recurrent or inoperable meningiomas,[4] but this approach is limited to small lesions far away from the critical brain structures. Fractionated stereotactic RT combines the precision of stereotactic positioning with the radiobiological advantage of fractionation. It might be an effective alternative treatment for large tumors and in lesions close to organs at risk.[5] The conventional dose of stereotactic RT varies from 50 to 54 Gy at 1.8–2 Gy/fraction, five times a week. Currently the most appropriate radiation doses and fractionation schemes are still undefined. Fractionated stereotactic RT can be administered using hypofractionated regimens (hFSRT) with the advantage of reducing the fraction number and treatment time. In the literature, few data on these regimens for treatment of meningiomas are available.[6] However comparative trials suggest the effectiveness of hFSRT and show no significant difference in LC and toxicity with respect to SRS or fractionated stereotactic RT.[7] In most cases a decision on the right approach to treat has to be decided based on the medical condition of the patient, the experience of the treating physician, the capabilities for RT, and the personal preferences of the patient. Only for patients with tumors with a spinal localisation or WHO Grade I meningiomas with a cortical localisation, a primary treatment surgery can be suggested. For all other localisations of tumors, an alternative treatment by means of stereotactic RT should be discussed.

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THE EMERGING ROLE OF IMMUNOTHERAPY IN HEAD AND NECK CANCER AND FUTURE DIRECTIONS

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Oncogenesis studies unveiled the capability of cancer cells to override the surveillance of the immune system through accumulation of genetic mutations and tumor heterogeneity.

Among immune-escape mechanisms that cancer cells are able to activate there are: the lack of recognition of the tumor-associated antigens; the enhanced negative co-stimulatory recognition and the alteration or suppression of the immune response induced by negative regulators of the immune system.[1,2]

Immunotherapy aim is to elicit an immune response against the tumor allowing its eradication or long-term suppression of its growth, and the generation of immu-

nological memory.[1,2] HNSCC are typically characterised by an inflamed phenotype with T-cell infiltration, and could potentially benefit from therapies that target the immune system. So far, the blockade of cancer cells and tumor microenvironment activation of inhibitory stimulus seems a promising strategy. PD-1/PD-L1 (Programmed Death Ligand protein 1) and CTLA4 (Cytotoxic T-Lymphocyte Antigen 4) are the most known costimulatory molecules and immune checkpoints.[1,2]

Preclinical data showed a synergistic effect of radiation and the concomitant administration of anti–CTLA-4 antibodies (Abs) not only in the radiation field but also out of it (abscopal effect).[3] The underlying hypothesis is that checkpoint inhibitors given before or concomitantly to radiation therapy can lead to antitumor immune responses.

Current immunotherapy clinical trials for HNSCC are evaluating: Ipilimumab, a monoclonal (m) Ab against CTLA-4, in combination with cetuximab and intensity-modulated radiotherapy (IMRT) (NCT01860430 and NCT01935921);Tremelimumab an anti-CTLA4 mAb, Durvalumab, a mAb that inhibits binding of programmed cell death ligand 1 (PD-L1) alone or combined with tremelimumab compared to standard treatment (NCT02369874), Pembrolizumab and Nivolumab, anti-PD1 Abs.[4] Both these latter showed a clinically significant activity and an acceptable safety profile in advanced pre-treated platinum and cetuximab-resistant HNSCC.[5,6]

A second broad category of immunotherapy is active immunization of the tumor-bearing host by increasing and activating preexisting anti-tumor T cells. Ongoing trials are assessing the safety and dosing of vaccine in HPV positive HNSCCC patients(NCT00019110)[7]

Finally, a most efficacious form of immunotherapy is adoptive T-cell transfer (ACT). This involves the transfer of activated immune T cells, which are capable of recognizing cancer cells and destroying them.[2] In a phase II study, ACT with EBV-specific CTLs in combination with chemotherapy has shown promising results.[8]

In conclusion, immunological therapy could become a new addition to the standard treatment of HNSCC. In order to improve patient outcome, many novel strategies are being explored in clinical trials .

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VERY HIGH RISK DISEASE: WHICH ANDROGEN DEPRIVATION THERAPY? ADJUVANT CHEMOTHERAPY?

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The use of Androgen Deprivation therapy (ADT) in combination with radiotherapy (RT) has traditionally been considered the standard option in high-risk prostate cancer patients (HRPC).[1,2] In this setting, chemotherapy (CT) in conjunction with RT has not an established role as part of a combined modality. However, results from three trials using docetaxel-based CT suggest that this treatment can be considered in selected cases.[3-5]

While EORTC 22863 trial[2] and RTOG 8531[6] have investigated the efficacy and optimal duration of ADT in combination to RT in HRCP, GETUG 15, CHAARTED and STAMPEDE compared ADT alone with ADT combined with immediate docetaxel based-CT.

The primary objective in all 3 studies was overall survival (OS).

In the EORTC 22863 at a median follow-up of 9 years, the 10-year disease-free survival (DFS) was significantly improved with the addition of ADT compared with RT alone. Similarly, the 10-year OS was better with the combined treatment, and prostate cancer mortality was decreased. In RTOG 8531 the addition of long-term ADT significantly decreased the rates of local failure and distant metastases (23 versus 38 and 24 versus 39 percent, respectively, compared with observation). The 10-year absolute OS rate was increased (49 versus 39%), and the disease-specific mortality rate was decreased (16 versus 22%).

In the GETUG 12 trial, the use of CT in conjunction with ADT for three years versus ADT alone, has shown an improvement in the eight-year relapse free survival (RFS) rate.

In the RTOG 0521 trial, patients were treated with ADT for two years beginning eight weeks prior to RT. Those randomly assigned to CT also received docetaxel after RT.[4] At a median follow-up of 5.5 years, OS and DFS were improved with adjuvant CT. Additionally STAMPEDE trial supporting a potential role for CT in high-risk patients including men with both metastatic disease and high-risk M0 disease.[5]

Docetaxel plus ADT significantly improved OS failure-free survival compared with ADT alone (median 81 versus 71 months).

Docetaxel plus ADT significantly increased the

duration of compared with ADT alone.

Considering the available discussed data we can conclude that: i) in HRPC the combination of RT and long-term (two to three year) course of ADT continued to be considered the standard of care; ii) a potential benefit from adding docetaxel based-CT to ADT has been suggested in randomized trials. Longer follow-up is needed to assess whether this benefit translates into improved metastasis-free survival and OS. Furthermore, data from "Latitude trial"[7] recently showed that the addition of abiraterone acetate and prednisone to ADT significantly increased OS and radiographic progression-free survival in men with newly diagnosed, metastatic, castration-sensitive prostate cancer.

Probably, this last result could further open a discussion on the most appropriate clinical approach also in the setting of HRPC.

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PAZIENTE METASTATICO E IRRADIAZIONE DEL PRIMITIVO PROSTATICO: MITO O POSSIBILE REALTA'?

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To date, Androgen Deprivation Therapy (ADT) with or without chemotherapy with Docetaxel is the first-line therapy for de novo metastatic prostate cancer (mPC) patients.[1]. Emerging, retrospective data suggest survival benefits in patients diagnosed with mPC after definitive loco-regional treatment such as surgery or radiotherapy on the prostate.[2,3] Mechanisms underlying the benefit of definitive treatment of the primary in mPC patients are still not completely understood. Biological evidences support this hypothesis. In fact, extensive pre-clinical experiments had confirmed the concept of "seed and soil", as proposed by Paget in 1889.[4] This theory hypothesized the existence of an interplay between metastatic properties of cancer cells (seed) and the favourable properties of the microenvironment (soil) conditioning the selective organ-preference of metastases therefore cancer cells growth. The primary tumour acts as a continuous source of metastatic cancer cells that circulate and generate metastases. These new lesions further release tumour cells that may again communicate with the primary site in a multidirectional process.[5] All this considered, "Hit the primary" with "curative" local treatment, could break this process. Moreover, in this emerging scenario, modern radiotherapy plays an important role owing to its better toxicity profile compared to other local treatments such as surgery. In conclusion, many clinical open questions concerning the potential role of local radiotherapy in the management of mPC patients will be probably answered in the next future by randomized, phase III trials among which STAMPEDE and PEACE-1.

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COMBINED TREATMENT IN UTERINE CERVIX CANCER: STATE OF ART AND FUTURE PERSPECTIVES

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Abstract. In 1999, on the basis of evidences from 5 large randomized studies showing improved loco-regional control and survival, the National Cancer Institute made a strong alert to include cisplatin based chemotherapy along with concurrent radiotherapy in uterine cervix cancer.[1] These data were confirmed in subsequent studies and meta-analyses.[2,3] A larger advantage was showed in earlier stage than in more advanced disease, without clear evidence regarding the best chemotherapeutic regimen.[2,3]

At present, concurrent chemo-radiotherapy plus brachytherapy is the standard treatment of stage IB2-IVA disease.[4,5] Moreover, concurrent chemo-radiothe-

rapy is also indicated in the adjuvant setting for high risk disease, as positive nodes, positive margin and parametrial invasion.[4,5]

The best chemotherapeutic drugs and treatment schedule are not well established. A meta-analysis of 8 randomized and non randomized studies evidenced a survival advantage for doublet chemotherapy schedule with different drugs over cisplatin alone.[6] However, some criticisms can be pointed out about patient selection and studies characteristics. Two randomized trials exploring the efficacy of concurrent chemotherapy with single cisplatin and cisplatin plus gemcitabina reported conflicting results.[7,8] Of note, in one of these trials, adjuvant chemotherapy was added after concurrent treatment completion.[8] To improve local control in patients with locally advanced disease, alternative treatments and new chemotherapeutic strategies have been evaluated. A study reported triweekly cisplatin (75 mg/ m^2) chemotherapy was more effective than conventional weekly cisplatin (40 mg/ m^2).[9] Many randomized trials, exploring the role of adjuvant chemotherapy after definitive chemoradiotherapy, neoadjuvant chemotherapy before definitive chemoradiotherapy and preoperative chemo-radiotherapy, are ongoing (EORTC 55994/NCT 00039338, INTERLACE TRIAL, OUTBACK TRIAL, GOG-RTOG 0724). Bevacizumab, a monoclonal antibody against the VEGF, witch has been recently introduced in the standard treatment of recurrent or persistent cervical cancer, is under investigation in addition to chemoradiation in bulky tumors.[10]

Results of ongoing studies to better define the more effective chemo-radiotherapy treatment in advanced and early uterine cervix cancer are pending.

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IMAGING FOR EXTERNAL BEAM RADIOTHERAPY PLANNING AND DELIVERY

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Aims: The improved efficacy of radiation treatment in cervical cancer (CC) results in part from tremendous imaging innovations. Advanced radiotherapy (RT) techniques may significantly benefit CC patients, in terms of reducing late toxicity and potentiating dose escalation. According to the dramatic changes of tumor, target and normal tissue topography during external beam radiochemotherapy need to be assessed by repetitive imaging studies to check the individual situation at a given time point during treatment. It is therefore important to consider the extent and patterns of organ motion and to investigate potential image-guided RT solutions before implementing advanced RT techniques for CC.

Methods: We summarize the advances in imaging that have potential applications in CC radiotherapy.

Results. Morphological MRI has become a standard imaging method for CC radiotherapy, its multiple planes allowing for a reliable volumetric definition of the target volume. Contouring guidelines recommend delineation for both target and OARs on T2 weighted MRI.[1,2] Concerning inter- and intrafraction mobility of pelvic organs MRI is particularly useful to measure motion variability due to its excellent soft tissue visualization, the absence of radiation, the availability of multiplanar imaging and fast 4D imaging. A practical solution is to incorporate intrafraction and interfraction MRI-guided soft tissue registration with adaptation of the treatment plan to adjust for the observed variations. Functional MRI sequences have been investigated as biomarkers for determination of radioresistance, as well as Dynamic contrast-enhanced MRI that is assumed to show vascular density and perfusion which is thought to be correlated with hypoxia and radioresistance. Further new imaging methods under investigation include blood-oxygen level dependent (BOLD) MRI[3] and diffusion-weighted high-resolution magic angle spinning magnetic resonance spectroscopy (MRS).[4]

The role of FDG PET/CT in the evaluation of patients with cervical cancer has expanded rapidly. Value of PET/CT has been found in the detection of locoregional and distant nodal metastases and subsequent change in management. Use of FDG PET/CT facilitates RT planning. The FDG PET–derived parameters SUVmax, metabolic tumor volume (MTV) and total lesion glycolysis (TLG) are emerging as predictive markers and possible stratification tools.[5]

Conclusions. MRI plays an important role in the development of adaptive radiotherapy as it provides 3D information about organ motion and tumor volume shrinkage.[6-8] With MRI-linear accelerator development on the horizon, real-time MR imaging during treatment will allow for excellent soft tissue delineation, image fusion, rapid adaptive radiation planning, and improved tumor targeting for women with CC. FDG PET/CT has become an essential modality for staging and restaging and for response assessment to therapy in the care of CC patients.[9,10] Integrated PET/CT precisely combines metabolic PET images with anatomic CT images and has proved more accurate than high-resolution CT alone, particularly in showing the presence of regional lymph node involvement and extrapelvic disease extension.

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IMAGE-GUIDED BRACHYTHERAPY IN LOCALLY ADVANCED CERVICAL CANCER: GOLD STANDARD AND POSSIBLE OPTIMIZATIONS

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For locally-advanced cervical cancer concurrent chemo-radiotherapy is the standard of care. External beam radiation therapy (EBRT) is tipically combined with a brachytherapy (BT) boost, currently considered "not optional".

In the last decade, the use of 4D image guided adaptive BT (4D-IGABT) based on the GEC- ESTRO recommendations has been successfully implemented in the clinical practice worldwide.

4D-IGABT integrates imaging and treatment in space and time and this image-based target approach improves the opportunities to prescribe, to optimize and to report doses in a reproducible way as well as the clinical outcome in terms of local control, overall survival and morbidity. Compared with a conventional CT-planning based approach, Magnetic Resonance Imaging (MRI) offers a superior soft tissue contrast and provides more detailed images for IGABT, helpful to reduce uncertainties in the definition of a shrinking target volume (GTV, CTVs) and OARs with a greater and more reproducible dose adaptation.

Advances in IGABT include improved individualization of BT applicators as well as tailored dose optimization. Intracavitary applicators are appropriate for residual disease (RD) confined to the uterus and hybrid applicators (obtained by combining the intracavitary and interstitial applicators) are suitable for targeting large RD involving paracervical tissues, essential for dose escalation without significant increase of dose to OARs.

Dose optimization is obtained adjusting the source loading and the dwell times manually by use of graphical tools or with inverse planning. The analysis of DVH parameters has become standard: dose to High-Risk (HR) CTV is evaluated in terms of dose covering 90% of the HR CTV (D90) and the dose volume constraints for OARs are 75 Gy EQD2 in 2 cc of rectum and sigmoid and 90

Gy EQD2 in 2 cc of bladder.

It is important for IGABT dose optimization to evaluate the cumulative dose delivered by EBRT and BT and the algorithm of image registration can be helpful to perform a volume registration. Furthermore, DWI parameters seem to be promising as prognostic biomarkers for clinical outcome. IGABT clinical experience indicates a very favorable therapeutic ratio with high local control rates

(>90%), even for advanced disease, with low morbidity rates (<5% G3/G4). Anyway these data has to be evaluated within prospective clinical multicenter studies such as the ongoing EMBRACE study.

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INTERNAL VALIDITY IN CLINICAL TRIALS

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The strength of randomised controlled trial (RCTs) relys on its excellent internal validity, which is based largely on the power of randomisation to ensure that the only difference between two treatment arms is their

exposure to the treatment itself. Although randomisation minimises the risk of confounding bias, there are other biases inherent to RCTs that reduce their applicability to patients usually seen on daily practice. In particular, patients, providers, and concurrent care in the general population are different from those in clinical trials, and the generalisability (or external validity) of RCTs may be limited. Although population-based observational research does not offer the same level of internal validity of RCTs, well-designed observational studies can offer superior external validity and provide a unique opportunity to evaluate the uptake of new treatments and their outcomes in routine practice.

MODERNO IMAGING: STUDIO DI BASE E APPROFONDIMENTO MIRATO IN PROSPETTIVA DEL TRATTAMENTO RADIANTE

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The primary purpose of this lecture was to discuss the role of imaging in palliative radiation therapy for skeletal metastases focusing on the role of magnetic resonance (MR) imaging in the characterization of spinal lesions. MR imaging is the imaging modality of choice for detecting axial and peripheral bone metastases, their extension from bone marrow as well as the possible involvement of surrounding soft tissue. However, differentiation between vertebral osteoporotic fractures and pathological neoplastic fractures may be a diagnostic challenge using routine MR imaging alone. Diffusion-weighted MR imaging is a non-enhanced functional MR imaging technique with short scanning time that can complement and augment routine MR imaging in the evaluation of vertebral body collapse.

In recent years, whole-body MR imaging, including anatomic and diffusion-weighted sequences, is increasingly used for the detection of metastatic disease with high diagnostic accuracy. Furthermore, this imaging modality provides morphologic and functional information in a unique examination.

In recent years, technological advances have enabled the development of hybrid imaging modalities such as positron emission tomography (PET)/CT which has already shown some advantages over PET alone. Furthermore, PET/MR imaging seems to be becoming a potentially superior alternative to PET/CT, although there is currently no published article comparing the accuracy of PET/CT and PET/MR imaging in diagnosing skeletal metastases.

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WHICH IMAGING IN THE ASSESSMENT OF TUMOR RESPONSE WITH INNOVATIVE DRUGS?

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The measure of tumor response with imaging has been proposed since 1980 by the WHO to assess the efficacy of new drugs within cancer clinical trials as a surrogate endpoint of patient overall survival. Most clinical trials now adopt RECIST imaging criteria version 1.1.[1] RECIST mainly defines response based on the change in the sum of target lesion diameter at Computed Tomography (CT) or Magnetic Resonance (MR) at different time points. While RECIST is accurate in measuring response to conventional chemotherapy it may not provide accurate information in patients undergoing therapy with new drug regimens (i.e. target therapy, immunotherapy, etc.), in those undergoing percutaneous tumor ablation or stereotactic surgery. Information on tumour internal features (e.g. measurement of tumor density) has been adopted first in Choi criteria for GIST treated with imatinib were tumor necrosis, not change in diameter, is commonly observed.[2] Choi criteria applied to GIST were more accurate that RECIST in predicting overall patient survival. Recently implemented hepatocellular tumor imaging criteria mRECIST also take into account response to percutaneous ablation procedures.[3] Specific criteria have been adopted for assessment of response in patients with lymphoma, keeping into account not only the anatomical information provided by CT but also the functional/metabolic data of FDG-PET.[4]

Novel immunotherapeutics have been seen to trigger different response patterns in tumours than classic chemotherapy drugs, including the so-called 'pseudo-progressions', leading to concerns about assessing changes in tumours using existing tools as an objective evaluation of response to the treatment and disease progression. The new iRECIST take into account responses not typically observed in traditional systemic treatment to be identified and better documented.[5]

Following multiple lines of therapy patient's individual cancer lesions may behave differently: some may continue to respond while others may progress. Mixed response is due to the presence of different tumour clones within lesions and may not be adequately assessed by conventional response criteria.[6] For the above reported reasons additional information needs to be extracted from images by means of texture analysis or receptor specific imaging performed, that may correlate phenotype with individual somatic mutations.[7] This new *on*

the edge approach represents one of the most promising frontiers of research in oncologic imaging.

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RUOLO DELL'IMAGING NELLA STADIAZIONE E VALUTAZIONE DELLA RISPOSTA DOPO TRATTAMENTO PREOPERATORIO

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The current guidelines for preoperative imaging of advanced rectal cancer recommend MR imaging for local staging and CT of the chest, abdomen and pelvis for detection of distant metastases. For invasive tumours, extramural spread has shown to be an independent prognostic factor in rectal cancer. MR imaging has been demonstrated to have a high accuracy in detecting extramural spread and to identify tumours with good *T3a,b , early T*3 (≤5 mm invasion) versus poor (T3c,d (>5 mm invasion) prognostic features. MR imaging is the best modality to identify patients at risk of local recurrence based on potential involvement by tumour within 1 mm of mesorectal fascia (MRF). The MERCURY Group, which has shown that MR imaging has a high specificity of 92% in determining a free MRF.

The rectum is traditionally divided into lower, mid and upper rectum with the latter being covered by peritoneum and MR imaging has demonstrated to be able to identify peritoneal involvement (T4a stage), infiltration of the other organs and structures (T4b) and known other imaging prognostic factors such as extramural venous invasion (EMVI) and mucinous component.

In low rectal cancer, MR imaging is capable of accurately defining the relationship of the tumour to the sphincter complex and demonstrating threatened resection margins for surgical road mapping, enabling precise preoperative planning.

Despite the fact that nodal staging remains challenging, it would be desirable to at least offer a practical guideline on MR imaging incorporating both size and morphology which were based on criteria described in Dutch evidence-based guidelines on rectal cancer treatment also applicable to extramesorectal (obturator and iliac) nodes. Mixed signal intensity and irregular edges are the features on MR imaging predicting nodal involvement with a sensitivity of 85% and specificity of 97%

The increasing interest in organ-saving treatment through local excision or even a nonoperative treatment (a watch-andwait strategy) demands a reliable method to identify patients with complete response.

Numerous reports have emerged investigating use of functional imaging techniques for rectal cancer (re)staging, of which diffusion-weighted imaging (DWI) and dynamic contrast enhanced (DCE) MR imaging have been researched most extensively. DWI should be performed routinely, in particular for restaging to evaluate response (the yT-stage) to chemoradiotherapy (CRT). Furthermore, DWI can improve the performance of MR imaging for T-restaging after CRT, specifically for differentiation between complete and partial response.

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INTENSIFICATION OF TREATMENT: WHAT IS THE CLINICAL EVIDENCE?

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The standard treatment of locally advanced extraperitoneal rectal cancer (II-III stage) is represented by long-

term preoperative chemoradiotherapy (CRT) fluoropyrimidine-based or short course radiotherapy both followed by total mesorectal excision. With improved surgical techniques and the addition of neoadjuvant radiation therapy, 5-year local recurrence rates have decreased from >25% to approximately 5% to 10% obtaining good local control of the disease. However, these advances have not appreciably decreased the approximately 30% risk of distant metastatic recurrence, which remains the leading cause of rectal cancer-related death. Adjuvant chemotherapy, while being recommended in the major international guidelines, based on risk factors and lymph node positivity at the time of surgery, did not actually yield satisfactory results in randomized trials.[1] Attempts to improve the results especially in terms of DFS and OS have been carried out on several directions. In the hypothesis that the unsatisfactory results of adjuvant chemotherapy are due to the delay in its administration at doses and with appropriate modalities for the control of micrometastases, several authors have proposed to anticipate all chemotherapy in the neoadjuvant setting according to two timing: in the interval between CRT and surgery or before CRT.[2] Other authors have evaluated the addition of other drugs to FU or Capecitabine normally used in neoadjuvant CRT: studies with Oxaliplatin,[3,4,5] Cetuximab[6] and Bevacizumab[7] have been performed. On the other hand, radiotherapy intensification studies have been carried out modifying total dose and fractionation. Mathematical models, extrapolated from the results of clinical dose-escalation studies on rectal cancer, confirmed a dose-response relationship after preoperative CRT for tumour dose levels in the range of 50.4 to 70 Gy.[8] With the use of new radiation techniques such as IMRT or the combined use of radiotherapy with external beams and brachytherapy or IORT, it is now possible to increase the total dose to the GTV without increasing the acute and late side effects.[9] IMRT can also provide a simultaneous concurrent boost (SIB), increasing the dose per fraction at GTV level. Such techniques result in greater radiobiological efficacy both by increasing the total dose and the dose per fraction, and by decreasing the total time of treatment.
Additionally, the search for optimum timing between radiotherapy and surgery to achieve the best results in pathological complete response (pCR), which seems to relate to DFS and OS, is added. The increase in pCR paves the way for more and more conservative surgical treatments even to watch and wait procedures.

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DOSE INTENSIFICATION IN RECTAL CANCER RADIOTHERAPY: GTV AND ITV DEFINITION

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Aims: Due to the increasing evidence for a dose-response relationship in rectal cancer, a boost dose to macroscopic disease could represent a potential strategy to improve oncological outcomes in not responder patients after preoperative long-course radiotherapy (LCRT) or to select patients for which organ-preserving strategies might be possible.

Methods: An overview on methods about boost volume delineation and organ motion evaluation was conducted using the Medline database over the past 10 years.

Results: Preoperative RT is effective to reduce pelvic recurrence (about 5-10%) when associated to total mesorectal excision. Moreover, pathological complete response (pCR) rate represents one measure of neoadjuvant treatment effectiveness, and was reported about 12-15% in patients treated with concurrent fluoropyrimidine.[1] The current consensus preoperative doses for LCRT are 45-50.4 Gy in 1.8-2 Gy per fraction. A pCR-rate up to 20% after preoperative RT with EQD2 doses >60 Gy, was reported with an acceptable toxicity.[2-3]

Intensity-modulated radiotherapy (IMRT) in rectal cancer reduces small bowel dose and allows to deliver a simultaneous integrated boost (SIB), with a potential higher biological tumor effective dose.[4] When IMRT is used, accurate delineation of the gross tumor volume (GTV) is mandatory. The integration of MRI and PET-TC imaging into the planning system could improve tumor localization and GTV delineation, and reduce inter-observer variability.[5-6]

In addition, organ motion evaluation is of particular importance for boost volume delineation. Some evidence using cone beam computed tomography (CBCTs) during the treatment examined intrafractional motion, mainly looking at the rectum and mesorectum. Tumor motion was correlated with tumor site, resulted greatest in the upper rectum, followed by mid then low rectum. Also, mesorectal movements were mainly in the anterior and lateral directions, minor in the posterior rectal wall, with different measurements in the several studies.[7-8] Our recent analysis on 133 CBCTs, with patients in prone position, reported a movement of GTV delineated by MRI less than 4mm in all directions. Due to these variations, an individualized margin should be evaluate and calculate for the Internal Target Volume (ITV) definition.

Conclusions. Rectal cancer patients could be benefit by different radiation treatment strategies including delivery techniques, doses, appropriate volume delineation, and organ motion evaluation.

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THE ROLE OF SURGERY IN THE MULTIMODALITY TREATMENT OF MALIGNANT PLEURAL MESOTHELIOMA

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Malignant Pleural Mesothelioma is a deadly disease with a poor prognosis even in the early- stage disease and an overall median survival from the time of diagnosis of only 9-12 months.[1] Though not yet clearly defined there does appear to be a subset of patients who benefit from surgery-based multimodal treatment plan, beyond what would be expected with current nonoperative therapies.[2] However, the real contribution and the true benefit of surgery remain controversial; even the extent of surgical resection remains a highly debated topic. In MPM it is generally not possible to achieve a microscopic complete resection with any operation. The goal of surgery in this setting, therefore, is to remove all visible and palpable disease – a macroscopic complete resection. To better compare results from different trials and Institutions uniform definition of surgical procedures, including Extrapleural pneumonectomy (EPP) and different types of pleurectomy decortication have recently been introduced.[3] EPP failed to show its benefit in the MARS trial[4] and Extended Pleurectomy Decortication (EPD) is currently under investigation in the MARS2 trial in UK. Due to the relative higher morbidity and mortality of EPP, there is currently a shift toward pleurectomy decortication, at least when a microscopic complete resection can be obtained by this procedure.[5] The transition from EPP to lung-sparing pleurectomy decortication has extended the role of surgery into a more elderly population.[6] In most recent trials induction chemotherapy was administered to improve surgical resection rate but pcr are infrequently observed.[7] Some centers including ours, are currently explored the role of adding hypertermic intrapleural chemotherapy in order to reduce the local recurrence that is the most frequent form of relapse, being present in 80% of the cases.[8] As stated in the ADRI and NCCN guidelines, radical surgery should be restricted in Institutions with significant surgical experience and high volume of cases and extensive cytoreductive surgery should only be used as part of multimodality treatment.[9] Surgery-based multimodality therapy for MPM may offer extended survival benefits when targeted in patients with best prognosis by careful staging. It can be made more accessible by lung preservation without compromising outcome. More randomized prospective trial data are needed to fully understand the role of radical surgery in the treatment of pleural mesothelioma.

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AVAILABLE TECHNOLOGY IN IMAGE GUIDED RADIATION THERAPY

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Aims. To highlight advantages and limits of Image Guided Radiation Therapy (IGRT).

Methods: Pubmed database was searched for reporting the technology and the techniques available 1) to reduce systematic and random errors both in planning (immobilization, simulation TC ,contouring) and in delivery phase; 2) to correct the set up error and to compensate organ motion and deformation.

Results: -Target (CTV) can be better delineated by deformable registration (DIR)[2] of functional images or RM with simulation TC. Moreover, patient motion is inevitably present in these processes, producing artifacts and uncertainties in target identification: 4DMI includes time-resolved volumetric CT, MRI, PET, PET/CT, SPECT, and US imaging.[3] - During treatment two-dimensional imaging (EPID, MV x-rays, kV x-rays, stereoscopic kV imaging 2D e.g. Cyberknife),[4] uses bone structures to correct set up or fiducials to compensate organ motion. Three-dimensional imaging (kV-CBCT, MV-CT, 4D-kV-CBCT, In-room CT scanning)[5,6] has been used to monitor organ motion and deformation. - IGRT frequency and modality have obvious implications in terms of overall health care costs: a randomized cost-analysis study for the prostate IGRT identified an additional cost per treatment course of Euro 679 when daily CBCT was performed over weekly CBCT (Euro 187). In addition, increase of control frequency from weekly to daily was followed by increase of mean therapy fraction period for 7.3 min (+53%) for CBCT and 1.7 min (+10%) for orthogonal electronic portal imaging with fiducial markers (EPI-FM). Daily control considerably takes more time from oncologist and intervention time of radiologist as well as occupation of operating room for both IGRT methods (CBCT and EPI-FM).[8] - One of potentially negative aspects of IGRT is its additional radiation dose. The use of MV image instead of KV-CBCT leads to an increase of dose to the patient until ten times over.[9] The dose is major for pelvic region, minor for head. Current on-board kV imaging devices result in much lower imaging doses compared to MV imagers even taking into account of higher bone dose from kV X-rays.

Conclusions. IGRT increases the agreement between the planned treatment and the dose delivered to the patient; it can detect gross positional errors, weight loss, substantial organ deformation, systematic changes in internal organs, and changes in respiratory motion . On the other hand IGRT is expensive and could increase the risk of secondary tumor. A residual error can be detected in spite of applied IGRT protocols so, an adapted CTV - PTV margin has to be used.[10]

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SET UP UNCERTAINTIES AND ORGAN MOTION, APPROPRIATENESS OF IGRT USE, CTV-PTV MARGIN INDICATIONS. LITERATURE RESULTS BY ANATOMIC REGION: HEAD & NECK AND LUNG

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Background: Radiation therapy (RT) technology has been rapidly developing recently, in order to improve effectiveness of cancer treatment. The implementing of Image-Guided Radiation Therapy (IGRT) before and/or during radiation allows a better accuracy and precision of RT. The clinical benefit of IGRT is clear in sites where the dose needed for tumor control is higher than the surrounding normal tissue tolerance. It is also particularly useful when targets present relevant inter- or intra-fraction motion. While IGRT can be used for any anatomical site, its benefit has been proven mainly in the treatment of prostate, bladder, head & neck (H&N) and lung cancers.

Aims: The purpose of this work is to provide a review of literature on the use of IGRT in H&N and thoracic malignancies.

Results: H&N cancers are close to several critical structures and the advent of Intensity Modulated Radiation Therapy (IMRT) has allowed the delivery of high doses to the tumor with sharp gradients next to organs at risk (OARs).[1] Randomized controlled trials have shown that IMRT can lead to a significant reduction in radiation-induced late toxicity.[2-3] As a result, imaging during treatment delivery is critical for ensuring that excessive radiation dose to normal tissues does not occur as a result of positioning errors. Furthermore, the decrease of set-up errors with IGRT can allow the reduction of PTV margins, thereby lowering the dose to normal tissues and permitting to escalate the dose to the tumor.[4-5]

During fractionated RT anatomical changes can occur in the H&N: the shrinkage of primary and nodal volumes might lead to an overdosage to OARs or underdosage of the tumor.[6] So in H&N cancers the question is "how much" rather than "if" IGRT is needed: some randomized trials demonstrated a direct clinical benefit with IGRT, while there is lack of studies suggesting that more intensive imaging can provide a dosimetric advantage.

Accurate RT delivery for lung cancer can be challenging: multiple factors can impact on treatment outcome, such as inadequate dose due to dose limiting OARs, inadequate volume coverage caused by geographic miss, and respiratory motion or set-up errors (both inter- and intra-fraction) impairing dose delivery and volume coverage.[7] A robust IGRT strategy, along with respiratory motion management, can help mitigating some of these effects and allows for reduction in PTV margins.[8] IGRT may be also helpful in monitoring anatomical changing during the course of treatment, which may require replanning.[9] The use of IGRT is mandatory in the stereotactic setting because of the high dose per fraction delivered.[10]

There are multiple IGRT tools, and the system choice depends on the facility resources and accuracy of the treatment to be delivered. This is influenced by the intent of RT, the dose prescribed and the subsite being irradiated.

Conclusions: IGRT is highly recommended, due to the possibility of decreasing toxicity and improving clinical outcomes. Each RT department should review literature available and choose which recommendations to adopt, according to factors such as accuracy of target delineation, PTV margins and imaging quality.

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SET UP UNCERTAINTIES AND ORGAN MOTION, APPROPRIATENESS OF IGRT USE, CTV-PTV MARGIN INDICATIONS. LITERATURE RESULTS BY ANATOMIC REGION: BREAST AND UPPER ABDOMEN

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On behalf of " AIRO Emilia Romagna e Marche".

Background: Today there is a wide literature that evidence the role of IGRT to reduce variations in terms of set-up errors and organ motion. IGRT permits moreover to detect and manage exceptional deviations, such as gross positioning errors, systematic changes in internal organs, organ deformation and so on.

Aims: Purpose of this review is to define which is real impact of IGRT different techniques applied to breast and upper abdomen treatments, also to analyse its role related to residual error.

Results: Respiration-induced motion and daily changes in the baseline tumour position of thoracic and upper abdomen targets have recently required the implementation of IGRT particularly for hypofractionated stereotactic treatments; but this intrafractional

breathing-related motion results in uncertainties in dose delivery and thus in target coverage. Even with breathing motion control techniques, such as abdominal compression, DIBH, setup uncertainties remain. As a consequence, generous margins have been used, which, in turn, increased organ at risk exposure. Movement of liver tumours has been measured using 4DCT/CBCT, MRI, real-time tracking of implanted fiducials: first it seems that magnitude measured by MRI was greater than those by other techniques; moreover magnitude of motion was greater than movements in other direction, up to 21 mm in CC (cranial-caudal) with MRI,[1] and a maximum of 17,9 mm CC with other techniques, up to 5.1 mm and 3 mm for AP (anterior-posterior) and RL (right-left).

The analysis of movement in pancreatic cancers confirmed similar results: magnitude up to 5.9 mm in CC direction [2] but up to 20 mm in cine MRI technique,[3] greater of a factor four, and about 3 mm in other directions and by other techniques.

Last, for esophageal tumours data from different studies are consistent among them, with major movement in CC direction, about 8 mm,[4] and greater for cine MRI (by approximately 5 mm).[5]

Finally, it has been reported that respiratory motion can cause anatomical movement within a planned radiation field[6] for breast RT. These anatomical movements may lead to decreased target coverage or normal tissue sparing (or both), resulting in an increased risk of treatment failure or complications such as late cardiac mortality and radiation-induced pneumonitis. Although such IGRT modality, as CBCT offers high quality verification images, this benefit needs to be balanced against the potential harm of additional radiation exposure to normal organs of patients and introduction of motion artefacts during its acquisition. However its application could increase if complex IMRT and partial breast irradiation are used.

Conclusions: The current literature shows that considerable residual error may remain even with daily IGRT. Organ motion due to breathing, peristalsis and deformation presents challenging problems for the delivery of radiotherapy to thoracic and upper abdominal targets, despite the many advancements in the technology of radiation planning and delivery.The goal is a potential increase in the likelihood of tumour control and reduction in normal tissue toxicity. Throughout treatment planning and delivery, imaging and image-guided radiotherapy (IGRT) are important tools to predict safe margins for tumour targets, and to assess daily residual geometric uncertainties that may impact the likelihood of tumour control and normal tissue toxicity

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SET UP UNCERTAINTIES AND ORGAN MOTION, APPROPRIATENESS OF IGRT USE, CTV-PTV MARGIN INDICATIONS. LITERATURE RESULTS BY ANATOMIC REGION: PROSTATE, RECTUM, UTERUS

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Aims: The aim of this work is to review the pattern of pelvic interfraction and intrafraction organ motion and deformation in cervical, ano-rectum and prostate cancer treatments.

Methods: Computerized literature search was performed to identify relevant articles about the role of IGRT to compensate uncertainties but also to highlight its limits to cancel residual error.

Results: Multiple studies have found that the uterus and cervix can move and regress substantially during treatment. Consequently, there is concern that such motion could lead to insufficient target coverage, compromising tumor control.[1] Up to 32 mm anterior - posterior, 20 mm superior-inferior and 17.5 mm laterally anisotropic motion was recorded, implying that the commonly used CTV- PTV margins of 1-1.5 cm could be insufficient.[2] Prostate organ motion is characterized mainly by shifts, while seminal vesicles (SV) motion results in deformation and tilt, so different IGRT protocols need to be applied when prostate only or prostate plus SV are treated; SV exhibits different and statistically significant greater mobility than the prostate in anterior (up to 2.8 cm), posterior (up to 1.8 cm) and caudal (up to 2.7 cm) directions; an anisotropic motion was observed for both prostate and SV. If Prostate (without SV) is treated with implanted fiducials, a CTV - PTV margin up to 5mm is needed despite IGRT. The cause could be found in the residual error due to prostate deformation and tilt, gold markers size, contouring as well as IGRT system uncertainties; in addition, small variations in the relative position of the markers (1,20 ± 0,67 mm) can be observed.[3] Finally, in rectal cancer patients, a substantial, heterogeneous and anisotropic deformation of the CTV mesorectum was found up to 2.3 cm in the upper-anterior part which lead to an ina-

dequate treatment of the mesorectal fascia. When the target motion is mainly tilt and deformation, simple translational shifts cannot compensate OM, even when a daily online imaging is used. In these cases an adapted margin can be required. [4,5]

Conclusions. Set up residual errors can be expected despite IGRT, mainly when six degrees of freedom couch is not available. Simple translational shifts cannot compensate for pelvic CTVs motion and deformation , even when a daily online imaging is used. Offline shape variation correction/ compensation can be obtained by averaging the shape of the CTV during the first 5 fractions . Individualized margins can maximize CTV coverage while minimizing OAR dose.

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INTEGRAZIONE DI IMAGING E CARATTERISTICHE BIOMOLECOLARI PER UNA TERAPIA PERSONALIZZATA

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Radiomics is a discipline based on medical image processing and analysis. Digital images possess quantitative data that can be extracted and analyzed through computer-assisted interpretation. More specifically, the increasing resolution quality of standard imaging modalities such as computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography scan (PET) has led to 3D image acquisitions containing millions of voxels available for computational analysis. The process is based on image acquisition and segmentation, feature extraction, 3D rendering and statistical learning. Eventually, radiomics data have to be integrated with clinical, pathologic and molecular data to improve precision medicine.

The goal of radiomics might be the setting of imaging biomarkers, which could have a significant impact on cancer diagnosis, prediction of response to treatment, and surveillance. Multidisciplinary working-groups including not only physicians but also medical physicist, computer scientists and mathematicians are needed to define and standardize reporting of radiomics studies. This will probably lead to the adoption of radiomics in routine clinical practice.

CONTROVERSIES IN BREAST CANCER UNIT

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Breast cancer is the most common cancer diagnosed in women, with approximately 50,000 new cases every year in Italy.[1] Based on stage disease at diagnosis, different treatment strategies can be propose to the patient, including surgery, radiation therapy and chemotherapy.[2] In the last decade, a multi-professional management has become commonly accepted and nowadays the breast cancer unit plays a crucial role in the high-quality care of breast cancer patients. The multidisciplinary collaboration is responsible for the diagnosis, staging, treatment and follow-up plan of breast cancer patients. Breast cancer unit requires a core team members specially trained in breast disease, as well as specific organization in order to guarantee the optimal treatment. This permits a consensual therapy plan, minimizes the burden of complicated decisions and promotes a complete view to the patient.[3]

Several controversies, including practical organization, technologic advances and cost will be discussed. The loss of patient's singularity will be also evaluated.

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TERAPIA MEDICA E MODIFICA DEI VOLUMI DI RADIOTERAPIA: PROS

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Although adjuvant radiotherapy for breast cancer has been shown to improve locoregional control and improve survival in selected patients, neoadjuvant chemotherapy (NAC) alters the key information used for decision making and poses new challenges to radiation oncologists. Pathological extent of disease is modified in 80–90% of cases and in 20–40% of patients lymph-node positive disease are converted to lymph-node negative

disease. Therefore, it is essential to accurately document the clinical extent of disease in the breast and lymph-node basins before NAC. Since there are no prospective randomised trials comparing outcomes with and without post mastectomy radiation therapy (PMRT) after NAC, retrospective studies have provided some guidance on who might benefit from PMRT in this setting. These series help to quantify locoregional (LRR) risk with and without radiotherapy for a variety of patient subgroups that underwent NAC and either breast-conserving surgery or mastectomy. In 2008, the National Cancer Institute Conference on locoregional treatments after neoadjuvant systemic therapies stated that chest-wall and regional nodal radiation should be considered for those who present with clinical stage III disease or have histologically positive lymph nodes after NAC. Nodal response is considered one of the most important prognostic factors, which can inform PMRT treatment decisions. Patients with residual nodal disease may even be candidates for intensification of PMRT. Clinical data on stage IIB (T2N1, T3N0) and II A (T2N0) remain limited: such patients should be discussed individually with respect to risks and benefits. Among the various LRR risk categories, age and biomolecular features are variables with a predictive value for local outcome. The MD Anderson data suggest that women younger than 35/40 years with clinical stage IIB disease or higher might benefit from PMRT. Breast cancer subtype and biologic features of primary cancer (hormone receptor negative, Her2 positive, triple negative) may be a significant predictor of LRR as well. For patients who achieve a pathologic complete response (pCR) after NAC, results from NSABP B18 and B27 showed low rates of LRR, but again molecular subtype may play an additional role in the decision making. To address the issue about the proper treatment for patients receiving NAC, two randomized trials are ongoing. Alliance A011202 will address whether axillary radiation is non-inferior to ALND following NAC, while NRG-B-51 will determine the need for PMRT or regional nodal irradiation in patients who convert to node-negative after NAC.

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TERAPIA MEDICA E MODIFICA DEI VOLUMI DI RADIOTERAPIA: CONS

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Multimodal approach for breast cancer led to de-escalation in adjuvant treatments. In details, endocrine therapy and radiation therapy omission have been studied for the early breast cancer patients. At the same time, an adequate selection of patients for primary systemic therapy led to a high rate of complete response of disease after surgery. Again, the omission or de-intensification (dose/volume) of adjuvant treatment has been advocated. The aim of the debate is to highlight the recently published experience concerning these challenging issues.

RESPONSABILITA' PROFESSIONALE

F. Lucà

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The law 24/2017, which puts our country at an equal pass with Europe is certainly a health precaution in favour of we doctors from the medical facilities .to the patients which involves not only the world of health,but also that of the law and insurance coverage .Law 24/2017"based on security material of treatment and the professional responsability of who exercises these treatments"guarantee a major protection of the public and gives back to the doctors the possibility to practice in serenity their profession restabalizing the relationship of trust between doctor and patient.

The civil and penal responsibility of the professionals undergo a change,and redraws the borders of medical fault (blame)"freeing the white coated professionals of the latches of defensive medicine,"used in the attempt to minimize legal cases and preconstituded justified evidence.

Above all regulates management of health risks introducing obligatorily in the public and private health structure the services of Risk management.

A fundamental step in terms of prevention of risks which will consent the reduction of damage to patients.This precaution obligates the introduction of a net of insurance coverage or similar measures of the public or private health structure of the employees,including the Free-lancing professionals.

Above all, they will be submitted to trial (Civil,Penal Corte dei Conti)only those cases that really

merit the weighing up of justice,and NOT unfounded claims used as a pretext to obtain unjustified compensation.

Thanks to preventive technical verification it will reduce civil judgement. The exclusion of responsibility following guide-lines and good steps for the objection of incompetence,penal judgement will decrease; while for the compensation the jurisdiction of the Corte dei Conti will guarantee impartiality of a grave charge,this court having the possibility of carrying out preliminary committal proceedings completely independantly of a civil/penal outcome.

The safeguard of patients and their rights of an adequate compensation in case of harm or damage the possibility of working without constant worry of facing trials , the National Health professionist, with the access of a suitable Insurance Coverage , the need of justice which is based on medical ,legal and also specialized verification .infact the judge who deals with bad health service should entrust the reconstruction of the specialistic and clinical case with the group involved.

The Gelli law represented a decisive moment for doctors because it excluded liability. In a case where incompetence had been proved and the doctor had respected all clinical rules and valid guide-lines recommended scientifically published online by The Superior Institute of Health.

The doctors' professional reputation is safeguarded considering virtuous behaviour, together with the reality of the case in question.

PRACTICE CHANGING STUDIES

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The medical knowledge is rapidly changing. New evidence is available based on the studies published in 2016-2017 and including radiotherapy. 1864 new reports are available at the 9th July 2017 (since 1st January 2016). Among the most significant studies are the following:

Brain: Mahajan A *et al.* Post-operative stereotactic radiosurgery versus observation for completely resected brain metastases: a single-centre, randomised, controlled, phase 3 trial. Lancet Oncol. 2017 Jul 4, showing that stereotactic radiosurgery (SRS) of the surgical cavity in patients who have had complete resection of one, two, or three brain metastases significantly lowers (halves) local recurrence compared with that noted for observation alone. Thus, the use of SRS after brain metastasis resection could be an alternative to whole-brain radiotherapy.

Lamba N, et al. Stereotactic radiosurgery versus whole-brain radiotherapy after intracranial metastasis resection: a systematic review and meta-analysis. Radiat Oncol. 2017 Jun 24;12(1):106, where based on retrospective cohort studies, the results of this study suggest that SRS of the resection cavity may offer comparable survival and similar local and distant control as adjuvant WBRT, yet may be associated with a higher risk for developing leptomeningeal disease.

Breast: Vrieling C, *et al.* Prognostic Factors for Local Control in Breast Cancer After Long-term Follow-up in the EORTC Boost vs No Boost Trial: A Randomized Clinical Trial. JAMA Oncol. 2017 Jan 1;3(1):42-48 showing that the association of high-grade invasive tumor with ipsilateral breast tumor recurrence (IBTR) diminished during follow-up, while the effect of DCIS adjacent to invasive tumor seemed to remain stable. Therefore, patients with high-grade invasive tumors should be monitored closely, especially in the first 5 years, while additional DCIS is an indication for longer follow-up, emphasizing the importance of long-term trial follow-up to estimate absolute effects accurately.

Lung: Gomez DR, *et al*. Local consolidative therapy versus maintenance therapy or observation for patients with oligometastatic non-small-cell lung cancer without progression after first-line systemic therapy: a multicentre, randomised, controlled, phase 2 study. Lancet Oncol. 2016 Dec;17(12):1672-1682 showing that local consolidative therapy with or without maintenance therapy for patients with three or fewer metastases from NSCLC that did not progress after initial systemic therapy improved progression-free survival compared with maintenance therapy alone.

Prostate:

James ND, et al. Failure-Free Survival and Radiotherapy in Patients With Newly Diagnosed Nonmetastatic Prostate Cancer: Data From Patients in the Control Arm of the STAMPEDE Trial. JAMA Oncol. 2016 Mar;2(3):348-57 showing that survival for men entering the cohort with high-risk M0 disease was higher than anticipated at study inception. These non-randomized data were consistent with previous trials that support routine use of RT with HT in patients with N0M0 disease. Additionally, the data suggest that the benefits of RT extend to men with N+M0 disease.

The list of new significant studies will be updated at the moment of the presentation.

Comparison of Gamma Knife Radiosurgery and Mi crosurgery for Small Size Meningiomas. World Neurosurg. 2017; 101:170-179.

Selected Oral Communications

B001

MRI TEXTURE ANALYSIS CAN PREDICT PATHOLOGICAL RESPONSE IN RECTAL CANCER PATIENTS UNDERGOING NEOADJUVANT CHEMO-RADIATION

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Aims: The present study was designed to evaluate MRI texture analysis (TA) in predicting the outcome in term of complete pathological response, of patients with locally-advanced rectal cancer undergoing radical treatment.

Methods: We performed a retrospective analysis on forty-nine patients with locally advanced rectal adenocarcinoma undergone neoadjuvant chemo-radiotherapy (C-RT) and radical surgery between January 2010 and December 2015. The gross tumor volume (GTV) was evaluated at baseline by MRI and contoured on T2, DWI, and ADC sequences, and multiple derivative parameters evaluated by means of a LifeX Software. By performing univariate analysis and a multivariate analysis (logistic regression), the TA parameters were then correlated with patients' pathological outcome. Complete pathological response (pCR, with no viable cancer cells: TRG 0) and good response (GR: pCR plus moderate response, with only small cluster or isolated cells remaining: TRG 0-1) were chosen as statistical endpoints.

Results: Eleven patients (22%) showed a pCR, whereas 26 patients (53%) showed a GR (TRG 0-1). TA parameters correlated with pCR included grading (OR 3.57), ADC Entropy (OR 2.25), ADC GLCM Dissimilariy (OR 1.93) and ADC ZP (OR 1.42), whereas TA parameters correlated with GR included DWI GLCM Homogeneity (OR 0.20), DWI ZP (OR 3.01) and ADC ZP (OR 2.22) (see Table for description of TA parameters). AUC for pCR was 0.834, whereas AUC for GR was 0.725.

Conclusions: Our results suggest that TA has a significant predictive and prognostic value and may lead to select the subset of patients who may achieve a complete pathological response and maypotentially avoid invasive surgery, according to some recent issues in the related literature.

Table 1 Texture analysis parameters calculated with Lifex Software, and corresponding description.

Type of TA Feature	TA Feature Name	Description
Co-occurrence Matrix (GLCM): takes into account the arrangements of pairs of voxels to extract textural indices.	**Homogeneity**	Homogeneity of gray-level voxel pairs
	Energy	Uniformity of gray-level voxel pairs.
	Correlation	Linear dependency of gray-levels in GLCM.
	Contrast	Local variations in the GLCM.
	Entropy	Randomness of gray-level voxel pairs.
	Dissimilarity	Variation of gray-level voxel pairs.
Gray-Level Run Length Matrix (GLRLM): gives the size of homogenous runs for each gray-level.	**SRE (short-run emphasis)**	Distribution of the short homogeneous runs in an image.
	LRE (long-run emphasis)	Distribution of the long homogeneous runs in an image.
	LGRE (low gray-level run emphasis)	Distribution of the low gray-level runs.
	HGRE (high gray-level run emphasis)	Distribution of the high gray-level runs.
	SRLGE (short-run low gray-level emphasis)	Distribution of the short homogenous runs with low gray-levels.
	SRHGE (short-run high gray-level emphasis)	Distribution of the short homogenous runs with high gray-levels.
	LRLGE (long-run low gray-level Emphasis)	Distribution of the long homogeneous runs with low gray-levels
	LRHGE (long-run high gray-level emphasis)	Distribution of the long homogeneous runs with high gray-levels
	GLNUr (gray-level non-uniformity for run)	Non-uniformity of the gray-levels of the homogeneous runs.
	RLNU (run-length non-uniformity)	Length of the homogeneous runs
	RP (run percentage)	Homogeneity of the homogeneous runs
Neighbourhood Gray-Level Different Matrix (NGLDM): corresponds to the difference of gray-level between one voxel and its 26 neighbourhoods in 3 dimensions.	**Coarseness**	Level of spatial rate of change in intensity.
	Contrast	Intensity difference between neighbouring regions.
	Busyness	Spatial frequency of changes in intensity.
Gray-Level Zone Length Matrix (GLZLM): provides information on the size of homogenous zones for each gray-level in 3 dimensions.	**SZE (short-zone emphasis)**	Distribution of the short homogeneous zones in an image.
	LZE (long-zone emphasis)	Distribution of the long homogeneous zones in an image.
	LGZE (low gray-level zone emphasis)	Distribution of the low gray-level zones.
	HGZE (high gray-level zone emphasis)	Distribution of the high gray-level zones.
	SZLGE (short-zone low gray-level emphasis)	Distribution of the short homogenous zones with low gray-levels
	SZHGE (short-zone high gray-level emphasis)	Distribution of the short homogenous zones with high gray-levels
	LZLGE (long-zone low gray-level emphasis)	Distribution of the long homogeneous zones with low gray-levels
	LZHGE (long-zone high gray-level emphasis)	Distribution of the long homogeneous zones with high gray-levels
	GLNUz (gray-level non-uniformity for zone)	Non-uniformity of the gray-levels of the homogeneous zones
	RLNU (zone length non-uniformity)	Length of the homogeneous runs
	ZP (zone percentage)	Homogeneity of the homogeneous zones
Indices from Sphericity	**Sphericity**	Measures how spherical a Volume of Interest is.
	Compacity	Measures the degree to which the Volume of Interest is compact
Indices from Histogram: provides informations derived from global histogram analysis	**Skewness**	measures the asymmetry of the gray-level distribution in the histogram.
	Kurtosis	measures whether the gray-level distribution is peaked or flat relative to a normal distribution.
	Entropy	mesures the randomness of the distribution
	Energy	measures the uniformity of the distribution

B002

COULD SURGICAL TIMING INCREASE PCR IN RECTAL CANCER? A POOLED ANALYSIS OF 3085 PATIENTS FROM 7 INTERNATIONAL RANDOMIZED TRIALS

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Aims: Optimal timing of surgery after neoadjuvant chemo-radiotherapy (NAD-CRT) is still controversial. Literature data suggest an improvement in pathological complete response (pCR) after a lengthening of surgical interval (SI) after NAD-CRT. The primary goal of this study was to determine the best timing to achieve the higher rate of pCR and secondly to evaluate the effect on surgical complications and survival outcomes in relation to a lengthening of surgical timing.

Material and Methods: Patient data were extracted from the following LARC international randomized trials: Accord 12/0405, EORTC 22921, FFCD 9203, CAO/ARO/AIO-94, CAO-ARO-AIO-04, INTERACT and TROG 01.04. Inclusion criteria were: age≥ 18 years old, cT3-T4 and cN0-2, no clinical evidence of distant metastasis at diagnosis, long-course NAD-CRT followed by surgery. The SI was calculated in weeks from the end of NAD-CRT. Pearson's Chi-squared test for categorial variables, Mann-Whitney test for continuous variables, Kaplan-Meier curves with log-rank test, univariate (uLRM) and multivariate logistic regression model (mLRM) were used for data analysis. A p-value<=0.05 was considered significant.

Results: The initial pooled dataset included 5247 patients (pts); 3085 pts met the inclusion criteria and were analyzed in this study. The pCR rate was 14%. Overall, the median time from NAD-CRT to surgery was 6 weeks(range 1-31 weeks). The cumulative pCR rate increased significantly when time between NAD-CRT and surgery lengthened, reaching a plateau at 16 weeks and 95% of pCR events was within 10 weeks from NAD-CRT (Figure 1). At uLRM and mLRM analysis, the lengthening of SI ($p<0.01$), the highest radiotherapy dose ($p<0.01$) and the addition of oxaliplatin to the neoadjuvant treatment ($p<0.01$) had a favorable impact on pCR. At uLRM the lengthening of SI appeared to be a protective factor for post operative complications ($p=0.05$). Furthermore lengthening of SI was not detrimental in terms of local recurrence, distance metastases and overall survival, on the contrary a positive trend in terms of survival outcomes was observed in the group of pts who achieve pCR after 6 weeks.

Conclusion: This pooled analysis suggests that the best time to achieve pCR is at 10 weeks with a plateau at 16 weeks. The lengthening of SI is not detrimental in terms of postoperative complications, conversely it could be a protective factor. Finally, in the group of pts achieving a pCR after 6 weeks, a positive trend in terms of survival outcomes was reported.

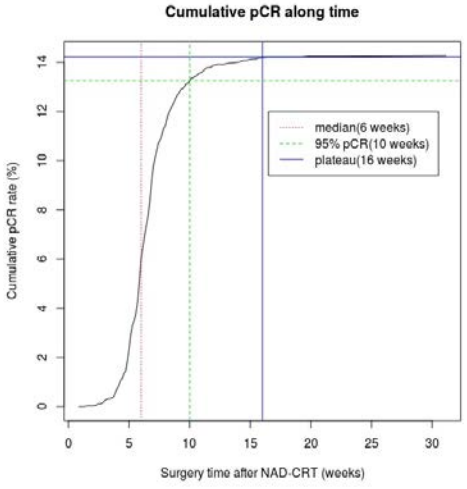

Figure 1.

B003

EVALUATION OF THE IMPACT OF DRUGS, CLINICAL AND FRACTIONATION FACTORS ON ACUTE AND LATE SKIN TOXICITY IN PATIENTS IRRADIATED AFTER CONSERVING SURGERY FOR BREAST CANCER: A SINGLE INSTITUTION STUDY

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Aims: The objective of this study was to evaluate possible drugs-related inference on acute and late toxicity in breast cancer patients treated with adjuvant conventional radiotherapy or with hypofractionated schedule

Methods: Between October 2011 and August 2014, 325 consecutive patients treated in our department with

breast conservative surgery and adjuvant radiotherapy were included in the analysis. One hundred sixty three patients were treated with 50 Gy to the whole breast (2.0 Gy/25 fractions) followed by a boost dose of 10 Gy in 5 days delivered by electrons on the tumoral bed, while 162 patients were treated with 45 Gy (2.25 Gy/20 fractions) with an additional daily concomitant boost of 0.25 Gy to the surgical cavity (2.5 Gy/20 fractions up to 50 Gy). Median age was 57 year (range 31-92). Acute and late skin toxicity was assessed by physical inspection during and after radiotherapy and was described and graded according to the RTOG scale. The impact of patients clinical and pathological characteristics, chemotherapy, hormone and biological therapy has been evaluated by univariate and multivariate analysis.

Results: At a median follow up of 36 months (2-65) estimated 5 year OS, LC, DFS, and CSS were 96.4, 97.8, 93.7, and 98.8%, respectively. Eighty four % of patients received hormone therapy and 51,2% of patients received also chemotherapy. 117 patients received both chemotherapy and hormone therapy. During radiation treatment 77,2% of patients developed G1/G2 acute skin toxicity and 22,8% developed G3 acute skin toxicity. By the end of RT, late skin toxicity was recorded in 19,3%; G1/G2 late toxicity occurred in 17% and G3/G4 toxicity occurred in 2,2% (1 patient developed nipple necrosis G4 at the site of the surgical scar). While no difference was found between fractionation schedule on late skin toxicity, a significant higher G3 acute toxicity was recorded for hypofractionation. Neither chemotherapy, trastuzumab or hormone therapy affected radioinduced skin toxicity. In the hypofractionated setting smoke resulted significantly linked to development of G3 acute skin toxicity.

Conclusions: In our study, drug therapy resulted not affecting radioinduced skin toxicity in patients treated with conserving therapy for breast cancer. Hypofractionation resulted in more acute severe skin toxicity that was significantly enhanced by smoke habit.

B004

TOXICITY AND OUTCOME IN MODERATELY HYPOFRACTIONATED RADIOTHERAPY FOR 590 PROSTATE CANCER PATIENTS: THE EUROPEAN INSTITUTE OF ONCOLOGY EXPERIENCE

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Aims: To report toxicity and efficacy of moderately hypofractionated external-beam radiotherapy (RT) in a large series of patients treated for prostate cancer in a 9-year period. Methods: Between January 2007 and December 2015, 590 T1-T3N0M0 prostate cancer patients received 70.2 Gy in 26 fractions at 2.7 Gy/fraction (equivalent to 84 Gy in 42 2-Gy fractions, considering / of 1.5 Gy) using image-guided three-dimensional conformal radiotherapy (3D-CRT) and intensity modulated radiotherapy (IMRT). Androgen deprivation was added to RT in 65% of pts. Radiation Therapy Oncology Group/European Organization for Research and Treatment of Cancer criteria (RTOG/EORTC) and Houston definition (nadir + 2) were used for toxicity and biochemical failure evaluation, respectively. Results: All patients completed radiotherapy. Mean age was 72.6 years (6.5 standard deviation). Fourteen patients were lost to follow-up. Information on gastrointestinal (GI) toxicity was available for 306 (54.4%) patients. Of these, 287 patients (93.7%) reported G0-G1 GI toxicity, with prevalence of G0 (84.6%), 13 (4.3%) G2 toxicity, 6 (2.0%) G3-G4 toxicity. Information on genito-urinary (GU) toxicity was available for 306 (54.4%) patients. Of these, 277 patients (91.2%) reported G0-G1 GU toxicity, with prevalence of G0 (68.8%), 26 (8.6%) G2 toxicity, 1 (0.3%) G3-G4 toxicity. After five years from the end of radiotherapy overall survival was 86%. After a median follow-up of 49 months (range 1-108 months) 69 patients (8.3%) had evidence of biochemical or clinical progression, or died from disease. At univariate analysis, age>80 years, increasing initial risk category, increasing Gleason score, increasing prostate-specific antigen (PSA) and the seminal vesicle involvement were associated with increased mortality. At multivariate analysis, Gleason score was the only predictor of mortality, even after adjustment for age. At univariate analysis, increasing risk, increasing Gleason score, increasing PSA and seminal vesicle involvement were associated with disease progression. At multivariate analysis, Gleason score was the stronger predictor of disease progression, even after adjustment for age.

Conclusion: Our study confirms that hypofractionated radiotherapy is a viable treatment option for localized prostate cancer in terms of toxicity and clinical outcome.Further analysis will be done in order to identify the patient subgroup that need more aggressive therapy.

B005

SBRT FOR UNRESECTABLE LIVER METASTASES: CLINICAL OUTCOMES AND PROGNOSTIC FACTORS

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Aims: Liver is a common site of metastases for several cancers. In selected patients with oligometastatic disease confined to liver, surgical resection improves overall survival (OS). Approximately 70–90% of liver metastases, however, are unresectable and a safe and effective alternative therapeutic option is necessary for these patients. The aim of this study was to evaluate clinical outcomes of SBRT for unresectable liver metastases and to analyze prognostic factors affecting overall survival (OS) and local control (LC) of these selected oligometastatic patients.

Methods: Patients with ≤ 3 unresectable liver metastases with diameter ≤ 6cm underwent to SBRT, with a prescription dose of 75 Gy on 3 consecutive fractions. LC, OS and toxicity rates were analyzed.

Results: Between February 2010 and December 2016, a total of 202 patients with 268 lesions were analyzed, with a median follow-up time of 33 months. One-, three- and five- years LC rates were 94%, 84% and 84%, respectively, with a median LC of 18 months. Median OS was 21 months and the survival rates were 79%, 27% and 15% at 1, 3 and 5 years, respectively. Univariate analysis showed four independent positive prognostic factors affecting survival: female sex (p=0.03), primary tumor (p=0.0001), intra- and extrahepatic progression (p=0.004 and p=0.05). At univariate analysis two independent variables affected local control: primary colorectal cancer (p=0.03) and prior local hepatic therapies (p=0.006). No cases of RILD were detected.

Conclusions: This study confirms the efficacy and safety of SBRT for unresectable liver metastases. Selection of cases with positive prognostic factors may improve survival and local control of these oligometastastic patients.

B006

ROLE OF CT PERFUSION IN THE EVALUATION OF NODAL TUMOR RESPONSE AFTER RADIOCHEMOTHERAPY (RCT) IN HEAD AND NECK CANCERS (HNCS): RESULTS OF A MONO-INSTITUTIONAL PROSPECTIVE STUDY

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Aims: To report the initial results of a prospective study aimed at evaluating the CT perfusion parameter changes (PCTp) of the primary gross nodal metastasis after radiochemotherapy (RCT) in head and neck cancer (HNCs) and to correlate with regional recurrence free-survival.

Methods: Eligibility criteria included HNC (Stage III–IV) candidates for RCT. Patients underwent perfusion CT (PCT) at baseline and at 3 weeks and 3 months after treatment. Blood volume (BV), blood flow (BF), mean transit time (MTT) and permeability surface (PS) product were computed. Moreover, according to our internal protocol, PET/CT was performed at baseline and 3 months after treatment. The PCTp were evaluated between baseline and 3-weeks/3-months, whereas PET/CT response was performed at baseline and 3 months after treatment.

Results: Between July 2012 and May 2016, overall 37 patients were enrolled in our study; among them 27 patients were evaluable for nodal response after RCT. Overall only 3 patients (11%) experienced tumor nodal recurrence (biopsy-proven) on the primary nodal site.

A significant reduction of all the PCTp values (p<0,0001), except MTT (from 6,3 to 5,7 sec; p-value 0.089), was observed early at 3-weeks post-RCT compared to the baseline. Indeed, all PCTp values including MTT (from 6,3 to 2,3 sec; p=0,04), were significantly lower compared to the baseline values at 3-months after treatment. Moreover, a statistical significant correlation was observed between tumor nodal persistence and high BF values (p=0,045) at 3 months after treatment that did not result for the other parameters.

Conclusions: Our preliminary findings seem to show that almost all PCTp are significantly reduced after RCT, whereas BF seems to come out as the strongest factor in predicting the regional recurrence free-survival.

AIRO GIOVANI
Oral Communications

CG001

PATTERN OF FAILURE IN HEAD AND NECK CANCER PATIENTS AFTER DEFINITIVE RADIOCHEMOTHERAPY BASED ON PER-TREATMENT 18F-FDG PET/CT UPTAKE

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Aims: To analyse the pattern of failure in relation to pre-treatment 18F-FDG PET/CT uptake in head and neck squamous cell carcinoma (HNSCC) patients treated with definitive chemoradiotherapy (CT-RT) (CTRT).

Methods: From 2012 to 2016, 87 head and neck cancer patients treated with definitive CT-RT with IMRT-SIB underwent pre-treatment 18F-FDG PET/CT (PETpre), and MRI/CT for RT planning purposes in our department. We focused on patients who experienced a recurrence at the site of primary tumour. All of them did an 18F-FDG PET/CT (PETpost) at the time of failure. In recurrent patients, the GTV-PETpre and the GTV-PETpost were contoured by means of an adaptive thresholding algorithm implemented on the dedicated iTaRT workstation (Tecnologie Avanzate, Italy). Both GTV-PETpre and the GTV-PETpost were transferred on the original planning CT scans by means of deformable co-registration of PETpost on PETpre in the Ray-Station treatment planning system. The overlapping volume of the pre-treatment volume and failure volume was generated: "GTV-PETpre GTV-PETpost". The dose delivered to the 99% of a volume (D99) was measured within GTV-PREpre GTV-PETpost and GTV-PETpost. The recurrent volume was defined as: ''In-Field (IF)'', ''Extending Outside the Field (EOF)'' or ''Out-of-Field (OF)'' if it had received >95%, 20–95% or <20% of the prescribed dose, respectively.

Results: We found 10/87 (11.5%) recurrences at primary site (2 oral cavity, 2 nasopharynx, 2 oropharynx, 3 hypopharynx and 1 larynx). The mean GTV-PETpre was 13.1 cc (4.6-37.4), while the mean GTV-PETpost was 4.3 cc (1.1-12.7). Mean D99 of GTV-PETpre GTV-PETpost was 68.1Gy, [66.5-69.2], considering a prescription dose of 70 Gy to the PTV. Two recurrences were 100% inside GTV-PETpre, 4 recurrences were mostly inside (61-91%) and 4 recurrences were marginal to GTV-PETpre (33-1%). Six recurrences (60%) were defined as IF, 3 (30%) as EOF and one (10%) as OF.

Conclusions: In all 10 patients an overlap existed between the planning 18F-FDG PET and the recurrence scan, which indicates a high probability of the recurrence to originate from the GTV-PETpre volume. Furthermore 60% of recurrences were IF while 10% were OF. Our study indicates, even though not conclusive, that the recurrence may come from the strongest FDG-signal These results support the hypothesis of an intensification of the dose on these volumes.

CG002

STEREOTACTIC BODY RADIOTHERAPY (SBRT) FOR PRIMARY AND METASTATIC LIVER TUMORS: CLINICAL-DOSIMETRIC CORRELATIONS IN A PRELIMINARY INSTITUTIONAL EXPERIENCE

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Aims: It is still widely debated what is the ideal treatment for patients affected by liver neoplasms, especially for those patients who are not candidates for surgery. With the main objective to assess local control and toxicities after SBRT for primary and secondary liver tumors, a group of 13 patients treated from October 2013 to March 2016 was retrospectively analyzed.

Methods: The patients were evaluated periodically at predetermined intervals (15 days and/or 1 month, 3-6-9-12-18-24 months) after the end of the treatment to assess local control and toxicity (according to CTCAE scale). Abdomen CT and mostly MRI with Gd-EOB-DTPA have been used to prospectively define the extent and severity of Focal Liver Reaction (FLR), atrophy and compensatory hypertrophy. Toxicity and radiological abnormalities have been related with dosimetric data, also evaluating the Conformality Index (CI).

Table 1

HCC

Patient	Age	IK	Volume GTV (cc)	Volume ITV (cc)	Volume PTV (cc)	Volume LIVER (cc)	DOSE (Gy)	Technique	FLR max	FLR min
1H	78	90	0,89	1,26	8,35	1695,9	20/60	VMAT	59,45	28,39
2Ha	68	80	40,26	51,22	74,93	1632,96	16/48	VMAT	283,56	214,15
2Hb			2,27							
3H	78	80	3,26	3,34	24,19	2630,92	20/60	VMAT	192,5	140,11
4Ha	63	80	6,47	12,66	44,49	1383,86	16/48	VMAT	123,09	/
4Hb			0,13							
4Hc			0,59							
4Hd			0,63							

METASTASES

Patient	Age	IK	Primary	Volume GTV (cc)	Volume ITV_ (cc)	Volume PTV (cc)	Volume LIVER (cc)	DOSE (Gy)	Tecnichnique	FLR max	FLR min
1M	63	70	Oropharynx	15,21	21,18	36,14	1788	20/60	VMAT	60,73	/
2Ma	71	90	Colon-Rectum	1	1,68	12,26	1630,46	20/60	VMAT	122,1	38,43
2Mb				5,11	7	16,46		20/60	VMAT		
3M	71	70	Colon-Rectum	34,69	50,81	134,97	1806,46	16/48	VMAT	431,46	125,41
4M	67	80	Colon-Rectum	0,29	/	17,8	1584,28	20/60	VMAT	/	/
5M	73	80	Pancreas	0,79	3,02	27,33	1003,08	20/60	VMAT	264,03	54,14
6M	65	90	Colon-Rectum	2,5	3,22	15,17	1452,1	20/60	VMAT	38,88	14,21
7M	52	90	Lung	0,83	1,65	9,13	2337,79	16/48	VMAT	52,65	11,22
8M	63	90	Oropharynx	3,96	5,51	10,76	1189,86	20/60	VMAT	112,84	48,24
9M	85	70	Colon-Rectum	6,11	8,9	28,29	1297,65	20/60	VMAT	205,18	125,41

Results: Disease and patient characteristics are reported in Table 1. Local control rate was 100% at a median follow-up of 15 months (6-26 months) in patients with oligometastases and of 10 months (3-19 months) in patients with primary Hepatocellular Carcinoma. Recorded toxicity was mostly Grade I-II in patients treated for oligometastases; Grade III toxicity was observed more frequently in HCC patients. FLR decreases with time and sometimes disappears; a larger FLR seems related to the severity of liver damage and to compensatory hyperplasia. Extent of FLR seems also related to a specific isodose of 25 Gy, as shown by CI.

Conclusions: Liver SBRT is an effective treatment, able to ensure high local control rates, in both subgroups of patients (oligometastases and HCC). Toxicity is manageable in most cases. Extension of FLR is related to the liver dose received and particularly to the volume included in the 25 Gy isodose, which could be used as an index to predict the grade of side effects. These data should be confirmed in larger patient series.

CG003

FDG PET/CT AFTER TOMOTHERAPY FOR CERVICAL CANCER: CORRECT TIMING IN RESTAGING/FOLLOW UP

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Aims: To identify the correct execution timing of [18F] FDG PET/CT (PET/CT) in restaging/follow up for the evaluation of the response to radiation treatment for cervical cancer (CC).

Methods: From October 2011 to October 2015, 34 patients with CC (stage IB1-IVA) were treated by radiotherapy (RT), 22 with curative intent and 12 with postoperative intent The mean age was 58 years (range 32-88). All patients underwent pre-treatment clinical examination and imaging staging: 32 with PET/CT (PET0) and with abdominal–pelvic MRI, 2 pts with PET/CT only. 25 patients received concurrent CHT with cisplatin and/or taxanes, while 2 patients received neoadjuvant CHT with TEP (paclitaxel, epirubicin and cisplatin). Tumor doses ranged between 54 and 70.4 Gy in 30-32 fractions (frs); dose to the pelvis ranged between 50.4 and 54Gy in 25-30 frs. Lumbar-aortic chain was treated in 4 pts (51 Gy/30 frs); 13 pts received a boost on PET/CT positive LN with doses ranging between 54 and 66Gy in 30 frs). Twenty-two pts were treated with HDR boost with a dose/fr equal to 6-15Gy in 1-3 frs. After treatment, patients periodically performed PET/CT to evaluate treatment response: PET1…x, up to a maximum of 5 PET (PET5) for each patient, with a variable timing from 1 to 3 months, according to oncological needs. The PET/CT response was evaluated by quantitative criteria (EORTC), qualitative analysis (Visual Score) and specialist report.

Results: 26 pts underwent a PET during the follow up: 18 pts showed a complete response (CR), 6 pts a partial response (PR), 2 pt had local stable disease (SD) but developed distant progression disease (PD). The time from end of treatment to the first PET/CT evaluation varied from 1 to 15 months (mean 5.7 months) . Among the 6 pts with PR at PET/CT, 3 showed CR at

the following PET (8, 12 and 14 months), 1 local stable disease (SD) but distant metastases and 2 showed local and distant PD. PET/CT study detected the response to treatment on average at 5.7 months, that is also mean time in which PET1 was performed .

Conclusions: In our study we have shown that PET/CT for restaging and follow-up is an excellent method of research for response and recurrence of disease after radiotherapy and the mean time for CR detection in our patients was 5,7 months. These results suggest that the first restaging PET/CT should be performed approximately 5-6 months after the end of treatment, but the optimal timing of execution remains to be defined by further studies.

CG004

PROGNOSTIC SIGNIFICANCE OF STANDARDIZED UPTAKE VALUE ON 18FLUORINE-FLUORODEOXYGLUCOSE POSITRON EMISSION TOMOGRAPHY/COMPUTED TOMOGRAPHY (PET/TC) IN PATIENTS WITH HEAD & NECK CANCER

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Aims: To evaluate the prognostic impact of maximum standardized uptake value (SUVmax) in patients (pts.) with locally advanced head and neck cancer (HN) undergoing pre-treatment [F-18] fluoro-D-glucose-positron emission tomography/computed tomography (FDG PET/CT) imaging.

Methods: Thirty pts. (22 men and 8 women; median age, 64 years; range 25-86 years) undergoing FDG PET/CT before radical treatment with definitive radiotherapy (± concomitant chemotherapy or ± neoadjuvant chemotherapy) or surgery + postoperative (chemo)radiation were analysed. We only included pts. with a histologically carcinoma diagnosis of oral cavity(n=6), nasopharyngeal (n=6), larynges (n=8), salivary galnds (n=1), paranasal sinuses (n=6), primary unknown cancer (n=3). Five pts. (17%) underwent neo-adjuvant chemotherapy; 5 pts. (17%) underwent concurrent chemotherapy; 3 pts. (10%) underwent both neo-adjuvant and concurrent chemotherapy. The planning treatment volume PTV for each pts. included the primary tumour site and regional lymph nodes. The median described dose was 70 Gy (range, 66–70 Gy) in 2 Gy per fraction, with 5 fractions per week. The effects of clinicopathological factors (age, gender, tumour location, stage, and treatment strategy) including primary tumour SUVmax on overall survival (OS), disease-free survival (DFS), were evaluated. The most appropriate SUVmax cut-off value for predicting overall survival (OS) and disease-free survival (DFS) was selected using receiver operating characteristic (ROC) curves.

Results: The median follow-up time for surviving pts. was 14 months, while the median survival time in the entire pts. cohort was 13 months. One-year OS and DFS rates were 73% and 70%, respectively. A SUVmax cut-off value of 16 showed the best discriminative performance. Of the 8 deceased, 7 had an SUV greater than 16. In univariate analyses, SUVmax (p=0.013, p=0.025), were identified as significant prognostic predictors for OS and DFS.

Conclusions: In our small and heterogeneous pts. series pre-treatment SUVmax is prognostic for OS and DFS. Pts. with SUVmax greater than 16 had a worse prognosis.

CG005

STEREOTACTIC RADIATION THERAPY AND PULMONARY PARENCHYMAL ALTERATIONS: THE FOLLOW UP ISSUE

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Purpose: To retrospectively evaluate pulmonary parenchymal CT alterations at 3, 6, 12 months after stereotactic body radiation therapy (SBRT). The aims of the study were to define which factors affect CT volumes and pattern of lung toxicity and to assess the isodose curves that better conform to the damaged pulmonary volume. CT alterations time course has been also addressed.

Materials and Methods: CT scan images of patients (pts) treated with SBRT for primitive or secondary lung nodules were reviewed. The characteristics of the patients in terms of performance status (using Charlson Comorbidity Index, CCI), type of cancer (primitive or secondary) and the patterns of lung toxicity (dense, ground glass or both) were considered. The study on volumes was performed using the software Velocity ®, Varian Medical Systems. To compare different variables -square test, Student t test and Anova test were used.

Results: From 2012 to 2015, 56 pts were treated with SBRT with the 55 Gy in 5 fractions schedule. The definition of how lung toxicity patterns change according to the type of tumor, the PTV and the CCI is reported in Table 1. No difference was found regarding the type of tumor. According to the dimension of PTV, the pattern of toxicity changes at 3 (p 0.009), 6 (p 0.001) and 12 (p 0.002) months; small nodules develop ground glass patterns and bigger nodules a dense one. As for the CCI, the pattern of toxicity changes at 3 (p 0.003), 6 (p 0.026) but not at 12 months; fit pts develop ground glass patterns and old pts with several comorbidities dense ones. The definition of how lung toxicity patterns change according to the lung toxicity volumes and iso-

dose curves is reported in Table 1. No difference was found in regard to the PTV, CCI and pattern of toxicity.

Conclusions: The "shape" of lung toxicity changes during the first year after SBRT, leading to fibrotic damage at 12 months. Old patients with several comorbidities or those who have undergone several therapies have different capability to repair lung damage and they consequently show a particular type of toxicity pattern. In addition to the knowledge of the "shape" of isodose curves this could allow to better distinguish radiation induced lung injury from disease progression.

Table 1

		3 months			6 months			12 months		
		Ground Glass	Dense	GG + dense	Ground Glass	Dense	GG + dense	Ground Glass	Dense	GG + dense
PTV (median 28.1)	Under median	77,3%	31,8%	44,4%	89,5%	40,0%	35,0%	83,3%	41,7%	27,3%
	Over median	22,7%	68,2%	55,6%	10,5%	60,0%	65,0%	16,7%	58,3%	72,7%
Charlson Comorbidity Index	≤ 4	68,2%	22,7%	55,6%	63,2%	13,3%	55,0%	50,0%	25,0%	63,6%
	≥ 5	31,8%	77,3%	44,4%	36,8%	86,7%	45,0%	50,0%	75,0%	36,4%
Tumor type	Primitive	59,1%	63,6%	55,6%	57,9%	40,0%	60,0%	50,0%	58,3%	63,6%
	Lung metastasis	18,2%	27,3%	44,4%	21,1%	46,7%	35,0%	29,2%	33,3%	27,3%
	Other organs metastasis	22,7%	9,1%	0,0%	21,1%	13,3%	5,0%	20,8%	8,3%	9,1%
Total		41,5%	41,5%	17,0%	35,2%	27,8%	37,0%	51,0%	25,5%	23,5%
		Tox Volume (mean cc)	Isodose (mean Gy)	CI (mean %)	Tox Volume (mean cc)	Isodose (mean Gy)	CI (mean %)	Tox Volume (mean cc)	Isodose (mean Gy)	CI (mean %)
PTV (median 28.1)	under median	35	43	47	52	40	49	50	35	46
	over median	49	49	51	76	37	46	73	38	48
Charlson Comorbidity Index	</= 4	42	44	49	69	37	52	71	34	51
	>/= 5	41	46	49	57	41	44	49	38	43
Pattern	Ground Glass	50	42	46	56	39	48	50	37	46
	Dense	27	50	49	50	37	43	63	35	50
	GG + dense	57	43	56	76	40	51	76	35	43
Total		42	46	49	63	39	47	59	36	47

CG006

HYPOFRACTIONATED IMRT FOR ANAL CANAL CANCER TREATMENT.WHAT'S THE GOOD IMAGING TO ASSESS RESPONSE

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Aims: The best time to assess complete clinical response after chemoradiotherapy in squamous cell carcinoma of the anus has been suggested to be around 26 weeks by the phase III study (ACT II). The aim of this report is to correlate the clinical outcomes with the sensitivity and the specificity of diagnostic imaging performed after six months from CT-RT

Methods: From March 2009 to April 2016 sixty-one patients with anal canal cancer have been treated with concurrent CT-RT. Radiotherapy was delivered by helical Tomotherapy and doses were adapted to two clinical target volumes according to the stage. Median dose simultaneously delivered was 55 Gy in 25 consecutive fractions for gross tumor volume T and N, while the pelvic and inguinal nodes received 45 Gy. Chemotherapy was 5-FU and mitomycin-based. All patients underwent to digital anal canal examination (DRE) every month after treatment until 26 weeks from the beginning of therapy. At this point, an imaging evaluation was performed. Commonly patients with positive imaging underwent to biopsy

Results: With a median follow-up of 31 months (5-73) the predicted 3 yy and 5yy overall survival was 84.3% and 77% respectively. The survival correlate with the stage at diagnosis. The three yy colostomy-free survival was 88.9%. Patients with not complete DRE at three and six months underwent to diagnostic imaging as MRI or TC or FDG-PET or EUS. After a minimum follow-up of seven months, the number of positive biopsies was twenty-two over the twenty-three performed. All these patients underwent magnetic resonance imaging of the pelvis (MRI) before the biopsy. On the basis of statistical analysis the positive predictive value of MRI to discriminate residual disease is around 66%. After treatment 38 patients (62%) did not perform biopsy. Twenty-one (35%) achieved a complete response (CR) at 6 months, defined by DRE and imaging. Within the group without a CR the integration of a negative FDG-PET excluded the biopsy.

Conclusions: While the best timing to assess the tumor response after CT-RT in the treatment of anal canal cancer is supported by evidence, the best imaging before biopsy for the uncertain cases is still to be defined. MRI should be predictive of residual disease in most of the positive exams

CG007

HYPOFRACTIONATED RADIOTHERAPY WITH SIB AND HORMONOTHERAPY IN ELDERLY WOMEN BREAST CANCER: WHAT IS OPTIMAL COMBINATION?

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Aims: In elderly women affected by breast cancer, the optimal combination of hormonotherapy (HT) and hypofractionated radiotherapy (RT) after breast-conserving surgery has not established, due to possible pulmonary and cardiac toxicities and breast fibrosis. Aim of the present analysis is to evaluate the feasibility of concomitant hypofractionated radio-hormone treatment in elderly women.

Methods: Between 03/2014 and 09/2015, 42 elderly women affected by early stage breast cancer were treated with concurrent administration of HT. Hypofractionated RT with simultaneous integrated boost (SIB) by Volumetric Modulated Arc Therapy (VMAT) was performed to irradiate the whole breast. Doses to whole breast and surgical bed were 40.5 Gy

and 48 Gy respectively, delivered in 15 fractions over 3 weeks. Acute toxicities were recorded according to RTOG scale.

Results: The main clinical and tumor characteristics of patients are summarized in Table 1. At median follow up of 24 months (range 18-36), all patients are alive and none developed local or distant relapse of disease. Quadrantectomy and sentinel lymph node biopsy were performed in all cases, 14 (33%) women received tamoxifen (TAM) and 28 patients (67%) aromatase inhibitors (AI) concurrently with RT. Only five patients underwent also adjuvant chemotherapy and two patients (HER2 positive) received trastuzumab. During RT, no acute complication were reported, and all women concluded their treatment without interruptions. At the end of treatment, acute skin G0, G1 and G2 toxicity was 43%, 52% and 5% of cases, respectively. Mild asthenia (G1) was referred by 17 women in absence of daily limitation activities. Regarding breast tissue acute toxicity, no edema or fibrosis was described. The pulmonary and cardiac toxicity profile was safe without acute events of pneumonia, pericarditis or coronary heart disease. During follow-up, no late side effects were registered and all women continued their hormonotherapy. No differences between patients received TAM versus AI were observed.

Conclusions: The concurrent administration of HT and hypofractionated RT with SIB is an effective and safe option for elderly women affected by early stage breast cancer. The type of HT seems to be not related to toxicity. Long-term follow-up data and larger population of study are needed to definitively assess late toxicity and clinical outcomes.

Table 1.

Patients' characteristics	
Patients number	42
Median age (range) [years]	71 (65-81)
Diabetes mellitus (No:Yes)	38:4
Hypertension (No:Yes)	18:24
Tumors' characteristics	
Laterality (R:L)	26:16
IDC:ILC:Other	29:8:5
Mean T dimension (range) [mm]	10 (5-43)
Grading (G1:G2:G3)	14:23:5
Margins (negative:close)	33:9
Ki67 (<15% vs >15%)	32:10
HER2 positive	2
ER-/PR+	1
ER+/PR-	12
ER+/PR+	29

R=right L=left IDC=Infiltrating ductal carcinoma ILC=Infiltrating lobular carcinoma ER=Estrogen receptor PR=Progesterone receptor

CG008

RADIOTHERAPY IN THE ELDERLY: FIVE-FOLD INCREASE OF PATIENTS WITH PACEMAKERS AND IMPLANTABLE CARDIOVERTER DEFIBRILLATORS TREATED AT RADIATION ONCOLOGY DEPARTMENT (2010-2016), CLINICAL AND DOSIMETRIC ASPECTS

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Aims: As the result of the aging, the number of patients with cardiac implantable electronic devices (CIEDs) that requires radiotherapy (RT) will continue to rise. RT can compromise electronic components of CIEDs, including pacemakers (PM) and implantable cardioverterdefibrillators (ICD), resulting in transiet malfunction as well as permanent damage. The presence of CIEDs could limit the therapeutic intent and make more difficult the management of these patients before and during RT.

Methods: In this work we present a retrospective analysis of all RT treatments of patients with CIEDs in different cancer site at European Institute of Oncology (EIO) of Milan from June 2010 to December 2016. Techniques used to treat patients were 3-Dimensional Conformal RT, Intensity-Modulated RT and Stereotactic RT. We collected clinical characteristics of cancer, models of CIEDs, data about RT treatment plan. Radiation dose to device, cardiological control and CIED dysfunctions after RT were evaluated.

Results: 17693 cycles of treatments were performed in our Institute from 06/2010 to 12/2016, 85 treatments get involved 56 patients (50 male, 6 female; median age 73.8, range 53.4–91.4) with a CIEDs (77% PM, 23% ICD). There was a five-fold increase of patients with CIEDs, from 0.2% of 2010 to 1.1% of 2016. The site of RT was chest and neck (50.5%), abdomen/pelvis (38%), head (10.5%) and arm/leg (1%). A subgroup analysis was performed (pts treated on chest and neck): of the 43 treatment (31 patients) on chest and neck, 69% were in presence of PM and 31% of ICD, all but one located in left chest. Median age of cardiac device at the time of RT was 30.3 months (range 1.4–159.4). Median maximum measured dose to PM was 1.19 Gy (range 0-4.2) and to ICD was 1.55 Gy (range 0-3.7). Two malfunctions occurred, both to ICDs (an altered electrode sensing and a reprogramming of device) receiving maximum dose > 2 Gy (2.09 and 2.1 respectively).

Conclusions: Nearly 3% of patients with CIED had experienced a damage of the device. Close cooperation

between radiation oncologists, cardiologists, physicians and technicians is needed to achieve the best practice management in these increased setting of patients.

Table 1.

	Patient 1	Patient 2
Age	55.3	85.5
Sex	Female	Male
Type of CIED	ICD	ICD
Manufacturer	Medtronic	Biotronik
CIED location	Left chest	Left chest
Type of cancer	Lung cancer	Lung cancer
Treatment region	Chest	Chest
GTV	RUL and mediastinal N	LUL and mediastinal N
Photon Energy MV	18 X	6-18 X
Radiation dose (measured)	2.09	2.1
Reprogrammed	No	Yes
Replacement	Yes	No

CIED: cardiac implantable electronic device; ICD: implantable cardioverter/defibrillators; GTV: gross tumor volume; RUL: right upper lobe; LUL: left upper lobe; N: lymph nodes

CG009

INOSITOL HEXAPHOSPHATE (INSP6) AS AN EFFECTIVE TOPICAL TREATMENT FOR PATIENTS RECEIVING ADJUVANT CHEMOTHERAPY AFTER BREAST SURGERY

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Aims: Inositol hexaphosphate (InsP6) has shown to be efficient in decreasing adverse effects in patients with breast cancer under chemotherapy. This study was aimed to evaluate and compare the efficacy of topical InsP6 in improving quality of life in women treated with anticancer drugs.

Methods: The study was a double-blind, randomized controlled trial (RCT) with allocation concealment of 20 patients in two groups, one (experimental) applied 4% topical formulation of InsP6 once a day, whereas the second one (control) a gel containing hyaluronic acid. Patients in both arms received the same polychemotherapy CMF for a total of 6 cycles. InsP6 therapy started 6 weeks after lumpectomy and were continued for 6 months. Blood tests were monitored in both groups and quality of life was assessed using standardized QLQ-C30 and QLQ-BR23.

Results: Patients who applied InsP6 on the breast significantly improved their quality of life and functional status reducing side effects compared to control group. Moreover, after treatment, a significant difference between the two groups was observed in the white blood cells and platelets count values. Complete blood cells count showed that the number of white blood cell (WBC) before treatment averaged 7.35 ± 2.5 x 10^9/L in treated group and 7.5 ± 2.5 x 10^9/L in control group. After treatment WBC remained at within the normal range in the InsP6 patients (6.85 ± 1.3 x 10^9/L), whereas it drastically decreased in control group (2.7 ± 1.5 x 109/L). Furthermore, in the InsP6 group platelets count was 285.12 ± 95.0 x 10^9/L before treatment and 268.98 ± 53.0 x109/L after treatment, whereas in control group platelets decreased significantly after treatment resulting in a mean value of 115.32 ± 52.0 x 109/L compared to 280.80 ± 81.0 x 10^9/L before treatment. Notably patient's compliance was high.

Conclusions: Data reported herewith showed that topical use of a formulation containing 4% phytic acid was effective in improving the QLQ and reducing the side effects of chemotherapy in women with breast cancer. Namely, a significant difference was observed between treated and control groups in the WBC and platelets count values after treatment. In addition, InsP6 group had three times less of postponed cycles over all the treatment period compared to control group. The results highlight the beneficial effect of InsP6 as an adjuvant of chemotherapy for breast cancer and the improvement in patients' quality of life.

CG010

ADJUVANT BREAST RADIOTHERAPY WITH AN HYBRID IMRT CLASS SOLUTION IN ELDERLY PATIENTS: PRELIMINARY TOXICITY RESULTS

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Aims: Elderly patients may have a scarce compliance to prolonged radiotherapy treatment. An hypofractionated treatment, by reducing the number of fractions, could be better accepted in this frail setting. Aim of the present analysis was to evaluate acute (TAC) and late cutaneous (TTC) and subcutaneous (TTSC) toxicity of a whole breast irradiation with simultaneous integrated boost using an hybrid IMRT class solution in a subgroup of elderly patients enrolled in the clinical study (MARA-3).

Methods: Patients > 70 years with low-moderate risk of recurrent disease (no positive nodes nor close resection margins) were enrolled in MARA-3 trial and treated with HMRT plans that were inversely optimized by combining two open fields with six-eight subfields in two tangential beams. Open fields were setup to include the whole breast with a 2 cm flash region and to carry the 80% of beams weight. Primary endpoints were TAC, TTC and TTSC scored by RTOG-EORTC scale. Secondary endpoints were local control and overall survival. All patients received 40Gy (2.5 Gy/fraction) to the whole breast and an additional simultaneous 4 Gy (2.75 Gy/fraction) to the tumour cavity over 16 fractions.

Results: 40 patients (median age: 74.5, range: 70-84; pT1N0: 85.0%, pT2N0: 15.0%) were selected and analyzed. The incidence of TAC was: G1: 35.0%, G2: 20.0%. No G3 acute skin toxicity was observed. The 18 months any grade late cutaneous and subcutaneous toxicity free survival were 62.9% and 65%, respectively. No G3 TTC nor TTSC were observed. With a 17-months median follow-up (range: 4-92), no patient showed local recurrence or lymph nodal disease.

Conclusions: An hybrid IMRT class solution in elderly patients seems to be tolerable and safe with negligible severe TAC as well as TTC and TTSC and an excellent local-regional control.

CG011

CETUXIMAB-BASED CHEMOTHERAPY IN ELDERLY PATIENTS AFFECTED BY RECURRENT/METASTATIC SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK (HNSCC): SINGLE CENTER EXPERIENCE

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Aims: The Extreme study (J Vermorken et al, NEJM 2007) showed that the addition of Cetuximab (CTX) to standard platin-based chemotherapy (CT) yielded a significantly improved outcome in patients affected by recurrent/metastatic (R/M) HNSCC, with a median overall survival (OS) of 10.1 months. However, the prognosis was shown to be worse in the 77 elderly patients enrolled, with a non-significant benefit in terms of OS and progression-free survival (PFS) in the CTX group. The aim of our study is to report the efficacy of CTX-based CT in elderly patients affected by R/M HNSCC.

Methods: We performed a retrospective, single-center analysis of R/M HNSCC elderly patients consecutively treated at our Radiotherapy department at Careggi Hospital, Florence, Italy. Following the definition of the National Institutes of Health, patients with age > 65 years were defined as old. Baseline comorbidities were evaluated according to the Charlson's Comorbidity Index (CCI). Treatment options for first-line CT were: standard Extreme regimen (Cisplatin or Carboplatin + 5FU + CTX); doublet chemotherapy regimen (Carboplatin + CTX) or monochemotherapy regimen (CTX). PFS was defined as the time from the start of first line CT to first radiological confirmation of disease progression or death. OS was defined as the time from the start of first line CT to death from any causes.

Table 1.

Characteristics	N° Patients
Sex	
M	34 (83%)
F	7 (17%)
Age	
Median Age	72.2 (range 65-84)
65-75	29 (70%)
>75	12 (30%)
PS	
0	22 (53%)
1	13 (32%)
2	5 (13%)
3	1 (2%)
Charlson's Comorbidity Score	
Median	5.5 (range 3-10)
≤3	6 (14%)
4-6	20 (49%)
≥ 7	15 (37%)
Smoke pack- years	
Never	8 (19%)
≤ 10	7 (17%)
10-20	11 (27%)
>20	15 (37%)
Primary Tumor Site	
Oropharynx	7 (17%)
Larynx	12 (31%)
Nasopharynx	1 (2%)
Ipopharynx	3 (7%)
Oral Cavity	17 (41%)
Unknown primary	1 (2%)
Previous Treatment	
No	6 (14%)
RT	20 (49%)
RT + weekly CDDP	9 (22%)
RT + cetuximab	4 (7.5%)
RT + carboplatin	4 (7.5%)
Extent of Disease	
Local Recurrence (T)	10 (26%)
Loco-regional Recurrence (T+N)	8 (19%)
Metastatic Disease	8 (19%)
Loco-regional and Metastatic disease	9 (22%)
Metastatic at diagnosis	6 14%)
Type of regimen	
CDDP+5FU+Cetuxiamb	8 (19%)
CBCDA+5FU+Cetuxiamb	12 (31%)
CBCDA+Cetuximab	17 (41%)
Cetuximab	4 (9%)

Results: Between February 2007 and April 2017, 41 patients were included in our analysis. The median age at diagnosis of R/M disease was 72.2 years (range: 65-84). Treatment and patients' characteristics are summarized in Table 1. Most patients had a loco-regional recurrence (85%; 35/41), whereas 15% of subjects (6/41) had metastatic disease. The median time to progression after the primary curative treatment was 20 months (range 0 – 101). Almost half the population (20/41; 50%) received triplet-based CT according to the Extreme schedule, whereas a doublet CT regimen and CTX monotherapy were delivered in 17 (41%) and 4 (9%) patients, respectively. At a median follow-up of 8.1 months (range 1-42), the median PFS was 4 months (SD: 2.4; 95% CI: 3.2 to 4.9 months). Finally, the median OS was 6.7 months (SD: 5.5; 95% CI: 4.6 to 8.8

months).

Conclusions: Our study confirms the efficacy of CTX-based regimen in the elderly HNSCC population in terms of PFS, in line with the results of the Extreme trial. The overall prognosis in this category of patients is particularly poor due to competing risks of mortality.

CG012

TOLERABILITY AND CLINICAL OUTCOMES OF ADDING OXALIPLATIN TO STANDARD NEOADJUVANT CHEMORADIOTHERAPY FOR LOCALLY ADVANCED RECTAL CARCINOMA IN ELDERLY PATIENTS: A RETROSPECTIVE COHORT STUDY

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Aims: To investigate the effects and report the long-term results after intensified neoadjuvant chemoradiotherapy (CRT) in elderly patients with locally advanced rectal cancer (LARC).

Methods: We identified a retrospective cohort of patients aged 70 years and older with LARC who received intensified neoadjuvant CRT, followed by surgery and adjuvant chemotherapy. At diagnosis, pre-treatment comorbid conditions were estimated using the adult comorbidity evaluation-27 (ACE-27) score. Intensified neoadjuvant CRT consisted of radiotherapy (total dose 50.4/54 Gy) plus concomitant oxaliplatin (50 mg/m^2/week) and 5-fluorouracil (200 mg/m^2/5 daily continuous infusion). Survival outcomes were evaluated by Kaplan-Meier method.

Results: A total of 26 patients were included. Globally, all patients received the RT prescribed total dose and the 85% of patients achieved chemotherapy protocol compliance. Conservative surgery was performed in 16 patients and pathologic complete response was achieved in 19.2% of cases. Gastrointestinal toxicity was the most common acute complication. Severe acute toxicity was recorded in 5 patients. Overall, 7 patients died. The 5-year overall survival and disease-free survival were 70.6% and 65.5%, respectively (Figure 1). Based on ACE-27 score, patients were divided into two groups: ACE-27 score 0 (9 patients) and ACE-27 score ≥ 1 (17 patients). ACE-27 score ≥ 1 was not associated with a poor treatment compliance or worst survival.

Conclusions: Intensified neoadjuvant CRT is an efficacious and well tolerated treatment option for LARC in elderly patients. These results could be potentially useful as a reference in the future for a solid scientific evidence in geriatric oncology.

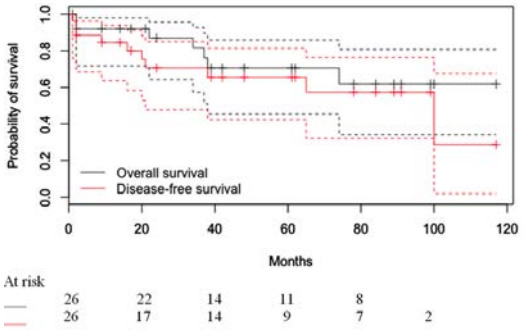

Figure 1

CG013

AGE-IMPACT IS SUBSITE DEPENDENT IN NASOPHARYNGEAL AND OROPHARYNGEAL CANCER

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Aims: Radio-chemotherapy impact over outcome in elderly (>65 years old) head and neck cancer (HNC) patients (pts) is controversial. Multimodal treatment showed a lack of benefit in comparative effectiveness analyses; however, retrospective highly selected series reported older pts to have similar outcome compared to younger ones although with higher toxicities rates.

Methods: We retrospectively evaluated locally advanced oropharyngeal (OPC) and nasopharyngeal cancer (NPC) pts treated at our institution with Intensity Modulated Radiation Therapy (IMRT) techniques and concurrent platinum based chemotherapy (CHT) from 2004 to 2015. Overall survival (OS) and Relapse Free Survival (RFS) Kaplan-Meier curves were estimated and compared with the log-rank test; acute toxicity rate ≥G3 according to Common Toxicity Criteria Adverse Event v4.0 and comorbidities scored with Adult Comorbidity Evaluation-27 (ACE-27) index were also analyzed.

Results: Overall, 375 pts received IMRT-CHT, 215 in OPC and 160 in NPC cohort. Elderly pts represented 26% and 11% of OPC and NPC pts, respectively. In both groups the platinum total dose was not decreased. Elderly pts had an higher ACE-27 score with respect to their younger counterparts (p=0.0078). HPV positivity

was similarly represented in older (73% of the cases) and younger OPC pts (66%) and maintained a significant prognostic role independently of age and also across different age groups. On the contrary, age did not significantly impact on survival in OPC. Five-years RFS was 68% in older versus 76% in younger pts (p=0.391); analogously for OS were 93% versus 87% (p=0.541). There was no significant difference in cumulative acute toxicity rate ≥G3 (39% in elderly vs 36% in younger p=0.778). When analyzed separately, no difference was shown for what concerns dysphagia and mucositis. Both in terms of 5-year RFS (41% in elderly vs 80% in younger pts, p<0.001) and 5-year OS (48% vs 90%, p<0.001) NPC pts showed a different outcome according to age, which turned out to be a negative prognostic factor in this disease. Also for NPC pts, the two age subgroups did not significantly differ in acute toxicity rate ≥G3 (56% vs 61%, p=0.800).

Conclusions: Age has a subsite-specific impact on treatment outcomes: older NPC pts showed markedly worse survival than their younger counterparts, while in OPC pts such an effect was inconsistent. HPV status confirmed its positive prognostic impact regardless of age.

CG014

THE INFLUENCE OF ADJUVANT RADIOCHEMOTHERAPY ON SURVIVAL IN ELDERLY PATIENTS WITH RESECTED PANCREATIC HEAD CANCER.

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Aims: A significant proportion of pancreatic cancer patients is over the age of 70 years at diagnosis. Older patients with pancreatic cancer continue to remain poorly represented in clinical trials. The aim of this study was to determine if age affects outcome in patients with resected pancreatic head cancer.

Matherials and Methods: An analysis of patients with upfront surgically resected pancreatic head cancer treated at our institution between 2005 and 2017 was performed to compare outcomes of patients ≥70 and <70 years. A retrospective review of 114 patients who underwent complete resection with macroscopically negative margins (R0-1) for invasive pancreatic adenocarcinoma was performed. Exclusion criteria included metastatic or unresectable disease at surgery, postoperative death and the use of neoadjuvant therapy. The primary endpoint was overall survival (OS).

Results: Sixty-six patients (39 males, 27 females) were included in the analysis. 41 patients aged <70 years (median age 59 years) and 25 patients aged ≥70 years (median age 75 years) were evaluated. Forty-nine patients (74.2%) received adjuvant radiochemotherapy, 17 patients (25.8%) received adjuvant chemotherapy alone. All patients received gemcitabine or fluoropyrimidine-based chemotherapy concurrently with radiotherapy. Overall, treatment protocols were well tolerated. The median follow-up was 31 months. For the entire cohort of patients no differences in survival was observed between patients receiving or not receiving adjuvant radiochemotherapy in terms of tumor diameter (p=0.36), tumor grade (p=0.5), surgical margins (p=0.75), perineural invasion (p=0.1) and lymph nodes positive disease (p=0.31). Moreover, the univariate analysis showed a trend towards decreased mortality with adjuvant chemoradiation (p=0.09).

There was no statistically significant difference in survival between patients aged <70 years and older patients. Median survival and 3-year OS were 35.5 months and 45% in patients <70 years and 29.5 months and 44% in those ≥70 years (p=0.5).

Conclusions: The data suggest that outcomes of patients ≥70 years who undergo upfront surgical resection and adjuvant therapy are not inferior to younger patients. Treatment decisions should be based on physiologic rather than chronological age.

CG015

PROSPECTIVE STUDY OF HYPOFRACTIONATED RADIOTHERAPY FOR ELDERLY PATIENTS WITH NEWLY DIAGNOSED HIGH GRADE GLIOMA

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Aims: Published studies showed that a short course of radiation therapy (RT) in elderly and frail patients with diagnosed anaplastic glioma is safe, feasible and better tolerated compared to standard RT fractionation. Based on this background we designed a prospective trial of hypofractionated radiotherapy (HFRT). The aim of this study was to evaluate patients' outcome in terms of progression free survival (PFS) and Overall Survival (OS) rate, and incidence of toxicity.

Methods: Elderly patients (≥70 years old) with poor Karnofsky performance status (KPS) ≤60 and histological confirmed high grade glioma (HGG) were enrolled. All patients received surgical resection or biopsy followed by HFRT, more or less associated to concurrent and/or adjuvant Temozolomide chemotherapy (TMZ-CHT) in relation to clinical condition and MGMT status. To precisely define the target volume, computer tomography (CT) scan with and without contrast and magnetic resonance images (MRI) scan were acquired and images were co-registered. All plans were optimized on PTV using volumetric modulated arc therapy (VMAT) mode. Dose prescription was 52 Gy in 15 consecutive daily fractions (BED10 70.88 Gy). Outcome evaluation was performed with neurological examination and brain MRI scan 1 month after RT and every 3 months thereafter. Response was recorded according to the Response Assessment in Neuro-Oncology (RANO)

criteria. Toxicities were graded according to Common Terminology Criteria for Adverse Events version 4.0.

Results: From February 2013 to March 2016, 30 patients were enrolled in this study. The median age was 75 years (range 71-83 years). Biopsy was performed in 17 patients and debulking surgery in 13. Concomitant and adjuvant chemotherapy was administrated in 7 and 11 patients, respectively. Median, 6- and 12- months PFS rates were 5.0 months, 43.3%, and 20% respectively. Median, 6- and 12- months OS rates were 8 months, 90%, and 30%, respectively. The treatment was well tolerated, no severe toxicity was recorded and no increase of steroid drugs has been required during radiation treatment. KPS=60, MGMT methylated status, concurrent and adjuvant CHT were associated with a better outcome.

Conclusions: In our experience, in elderly and frail patients, HFRT with VMAT given at therapeutic doses has proven to be feasible with limited morbidity.

Oral Communications

C001

TEN DAILY FRACTIONS FOR PARTIAL BREAST IRRADIATION. LONG-TERM RESULTS OF A PROSPECTIVE PHASE-2 TRIAL

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Aims: Partial breast irradiation (PBI) is an effective adjuvant treatment after breast conservative surgery for selected early-stage breast cancer patients. However the best fractionation scheme is not well defined. Hereby, we report the 7-year clinical outcome and toxicity of a phase 2 prospective study of a novel regimen to deliver PBI, which consists in 40 Gy delivered in 10 daily fractions.

Methods: Patients with early-stage (pT1-pT2, pN0-pN1a, M0) invasive breast cancer were enrolled after conservative surgery. The minimum age at diagnosis was 60 years old. PBI was delivered with 3D-conformal radiotherapy technique with a total dose of 40 Gy, fractionated in 10 daily schedule (4 Gy/fraction). Treatment volumes and radiation therapy planning were based on NSABP B-39/RTOG 0413 guidelines. Regular follow-up was performed by a radiation oncologists, toxicity was scored with Common Terminology Criteria version 4.0 scale and cosmetic outcome was categorized with Harvard scale. Local control (LC), disease-free survival (DFS) and overall survival (OS) were estimated by Kaplan Meyer method.

Results: Eighty patients were enrolled. The median follow-up was 66 months. A total number of 4 ipsilateral breast recurrences were registered, with a 7-year LC rate of 95%. The 7-year DFS and OS were 91% and 96%, respectively. The presence of lymphatic vessels infiltration and an age <70 years at diagnosis were found to be independent risk factors for DFS at the univariate analysis (p=0.05). One case of severe acute pain occurred during the weeks immediately subsequent to PBI and then resolved. No cases of late Grade-3 toxicity were reported. Grade 1 and 2 subcutaneous fibrosis were documented in 23% and 5% of cases respectively. Cosmetic results were judged by physicians as "good/excellent" in 77 (96%) patients and "fair/poor" in 3 (4%).

Conclusions: PBI delivered with 40 Gy in 10 daily fractions provided good clinical results and was a valid radiotherapy option for early-stage breast cancer patients.

C002

RANDOMIZED PHASE II STUDY OF HYPOFRACTIONATED WHOLE BREAST IRRADIATION VERSUS ACCELERATED PARTIAL BREAST IRRADIATION (HYPAB TRIAL) USING VOLUMETRIC MODULATED RADIOTHERAPY (VMAT): FEASIBILITY AND EARLY TOXICITY RESULTS IN THE FIRST 82 PATIENTS

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Aims: We designed a study to evaluate toxicity and cosmesis of Accelerated Partial Breast Irradiated (APBI) using external intensity–modulated radiotherapy (VMAT-RA), compared to hypofractionated WBI in postmenopausal women with early breast cancer undergoing conserving surgery.

Methods: Postmenopausal women affected by low risk early BC, were randomly assigned in a 1:1 ratio to receive either Hypofractionated WBI or APBI using VMAT. Patients in the APBI arm receive a total dose of 30 Gy to the tumour bed in five fractions every other day. The Hypofractionated arm receive 40.5 Gy to the WB, and 48 Gy to the tumour bed in 15 fractions with SIB tecnique. Primary end-point is the evaluation of toxicity and cosmesis outcome. This trial is registered with ClinicalTrials.gov, number NCT02375048. Acute toxicity and late toxicity were scored according to CTCAE v.4.0. Cosmesis was assessed according to the Harvard scale.

Results: From November 2014 to April 2017 we enrolled 139 patients. Here we present data on the first 82 patients with at least 6 months follow up. All patients had hormonal receptor positive early stage (less than 3 cm) breast cancer, node negative. 40 patients were randomized to APBI arm, 42 patients received hypofractionated RT. Treatment was globally well tolerated. No G3-4 toxicity was recorded. In the APBI arm, acute toxicity was reported in 10 patients (25%), mostly asthenia (G1 3 cases, G2 1 case) and skin erythema (G1 5 cases). In the whole breast arm, toxicity was reported in 30 patients (71.4%), mostly asthenia (5 patients G1, 1 patient G2), skin toxicity (G1 in19 cases, G2 in 7 cases) and breast pain (7 cases). With a median follow up of 7.8 months (range 6-25 months), no patients experienced local or distant recurrence. In the APBI arm, twelve patients (30%) reported G1 toxicity, mostly fibrosis (5 cases) and breast pain (4 cases). In the WBI arm, 30 patients reported (71.4%) late side effects, in three cases G2 (2 cases of skin erythema and 1 case of fibrosis). Concerning cosmetic outcome, at 6 months follow up cosmesis was rated excellent in 52 patients (63.4%), good in 27 (32.9%) and fair in 3 (3.7%).

Conclusions: The current trial is still ongoing, however the preliminary results here reported seems to confirm that APBI with VMAT technique is feasible and safe. More patients and longer follow up data are needed.

C003

DOSIMETRIC RESULTS AND TOXICITY OF A 3-WEEK SCHEDULE HYPOFRACTIONATED RADIOTHERAPY WITH SIMULTANEOUS INTEGRATED BOOST IN 224 EARLY BREAST CANCER, USING TOMODIRECT: MONOINSTITUTIONAL PROSPECTIVE STUDY

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Aims: To evaluate dose distribution, toxicity and cosmesis in breast cancer patients (pts) treated with hypofractionated radiotherapy (RT) to the whole breast (WB) with simultaneous integrated boost (SIB) to the tumor bed (TB) using Tomotherapy (Accuray Inc., Sunnyvale, CA) in Direct modality.

Methods: Pts with early breast cancer undergoing breast conserving surgery followed by RT in 15 daily fractions to WB (40.05 Gy, 2.67 Gy/fr) and to the TB with SIB (48 Gy in 15 fractions, 3.2 Gy/fr), were evaluated. Acute and late toxicity were prospectively assessed according to RTOG and LENT-SOMA scale respectively. Cosmesis was evaluated using Harvard criteria.

Results: Pts were enrolled were 124. The dose distribution was the following. Regarding WB planning target volume (PTV), the median volume receiving the 95% of the prescribed dose was 99.2% (range 93.5%-100%), the median maximum dose (D0.03cm3) was 118% (range 113.8%-125%) of the prescription dose, the median value of the prescribed dose delivered to 50% of breast volume was 102% (50%-106%) and the median value of the breast volume receiving the boost dose prescription was 0.1% (range 0%-13.6%). Regarding the boost PTV to TB, the median volume receiving the 95% of the prescription dose was 97.6% (range 70%-100%), the median maximum dose was 102% (range 100%-107%) of the prescription dose. Acute toxicity evaluated at the end of RT, was the following. Concerning erythema, G0 was recorded in 14.3% and 35.7%, G1 in 72.8% and 56.3%, G2 in 12.9% and 8.0% on WB and on TB, respectively. Concerning desquamation, G0 was observed in 91.5% and 96.4%, G1 in 6.7% and 2.7%, G2 in 1.8% and 0.9% on WB and TB respectively. Concerning edema, G0 was seen in 78.1% and 84.4% and G2 in 21.9% and 15.6% on WB and TB, respectively. One month afterwards, (data available for 127 pts), G2 erythema

was present in one pt (0.8%), while 14.2% and 11.8% of the pts showed G1 erythema on the WB and TB respectively. Grade 1 desquamation affected 3.1% of the pts, while G2 edema (symptomatic) affected 26.8% of the pts. Late skin toxicity and cosmetics evaluation was available for 63 and 60 pts with a median follow-up of 14 months (Table 1). Correlation of dose distribution and clinical features with toxicity is ongoing.

Conclusions: Hypofractionated RT with TomoDirect was characterized by high dose homogeneity and high PTV boost conformality, leading to limited maximum dose outside the PTV boost. Acute and late toxicity were mild and acceptable.

Table 1. Evaluation of late skin toxicity according to LENT/SOMA scale and cosmetic outcome according to Harvard criteria on 63 patients with a median follow-up of 14 months. *Cosmetic outcome evaluation was available for 60 patients.

LENT-SOMA	G0	G1	G2	G3
Pain	74.6%	19.0%	6.3%	-
Edema	74.6%	14.3%	11.1%	-
Fibrosis	81.0%	17.5%	-	1.6%
Telangiectasia	100%	-	-	-
Lymphedema arm	96.8%	3.2%	-	-
Retraction	63.5%	27.0%	9.5%	-
Atrophy	95.2%	3.2%	1.6%	-
Ulcer	100%	-	-	-
Radiological fat necrosis	YES			
	9.5%			-
COSMESIS*	**Excellent**	**Good**	**Fair**	**Bad**
Patient's view	42.9%	41.3%	9.5%	1.6%
Physician's view	38.1%	49.2%	6.3%	1.6%

C004

ACUTE RADIATION TOXICITY OF TWO HYPOFRACTIONATED SCHEDULES OF RADIOTHERAPY (RT) IN PATIENTS TREATED FOR EARLY STAGE BREAST CANCER: A MONOCENTRIC EXPERIENCE

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Aims: The use of hypofractionated accelerated radiotherapy (HypoRT) suggests satisfactory results in terms of clinical outcomes and toxicity, also if concomitant or sequential tumor boost was delivered. Aim of this study is to report and compare acute toxicity of patients treated with two different hypofractionated schedules of RT as adjuvant treatment after breast-conserving surgery.

Methods: Three hundred and five patients (pts) with early-stage breast cancer, treated after breast-conserving surgery, were evaluated. All the pts were stage I-II, all but 6 had negative margins and most of them were LUMINAL A. Systemic adiuvant was allowed but chemotherapy. All pts underwent to HypoRT to irradiate the whole breast and the tumor bed, identified by surgical clips. A first group of pts underwent 3DCRT technique (Hypo-3DCRT) with a sequential boost on the tumor bed. Doses were: 42.56 Gy to whole breast delivered in 16 fractions over 3 weeks and 10 Gy on surgical bed delivered in 4 or 5 daily fractions. A second group of pts, underwent VMAT-SIB technique (Hypo-SIB); doses to whole breast and surgical bed were 46 Gy and 54 Gy, respectively, delivered in 20 fractions over 4 weeks, or 40.5 Gy and 48 Gy, delivered in 15 fractions over 3 weeks. Pts in the second group were treated after April 2014. Acute skin toxicity according to RTOG scale, patients and disease characteristics, and target volumes were recorded.

Results: Pts were treated between June 2010 and December 2016: 100 pts with Hypo-3DCRT technique and 205 pts with Hypo-SIB. Median age was 65 years old (range 40 – 85). The maximum acute skin toxicity was G2 in 33 pts: 15 (15%) pts in Hypo-3DCRT group and 18 (9%) pts in Hypo-SIB. This difference was not significant (OR= 0.545 with p-value= 0.101). None of pts experienced acute toxicity G3-G4. We also evaluate correlation between toxicity grade and breast volume, using 700 cc (50th percentile) as a cut-off. If breast volume < 700 cc, we recorded toxicity G2 in 15% of Hypo-3DCRT pts while it is 9% in Hypo-SIB group. Similarly, in pts with breast volume > 700 cc, toxicity G2 was 17% in Hypo-3DCRT group versus 9% in Hypo-SIB. Nevertheless this difference between two groups was not significant (respectively OR 0.478 with p-value=0.358 and OR 0.619 with p-value=0.159).

Conclusions: At a first analysis Hypo-SIB course as adjuvant treatment after breast-conserving surgery, showed to be well tolerated and the toxicity profile seems to be comparable or better then Hypo-3DCRT technique.

C005

CONCOMITANT HYPOFRACTIONATED RADIOTHERAPY (RT) AND TRASTUZUMAB IN EARLY BREAST CANCER (BC): ACUTE AND LATE TOXICITIES

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Aims: Trastuzumab combined with chemotherapy improves outcome in HER2-positive BC. However most important studies of hypofractionated RT did not include these patients (pts), usually receiving after chemotherapy concomitant trastuzumab and RT. The aim of our analyses was to evaluate acute and late toxicities of this combined treatment.

Methods: We retrospectively analysed 376 pts consecutively treated in our Institute after breast-conserving surgery with hypofractionated RT (2.66 Gy x 16 or 2.25 Gy x 21, both schedule ± boost) from June 2014 to July 2016. Acute and late toxicities were assessed according to the CTCAE-v3 criteria. Breast erythema, moist desquamation, pain, fibrosis/induration, telangiectasia, hyperpigmentation, scar retraction, ulceration, breast/arm lymphedema, late mastitis were evalua-

ted.

Results: Median follow-up was 20 (6-32) months. Hormonotherapy was administered in 328 (87.3%) cases. Eighty-six (22.9%) pts received adjuvant chemotherapy and 33 (8.8%) pts received, after chemotherapy, concomitant trastuzumab and RT. Age at diagnosis, diabetes, postsurgical mastitis, fractionation schedule, breast volume, hormonal therapy were similar in trastuzumab and non-trastuzumab group. No grade 3-4 acute and late toxicity occurred. Observed acute toxicities were: grade 0-1 and grade 2 erythema respectively in 192 (51.1%) and 182 (48.4%) pts, moist desquamation in 136 (36.2%) pts. Observed late toxicities were: pain in 169 (44.9%), fibrosis/induration in 161 (42.8%), telangiectasia in 5 (1.3%), hyperpigmentation in 131 (34.8%), scar retraction in 64 (17.0%), ulceration in 6 (1.6%), breast/arm lymphedema respectively in 78 (20.7%) and 38 (10.1%), late mastitis in 19 (5.0%) pts. In the total group mainly factors significantly associated with acute and late toxicity were large breast size, younger age and V95. The small group of pts receiving after chemotherapy concomitant trastuzumab and RT did not show an increased risk of acute dermatitis but late toxicities were significantly increased, particularly fibrosis and lymphedema.

Conclusions: In our experience, hypofractionated RT was overall well tolerated: however special attention is required in pts receiving after chemotherapy concomitant trastuzumab and RT, because long-term effects of this concurrent treatment are not yet known.

C006

CLINICAL OUTCOME AND MANAGEMENT FOLLOWING LOCOREGIONAL RELAPSE IN 248 PATIENTS TREATED WITH INTRAOPERATIVE ELECTRON AS THE SOLE RADIATION TREATMENT FOR BREAST CANCER: MULTICENTER STUDY OF THE AIRO IORT WORKING GROUP

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Aims: The intraoperative radiotherapy (IORT) working Group of the Italian Association of Radiation Oncology (AIRO) set up a database to collect on a national basis patients (pts) who presented local relapse (IBTR) after IORT full dose with the aim to evaluate clinical outcomes, patterns of failure and salvage treatment.

Materials and Methods: From Sept 2000 to Sept 2013, data of pts treated for the primary tumor with quadrantectomy and IORT full dose in 7 Italian centers, with local/locoregional recurrences, entered the database. Clinical outcome was based on local and distant disease-free survival (DFS) and overall survival (OS) were evaluated.

Results: The study included data of 248 patients. Median age was 59.5 years and 64.5 years at the time of primary tumor and IBTR, respectively. The median time interval to IBTR was 4 years (range: 0.4–15.1). The primary tumor features revealed an unfavorable profile (primary tumour size was > 2 cm in 25%, positive axillary nodes in 30%, grade 3 in 38% etc). The first IBTR showed very similar biological and histopathological features. The median dose of IORT was 21 Gy. IBTR site was close to the primary site in 142 pts (57%) (median time 4.4 years, range 0.6-15.1), and 81 pts (15%) had other quadrant involved (median time 3.8 years, range 0.6-10.2). In 24 pts (10%) the local relapse was multicentric. In univariate analysis, prognostic factors for second local recurrence (LR) or death were median time to first relapse < 2 years, pathological size of the first IBTR > 1cm, presence of vascular invasion, and ≥4 positive nodes. Type of salvage surgery (mastectomy or quadrantectomy) were reported to be at least equivalent (interesting to note, 67% of pts received radiotherapy (RT), either with whole breast radiotherapy (WBRT) or second partial breast irradiation (PBI)). In multivariate analysis the only factor which remained significant was 4 or more positive nodes. The median follow-up after the second oncologic event was 51 months. Regarding the pattern of second failure, 10% of pts presented a second LR, 4% presented a regional relapse, 13% had distant metastases with or without locoregional failure. Thirty-eight pts died. Five-years OS was 89%.Mastectomy and quadrantectomy with RT had the same DFS.

Conclusions: A second conservative approach can be safely performed. The 5–year DFS was slightly lower than that shown in the GEC-ESTRO re-irradiation study with brachytherapy after WBRT, although 5-year OS was comparable.

C007

EFFICACY AND SAFETY OF EVEROLIMUS AND EXEMESTANE FOR METASTATIC BREAST CANCER PATIENTS: A REAL-LIFE EXPERIENCE OF THREE ONCOLOGY DEPARTMENTS

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Aims: Everolimus and exemestane regimen for metastatic breast cancer (MBC) is an effective and widely adopted treatment in hormonal receptor positive (HR+) and human epidermal growth receptor factor 2 negative (HER2-) patients. The pivotal phase 3 BOLERO-2 trial showed a significant progression-free survival (PFS) improvement in patients previously treated with nonsteroidal aromatase inhibitors (4.6-months prolongation in median PFS). Conversely, adding everolimus to exemestane did not confer a significant improvement in the secondary endpoint overall survival (OS). Many other experiences reported results in patients mostly endocrine-treatment naive or treated with tamoxifen only. Therefore, the real-life translation of these evidences is still debated.

Methods: We evaluated the efficacy rates obtained from a cohort of consecutive treated patients at three different Oncology Departments. We compared our PFS and OS results to the outcomes showed in the BOLERO-2 trial (published as a pre-planned interim analysis after 359 observed PFS events), in order to evaluate if applicable also in out-of-trial real-life series. Adverse events were graded according to the NCI CTCAE, version 4.0.

Results: We overall analysed 95 patients. The median age of patients was 51 years (range 30-86). 70 patients (73.7%) received previous adjuvant endocrine treatment; 35/70 patients were treated with adjuvant aromatase inhibitors. Median PFS was 6 months (BOLERO-2 trial showed a local-assessed PFS of 6.9 months). Visceral disease (62/95; 65%) showed a significant worse outcome compared to bone metastases group of patients (p=0.043). Concerning age, median PFS was 7 months (<=65 years) versus 6 months (>65 years), no significant (p=0.61). If used in I-II line of chemotherapy the median PFS showed a significant improved outcome (8 months versus 5 months in case of >2 line; p=0.03). The OS of our series was 20 months; patients affected by visceral disease at time of treatment had a comparable median OS compared to the bone metastases group of patients (17 versus 15 months; p=0.64).

Conclusions: Real-life use of everolimus plus exemestane regimen in our clinical routine practice supported the BOLERO-2 trial outcomes, confirming the expected efficacy in several subgroups of patients affected by HR+/HER2- MBC patients.

C008

OUTCOMES OF STEREOTACTIC RADIOTHERAPY FOR BRAIN METASTASES IN BREAST CANCER WITH DIFFERENT MOLECULAR SUBTYPES

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Aims: To evaluate the response to stereotactic radiotherapy (SRT) among patients with brain metastases of different molecular subtypes of breast cancer (BC) treated with or without targeted therapies.

Methods: Patients diagnosed with BC brain metastases were retrospectively evaluated. Molecular subtypes were defined as luminal A (LA), luminal B (LB), HER2 and triple negative (TN) based on the 2015 St. Gallen Consensus Criteria. For all patients stereotactic plans were generated using BrainLab's iPlan. Patients were treated using a thermoplastic mask. The primary outcome was local failure (LF), whereas secondary outcomes included overall survival (OS) and radiation necrosis (RN).

Results: Between February 2009 and March 2017, 43 BC patients with 73 brain metastases were retrospectively reviewed. The histology of 49% of lesions was infiltrating ductal carcinoma. The most common molecular subtype was HER2 (54.5%), followed by LB (27.3%), TN (10.9%) and LA (7.3%). Patients with HER2 disease received HER2 antibodies or HER2/EGFR TKI. Among all patients, 63% received a course of cytotoxic chemotherapy after brain metastases diagnosis. The mean delivered dose was 36.76 Gy (range 12-45). 15 patients (34.8%) underwent whole brain RT (WBRT) prior or after stereotactic radiotherapy. No acute toxicities has been reported. At the first MRI, we recorded: complete response (CR) in 12.3%, partial response (PR) in 58.9%, stable disease (SD) in 28.8%. The response found at the last follow-up was: CR in 34.2%, PR in 30.1% and SD 16.4%; 19.2% of brain metastases presented progression. At a median follow-up of 9.8 months (range 1-70), the incidence of LF and RN was 13.7% and 8.2%, respectively. At the time of our analysis, 38 patients were alive. The median 1-year LF free survival rate was 89%; among molecular subtypes 1-year LF free survival rate was: LA 75%, LB 100%, Her2 87% and TN 100%. No difference in LF rate was observed according to molecular subtypes. Only the delivered dose (p=0.002) and WBRT (p=0.004) were predictive of local control. The median 1-year OS was 65.8%; among molecular subtypes 1-year OS rate was: 27.6, 27.5, 69.58, 8.4 in LA, LB, HER2 and TN, respectively. OS was significantly shorter in the TN cohort, instead of HER2 group probably due to targeted therapies.

Conclusions: SRT provides a good local control on brain metastases in patients affected by BC. In this analysis molecular subtypes are not predictive of response to SRT.

C009

IDENTIFICATION OF THE MOST SIGNIFICANT MAGNETIC RESONANCE IMAGING (MRI) RADIOMIC FEATURES IN ONCOLOGICAL PATIENTS WITH VERTEBRAL BONE MARROW METASTATIC DISEASE: A FEASIBILITY STUDY

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Aims: Recently, radiomic analysis has gained attention as a valuable instrument for the management of oncological patients. The aim of the study is to isolate which features of magnetic resonance imaging (MRI) based radiomic analysis have to be considered the most significant predictors of metastasis in oncological patients with spinal bone marrow metastatic disease.

Methods: Eight oncological patients (3 lung cancer; 1 prostatic cancer; 1 esaphageal cancer; 1 rinopharyngeal cancer; 1 hepatocarcinoma; 1 breast) with pre-radiotherapy MR imaging for a total of 58 dorsal vertebral bodies, 29 of which metastatic and 29 non-metastatic, were included. Each vertebral body was contoured in T1 and T2 weighted images at a radiotherapy delineation console. The obtained data were transferred to an automated data extraction system for morphological, statistical and textural analysis. Eighty-nine features for each lesion in both T1 and T2 images were computed as the median of by-slice values. A Wilcoxon test was applied to the 89 features and the most statistically significant of them underwent to a stepwise feature selection, to find the best performing predictors of metastasis in a logistic regression model. An internal cross-validation via bootstrap was conducted for estimating the model performance in terms of the area under the curve (AUC) of the Receiver Operating Characteristic (ROC).

Results: Of the 89 textural features tested, 33 were found to differ with statistical significance in the metastatic vs non-metastatic group. The best performing model was constituted by two predictors, namely one morphological feature (center of mass) (p value: 0.001) and one textural feature (gray level co-occurrence matrix sum entropy) (p value: 0.01), in T2 images. The internal cross-validation showed an AUC of 0.918 (95% CI: 0.847-0.988).

Conclusions: The results suggest that MRI based radiomic analysis on oncological patients with bone marrow metastatic disease is able to differentiate between metastic and non-metastatic vertebral bodies. More interestingly, the most significant predictors of metastasis were found to be based on T2 sequence and were one morphological and one textural features. On this basis, the study demonstrates that when facing with patients with bone marrow metastatic disease, the radiomic analysis selectively based on these features might represent a valuable assisting tool for the diagnosis and management of oncological patients with metastatic lesions.

C010

ROLE OF [18F]CHOLINE PET/CT GUIDED STEREOTACTIC BODY RADIOTHERAPY IN PATIENTS WITH OLIGOMETASTATIC PROSTATE CANCER

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Aims: in an attempt to achieve a PSA control, patients with oligometastatic disease could eventually be managed by treating all the active lesions revealed by [18F]Choline ([18F]FMCH) PET/CT with local therapy, either surgery or ablative stereotactic body radiotherapy (SBRT). This study aims to assess in a prospective manner the impact of [18F]Choline ([18F]FMCH) PET/CT guided SBRT in patients with oligometastatic Prostate Cancer (PCa).

Methods: Between May 2011 and December 2016, 53 patients with oligometastatic PCa (defined as $\leq$3 synchronous active lesions detected with [18F]FMCH-PET/CT) out of 98 patients with biochemical relapse of PCa were enrolled in the present prospective clinical trial. All patients were treated with repeated salvage SBRT until the occurrence of a multimetastatic disease (>3 active synchronous metastases). Systemic therapy were delivered after the detection of 4 synchronous metastatic lesions. Primary endpoint analyzed was the length between the baseline PET/CT and the beginning of systemic therapy.

Results: A total of 85 lesions were treated with SBRT. After a median follow-up of 20.3 months, 32 pts started systemic therapy after 39.7 months from the first PET/CT whereas 23 did not. Toxicity related to SBRT greater than G2 where not recorded. Results of semi-quantitative parameters and texture features analysis are under evaluation.

Conclusions: Salvage [18F]FMCHPET/CT-guided SBRT is feasible, well tolerated and succeeded in deferring the initiation of systemic therapy in selected patients with oligometastatic PCa.

C011

VMAT STEREOTACTIC ABLATIVE RADIOTHERAPY FOR OLIGOMETASTATIC PATIENTS: FDG PET/CT AS PREDICTIVE TOOL OR METABOLIC ATLAS?

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Aims: To explore the role of FDG positron emission tomography/computed tomography (FDG PET/CT) in Volumetric-Modulated Arc Therapy (VMAT) Stereotactic Ablative Radiotherapy (SABR) of oligometastases.

Methods: Twenty consecutive patients with oligometastases underwent FDG PET/CT scanning for staging and radiation treatment planning. CT-based gross tumor volumes (GTVCT) was first delineated using clinical information and CT imaging data, and after by a gradient autosegmented PET/CT-based GTVs (GTVPETCT). The mean GTV, proximal and distal margins were compared. For lung oligometastases, 4D CT was used and ITV derived for comparison with GTVPET CT. The differences in the volume, position, matching index (MI) and degree of inclusion (DI) of the GTVPET CT and GTVCT were investigated. The maximal standardized uptake value (SUVmax) and metabolic tumor volume (MTV) were correlated with outcome.

Results: From December 2013 to September 2014, 20 oligometastatic patients were treated with VMAT SABR (median dose 45 Gy, range 30-50, in 1-5 fractions) at the Radiotherapy Unit of San Donato Hospital – Arezzo. Site of oligometastases were lung (8 patients), bone (7), lymphonodes (5) from lung (9), breast (7) and colorectal cancer (4). The mean GTVPETCT was significantly smaller than the mean GTVCT volumes (P = 0.04). Interobserver variability in target delineation was reduced if FDG PET CT was used. The proximal and distal margins of GTVCT volumes were altered by a mean of 0.5 ± 0.3 cm and 0.4 ± 0.2 cm, respectively. For 4D CT, ITV encompassed GTVPET CT in most cases: the GTVPET approximated to the ITV and the spatial mismatch is apparent between them. After a median follow up of 15.5 months (range 18.2- 32.8), 2 years local control (LC) was 90%. MTV and SUVmax did not significantly correlate with LC (p=0.16 and 0.4 respectively).

Conclusions: FDG PET/CT for dose planning improved target definition in oligometastatic patients. If VMAT SABRT is used, PET/TC parameters did not correlate with outcome. GTVPET CT can not replace ITV in spatial position and form for lung oligometastases. The advent of 4D PET/CT may improve the accuracy of contouring the perimeter for moving targets.

C012

INCREASED EFFICACY OF STEREOTACTIC ABLATIVE RADIATION THERAPY IN COMBINATION WITH BEVACIZUMAB IN LUNG OLIGOPERSISTENT/OLIGOPROGRESSIVE METASTASES FROM COLON CANCER

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Aims: metastases from colorectal cancer are poor responsive to SABR probably due to intra-tumor hypoxia. Intratumoral oxygenation is improved by angiogenesis inhibitors administration. Thus, a possible clinical synergistic efficacy of SABR with Bevacizumab could exists in metastases from colorectal cancer. Aim of the analysis is to evaluate the feasibility and efficacy of SABR in combination with Bevacizumab in the setting of lung oligopersistent/oligoprogressive metastases from colon cancer.

Methods: Dataset of lung metastases from colon cancer underwent to SABR were retrospectively evaluated according to the following inclusion criteria: number of metastases ≤ 3; oligopersistent and oligoprogressive disease underwent to SABR; patients underwent to previous chemotherapy alone or in combination with Bevacizumab; Karnofsky performance status > 80; life-expectancy > 6 months; at least 6 months of follow up after SABR; a mutational K-RAS status. Results were compared with a similar cohort of irradiated lung lesions from colorectal cancer in which Bevacizumab was not previously administered.

Results: twenty-three patients for a total of forty lung metastases met the inclusion criteria. The rate of complete response after SABR was higher in the cohort of lesions previously underwent to Bevacizumab, comparing to the remaining (p 0.04). Additionally, in the Bevacizumab group, higher rate of complete response post-SABR was observed in case of oligopersistent versus oligorecurrent metastases (p 0.001).

Conclusions: in the setting of lung oligopersistent/oligoprogressive metastases from colon cancer present study attested the feasibility/efficacy of SABR in combination with Bevacizumab. Further studies in this field of research are strongly advocated.

C013

STEREOTACTIC BODY RADIOTHERAPY (SBRT) FOR BONE OLIGOMETASTATIC CASTRATION-SENSITIVE RECURRENT PROSTATE CANCER (MCSPC): SERIES OF 55 PTS TREATED AT EUROPEAN INSTITUTE OF ONCOLOGY

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Aims: To evaluate outcome in pts treated with SBRT with or without androgen deprivation therapy (ADT) on bone oligorecurrences (BM) from mCPSC after primary treatment (RT or surgery).

Methods: We retrospectively collected data of pts treated on BM from mCPSC with SBRT between 03/2012 and 11/2016. Inclusion criteria were: <3 lesions at time of SBRT detected with positron emission tomography/computer tomography (PET/CT), Magnetic Resonance Imaging (MRI) and CT, hormonenaïve disease at first extra-regional localization, no evidence of local recurrence. PSA was measured every 3 mos after SBRT. Biochemical response was evaluated with PSA level variation (PSA) between pre-SBRT and post-SBRT: biochemical response (BCR) as PSA lower than -20%, progression (BCP) for PSA>+20% and stability (BCS) -20%< PSA<+20%. Imaging was performed in case of BCP. Biochemical and clinical progression free survival (PFS) as well as in field recurrence curves were elaborated with Log-Rank Test.

Results: Fifty-five pts were treated on 77 BM. Median age, initial PSA (iPSA) and pre-SBRT PSA score were 72 years, 9.12ng/mL and 3.5ng/mL, respectively. Initial NCCN class risk was low, intermediate and high in 2, 12 and 41pts, respectively. Median dose was 24Gy/3 fractions. All pts received Image Guided RT. In 30(55%) pts, ADT was added to SBRT. Median follow-up was 17.6mos. No acute or late toxicity was reported. BCR, BCS and BCP were observed in 38(69%), 5(9%) and 12(22%), respectively. Clinical progression was observed in 30(55%) pts after a median time of 7.24mos. In-field progression occurred in 8(15%) pts. One-year biochemical, clinical and in-field PFS (b-, c- and if-PFS) rates were 52%, 55% and 89%, respectively. b-PFS was significantly lower in pts treated with SBRT alone (p=0.0246). On the contrary, c-PFS was similar (fig.). In those pts, ADT was started after a median time of 4.5mos (range: 2.3-34.5mos). At the time of analysis 14(25%) pts were alive with no evident disease, 36(65%) alive with disease, 3(5%) pts dead of disease and 2(5%) dead for other causes.

Conclusions: SBRT is safe and allows high local control rate (85%). One out of two patients is free of biochemical progression at one year after SBRT. Addition of ADT to SBRT improved b-PFS but not c-PFS. Further investigation is warranted to identify pts that could benefit most from this treatment modality and the optimal combination with androgen deprivation or other systemic treatments.

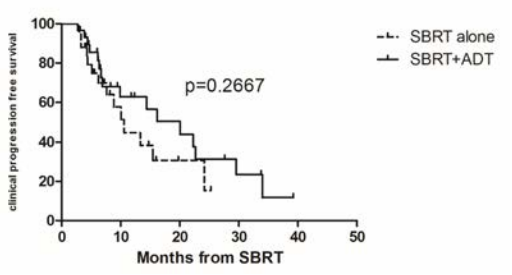

Figure 1. Comparison in PFS in patients receiving SBRT alone or in combination with ADT.

C014

HYPOFRACTIONATED RADIOTHERAPY IN BONE METASTASES

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Aims: External beam radiotherapy (EBRT) is a effective local treatment modality for patients with painful bone metastases. In the clinical practice the use of conventional EBRT (daily fractions of 2-3 Gy to a total dose of 30-40 Gy) has been abandoned in favour of EBRT regimens requiring a smaller number of fraction. We evaluated the efficacy of short fractionated schedules of 8 Gy as a single dose and 8 Gy in 2 weekly fractions.

Methods: Between May 2007 and April 2017, 1162 patiens with diagnosis of multiple bone metastases were treated with hypofractionated external beam radiotherapy. Male/female ratio was 697/465, median age 57 years (range, 32-81) and median KPS 80% (range, 50-90%). The primary tumors were in the prostate (569, 49%), breast (477, 41%), lung (58, 5%), rectal (23, 2%), and other sites (35, 3%). The choice of 8 Gy or 8 Gy in 2 weekly fractions was based on the number of metastases, site and performance status.

Results: All patients completed the established treatment. There was no significant difference in complete response rates between treatment schedules. Complete pain relief was achieved in 162/523 patients (31%) in the fractionated group and in 185/639 patients (29%) in the single dose group. Also the partial respon-

se was similar: 335/523 patients (64%) in fractionated group and 396/639 (62%) in single dose group. The median duration of pain relief was similar: 5 months in fractionated group and 4.5 months in single dose group. No particular side effects were recorded in either group.

Conclusions: In our experience hypofractionated radiotherapy (8 Gy in a single dose or 16 Gy in 2 fractions) is effective in the pallation of symptomatic bone metastases with no severe side effects

C015

VMAT RADIOSURGERY BOOST AFTER EXTERNAL RADIOTHERAPY IN OLIGOMETASTATIC PATIENTS WITH VERTEBRAL METASTASES: PRELIMINARY EVALUATION OF A FEASIBILITY TRIAL

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Aims: To report early clinical experience about volumetric intensity modulated arc radiosurgery boost (VMAT-RCH) after 3D-conformal radiotherapy (3D-CRT) in patients with vertebral metastases.

Methods: Patients with vertebral metastases alone or plus < 5 visceral metastases were included in a phase I study and sequentially assigned to a established dose level of VMAT-RCH (8, 10 or 12 Gy) following 25 Gy in 10 fractions delivered to adjacent vertebrae. Herein, we report preliminary results in terms of acute toxicity (CTCAE 4.03 scale), tumour response and early local control.

Results: 27 lesions accounting for 24 consecutive patients (M/F: 17/7; median age: 71; range 40-85) were treated from April 2011 to April 2017. The majority of patients had a primary prostate (16) or breast cancer (6). Planning Target Volume was defined as the vertebral lesion + 3 mm isotropic margin. 17 patients received 8 Gy VMAT-RCH boost (total BED10: 45.7 Gy) and 7 patients received 10 Gy (total BED10: 51.3 Gy). With a median follow-up of 18 months (range 1-42), 6 (22%) patients had grade 1acute toxicity (skin erythema: N=3, esophagitis: N=2 and nausea: N=1). Overall response rate based on CT/PET-CT was 74.1% (CI 0.95: 49.3%-89.6%) with a complete response rate of 66.7% (CI 0.95: 41.9%-84.4%). One year-actuarial local control (defined as irradiated site progression-free) was 89%.

Conclusions: A VMAT-RCH boost on vertebral lesion delivered after a 25 Gy 3D-CRT to adjacent vertebrae resulted to be feasible with encouraging tumour response, local control rate and acute toxicity profile. The maximum tolerable dose has not yet been reached and the study is actually on going.

C016

PERSONALIZED RADIOTHERAPY FOR OLIGO-METASTATIC/OLIGO-RECURRENT PROSTATE CANCER: PRELIMINARY EXPERIENCE

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Aims: Recent technology advances in diagnostic field, by multiparametric MRI or choline/PSMA-CT-PET, have allowed to early detect oligo-metastasis oligo-recurrences from prostate cancer, so as to perform more and more an early and personalized treatment. The aim of this work is to report a preliminary analysis of our experience about radiotherapy in oligo-metastatic/oligo-recurrent patients.

Methods: Between October 2010 and December 2016 we treated 44 oligo-metastatic/oligo-recurrent prostate patients, by IMRT-SIB-IGRT technique, for a total of 72 metastatic lesions (37 patients were metastatic only on lymph nodes, 7 in both nodes and bone). The mean age was 65 years (range 47-81). CT scan was performed in 6 cases; bone scan in 5 cases; multiparameter MRI in 4 cases; finally, all patients received also choline-CT-PET. The site number of nodal metastasis ranged between 1 and 7 (mean 2.5). Eleven patients were hormonal naïve and recurred after primary therapy (surgery, radiotherapy, HIFU), the remaining had already been submitted to hormone therapy and were castration resistant. Four patients received also second line hormone therapy with Abiraterone acetate, 2 patients chemotherapy with Taxanes; 2 patients received a previous surgery on lymph nodes, without success. Our treatment philosophy involves the irradiation of lymph node chains close to the relapsed nodes with prophylactic doses (ranging between 51-54 Gy) and the choline CT-PET-positive nodes with higher doses (ranging between 66 to 70,5 Gy); moreover, we treat bone metastasis with doses ranging between 45-54 Gy. Thirty-two patients received hormone therapy during radiotherapy course with analogous-LH-RH.

Results: With a mean follow up of 41 months (range 12-72 months) we observed a loco regional control of 81% (36 pts). Median time to progression was 18 months (6-34 months). At last follow-up 2 patients were dead, 8 have disease progression (3 bone, 4 nodal, 1 in lung). The treatment was well tolerated, no patient experienced acute or late RTOG toxicity ≥ G2 (15 pts G1 gastrointestinal, 13 G1 hematological and 3 G1 genitourinary acute toxicity).

Conclusions: In our experience, high-precision

radiotherapy, in a multidisciplinary context, can be used to manage oligo-metastatic/oligo-recurrent disease in order to obtain local control and a delay in systemic therapy, with a low profile of acute and late toxicity.

C017

TRANSPERINEAL APPROACH FOR FIDUCIAL MARKERS IMPLANTATION IN PROSTATE IMAGE-GUIDED RADIOTHERAPY: SINGLE CENTER DATA ON THE FIRST 92 PATIENTS

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Aims: In the external beam prostate cancer radiation therapy, daily gland displacement could lead to a target missing. Prostate pelvic motion up to 2 cm are reported, so that the use of intra-prostatic gold fiducial markers for daily prostate position verification and correction before treatment delivery (image-guided radiotherapy, IGRT) is widely used in the radiation therapy centers. The most commonly used implantation procedure involves transrectal ultrasound-guided insertion of fiducial markers, with not negligible complications. We report our experience in prostate fiducial markers implantation through a transperineal approach.

Methods: Between September 2011 and May 2017 at our center 92 patients underwent gold seed fiducial marker implantation for prostate IGRT by a Radiation Oncologist with expertise in prostate brachytherapy. The procedure was done using transrectal ultrasound guidance; local anesthesia was performed by subcutaneous and transperineal peri-prostatic Mepivacaine injection. Three gold markers of 1,2 x 3 mm or 1 x 5 mm were inserted into the prostate gland through the perineum in a sterile field. No antibiotic prophylaxis was used. Patients were instructed to contact the treating radiation oncologist if there were complications.

Results: All procedures were uncomplicated. In one patient a single episode of self-limiting urinary bleeding occurred just after. No other complication was recorded. No rectal bleeding, no urinary obstruction or infection, no episode of hematospermia occurred.

Conclusions: The insertion of intra-prostatic markers for IGRT is commonly done through the rectum; despite antibiotic prophylaxis, a rate of urinary infection of 7.7% with a total of 2.8% of patients requiring hospital admission for infective complication is reported. Rates of 3.8-15% of hematuria, 18.5% of hematospermia, 4-9.1% of rectal bleeding are reported. In our series only one patient (1%) showed a single episode of self-limiting hematuria. No worsening of baseline urinary obstruction symptoms was reported by the patients. According to our experience, prostate fiducial markers implantation through a transperineal approach is safe and should be recommended.

C018

CAN PROSTATE IGRT PROTOCOL WITH INTRA-PROSTATIC GOLD MARKERS BRING CTV – PTV MARGIN TO ZERO?

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Aims: The aim of this study was to investigate if a CTV-PTV margin is needed after prostate organ motion correction using CBCT marker match. For the same purpose the stability of fiducials markers (FM) within the gland, during radiotherapy was also assessed.

Materials and Methods: 62 prostate cancer patients were studied. 3 markers were implanted at the base (A), middle (B) and apex (C) of the gland. All patients underwent a 1-mm CT (CT sim) within 10 days; a prostate CTV (CTVP) was delineated. A daily CBCT was used to correct prostate organ motion (OM) by checking markers position. 5 CBCTs per patient were used to evaluate CTV P position residual error after marker match; the daily CTVs P 1-5 were delineated on CBCTs1-5; an ITV (re PTV) was created. The maximum distance CTV P – re PTV, for each directions, cranial, caudal, anterior, posterior, left and right, was assessed for each patient. The median value of the measured distances was reported. Retrospectively CT sim and CBCTs acquired at 1^, 10^, 20^ , 30^ and 39^ fraction were used to record FM coordinates (x,y,z) in 55 out 62 patients. The distances between markers (FMD) as AB, BC, CA were measured in mm as:

$$X1X2=\sqrt{(X1-X2)2 + (Y1-Y2)2+(Z1-Z2)2}$$

FMDs variations before and during the full course of radiotherapy were then calculated as the differences between CBCTs and CTs data.

Results: 310 CBCTs, were used to define re PTVs and 2418 CBCTs to check their adequacy. The median value of residual error resulted 1 mm cranial, 1 mm caudal, 3.5 mm anterior, 3 mm posterior, 2 mm left and 2.5 mm right. 990 FDMs (mm) were recorded . The average absolute variation of all FMDs was 1,20±0,67 mm. 94% of recorded variations were 3 mm or less , while 80% were 2 mm or less. A simultaneous progressive reduction of FMDs (negative values in mm) was seen in 77% of patients and it was related to the shrinking of the prostate volume during the treatment.

Conclusions: A 5mm CTV P - PTV margin is needed despite IGRT. The cause could be found in the residual error, due to multiple factors (prostate deformation and tilt , gold markers size, contouring as well as IGRT system uncertainties). In addition, small variations in the relative position of the markers (1,20 ± 0,67 mm) were recorded even if they could be related to the uncertainties of our IGRT System or marker length (= 3 mm) rather than to the markers migration.

C019

PRELIMINARY EXPERIENCE WITH SYMMETRY ELEKTA X-RAY SOFTWARE FOR 4D-CBCT ACQUISITION IN THORACIC STEREOTACTIC RADIOTHERAPY

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Aims: To evaluate set up and organ motion errors in patients treated with stereotactic radiotherapy for lung cancer or mediastinal lymphadenopathy, using 4D-Cone Beam CT (CBCT) (Symmetry Elekta X-Ray volume imaging system).

Methods: From September 2016 to April 2017, 6 patients were selected to receive stereotactic radiotherapy to thoracic lesions. Patients characteristics were the following: mean age 75 years (range 68-85); M/F: 6/0; pulmonary nodules: 4 (66.7%), mediastinal lymphadenopathy: 2 (33.3%). Patients underwent a simulation computed tomography (CT) without contrast, with 3 mm slice thickness and acquired from humeral heads to include the 12th rib. A 4 fixation points thoracic thermoplastic mask was used with manual abdominal compression. CT images were exported to the TPS Oncentra External Beam v.4.5 (Elekta, Crawley) to contour pulmonary lesions as a Gross Tumor Volume (GTV). A preliminary isocenter at the center of the GTV was defined to allow the 4D-CBCT acquisition on Elekta Agility Linear Accelerator. The patients underwent 4D-CBCT with Symmetry software that sorted in 10 breath phases. Subsequently, GTVs were delineated on all phases of 4D-CBCT to define Internal Target Volume (ITV). ITVs were expanded of 5 mm. Definitive VMAT treatment planning were created. According to constraints, 3 patients received 50 Gy (10 Gy/fraction) and 3 patients received 35 Gy (7 Gy/fraction). A total of 30 4D-CBCT on treatment were acquired. Translations were measured in medio-lateral (x), supero-inferior (y) and antero-posterior (z) directions, as well as in rotation around axes. Translational displacements ≥ 2 mm were corrected on-line. Cut-off rotation should be ≤ 3°; if rotation was > 3°, the patients were repositioned. Mean (M) and standard deviation (SD) of the 4D-CBCT displacements were calculated.

Results: The mean setup error was 0.05 ± 0.21 mm in lateral direction, 0.06 ± 0.30 mm in longitudinal direction, and 0.13 ± 0.26 mm in vertical direction. Mean values distribution of translation displacements for each patient were reported in Figure 1.

Conclusions: From our preliminary experience, acquisition of 4D-CBCT with Symmetry Elekta X-Ray software, seems to be a useful method for planning and delivery of thoracic stereotactic radiotherapy. It is certainly necessary increase the number of patient to confirm these data and a longer follow-up to evaluate late response of treatment.

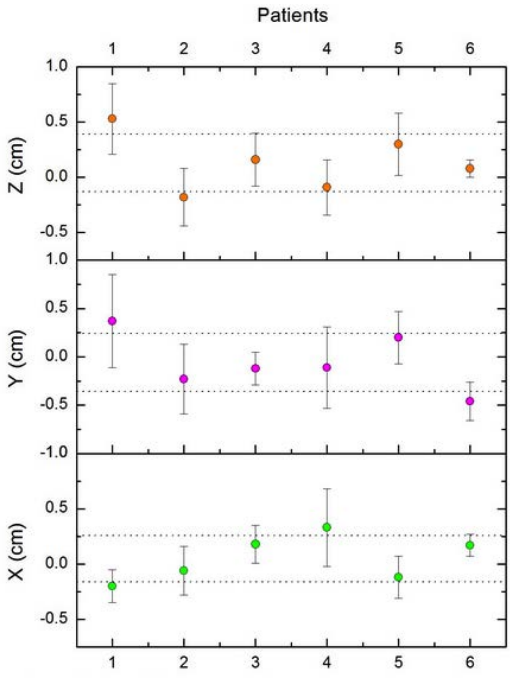

Figure 1. Mean values distribution of translation displacements for each patient.

C020

IMPACT OF IGRT ON PATIENTS POSITIONING WITH PROSTATE CANCER AND DECREASE OF RECTAL TOXICITY: EXPERIENCE OF OUR CENTER

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Aims: The purpose of this study is to evaluate the impact of image-guided radiotherapy (IGRT) on the quality of radiotherapy treatments in prostate cancer patients in terms of rectal toxicity and the potential benefit of daily verification in reducing adverse effects.

Methods: In our center, from January to May 2017, 32 patients with prostate cancer were treated; all patients were planned with volumetric-modulated arc therapy (VMAT) technique. 14 patients received hypofractionated radiotherapy for a total dose of 67.5 Gy in 25 fractions to prostate with or without seminal vesicles and 18 patients received conventionally fractionated radiotherapy for a total dose of 70-80 Gy in 35-40 fractions to prostate surgical bed or prostate with or without seminal vesicles. Daily IGRT using cone-beam computed tomography (CBCT) was performed for all patients. Weekly clinical visits were made to all patients; rectal toxicity was evaluated according to CTCAE scales, version 4.02 and compared with 32 patient's rectal toxicity.

These latter patients represented a group with similar characteristics that are part of patients treated in our center from January 2013 to July 2014 with intensity-modulated static fields technique, without daily IGRT (only two weekly MV-paired images).

Results: No rectal toxicity was observed in 78% of patients treated with daily IGRT and in 47% of patients treated without daily IGRT, whereas Grade 1 (G1) rectal toxicity was recorded in 22% and in 49% of patients, respectively. No patients treated with IGRT showed G2 rectal toxicity while it was found in 4% of patients treated without IGRT.

Conclusions: Daily IGRT allows real-time verification and correction of set-up and organ-motion errors and greatly improves treatment quality by reducing rectal toxicity. We need more cases to confirm the preliminary results of this study.

C021

CONE-BEAM CT-BASED INTER-FRACTION LOCALIZATION ERRORS FOR TUMORS IN THE PELVIC REGION

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Aims: To evaluate inter-fraction tumor localization errors (TE) in the volumetric modulated arc therapy (VMAT) treatment of a large series of patients with pelvic cancers based on a kilovoltage cone-beam computed tomography (CBCT). Appropriate clinical target volume (CTV) to planning target volume (PTV) margins in non image-guided radiotherapy (IGRT) scenario have been proposed.

Methods: A total of 13,224 CBCTs of 928 patients with prostate, gynecological, and rectum/anal canal cancers were retrospectively analyzed to determine the mean systematic error (mean of the means of each patient), systematic error (SD of the means of each patient) and random error (root mean squared sum of SDs of each patient). Two IGRT protocols were used: daily online IGRT and weekly IGRT, consisting in acquiring a CBCT at the first 3 fractions, correcting for the systematic errors, and subsequently once a week. The first was applied to hypofractionated treatments and reirratiations, while the second to conventional fractionation treatment. The difference between TE evaluated after 3 fractions and those determined using all CBCTs was assessed.

Results: The systematic (and random TE) in the antero-posterior (AP), latero-lateral (LL), and supero-inferior (SI) directions were: for prostate bed, 2.7(3.2), 2.3(2.8) and 1.9(2.2) mm; for prostate, 4.2(3.1), 2.9(2.8) and 2.3(2.2) mm; for gynecological, 3.0(3.6), 2.4(2.7) and 2.3(2.5) mm; for rectum, 2.8(2.8), 2.4(2.8) and 2.3(2.5) mm; for anal canal, 3.1(3.3), 2.1(2.5) and 2.2(2.7) mm. The CTV-to-PTV margins considering all CBCTs were similar for all groups of patients: 10 mm in AP, 7.5-9.5 mm in LL and 8-9 mm in SI directions. When considering the first 3 CBCTs, the CTV-to-PTV margins were larger: 12-14 mm in AP, 7-10.5 mm in LL and 9-10.5 mm in SI directions. The systematic and random tumor localization errors for the total and first 3 CBCTs are shown in the table. The largest difference (4.2 mm) was observed in the AP direction for the prostate.

Conclusions: Without IGRT, large CTV-to-PTV margins up to 14 mm are required to account for inter-fraction tumor localization errors. Although we believe that a daily on-line IGRT could be beneficial for all patients treated with VMAT, a compromise between increased accuracy and workload in a busy department should be accepted. Daily IGRT should be proposed to all hypo-fractionated treatments that require smaller margins to avoid increased toxicity to the critical organs.

Table. Systematic and random tumor localization errors for the total and first 3 CBCTs.

Tumor site/ n° of patients	n° of CBCT	Tumor localization error (mm)														
		AP			LL			SI			3D			Yaw (°)		
		M	Σ	σ	M	Σ	σ	M	Σ	σ	M	Σ	σ	M	Σ	σ
Prostate bed (334)	All (mean= 12.1)	0.6	2.7	3.2	0.5	2.3	2.8	0.3	1.9	2.2	5.0	1.5	2.9	-0.1	0.3	0.4
	first 3	0.6	4.4	2.3	0.6	3.4	2.2	0.5	2.8	1.9	5.7	2.9	2.4	0.0	0.4	0.3
	Diff	0.0	-1.7	0.9	-0.1	-1.1	0.6	-0.2	-0.9	0.3	-0.7	-1.3	0.5	0.0	-0.1	0.1
Prostate (190)	All (mean= 22.1)	1.7	4.2	3.1	0.5	2.9	2.8	0.7	2.3	2.2	6.2	2.4	3.0	-0.1	0.3	0.4
	first 3	1.7	4.7	2.5	0.4	3.2	2.4	0.7	2.6	1.7	6.1	3.0	2.5	-0.1	0.4	0.3
	Diff	0.0	-0.5	0.7	0.1	-0.4	0.4	0.0	-0.4	0.5	0.1	-0.6	0.5	0.0	-0.1	0.0
Gynecological (231)	All (mean = 13.7)	-1.0	3.0	3.6	0.6	2.4	2.7	-0.4	2.3	2.5	5.4	2.3	2.9	0.0	0.4	0.5
	first 3	-1.6	4.4	2.6	1.0	3.5	2.1	-0.5	3.2	2.0	6.0	3.4	2.4	0.0	0.5	0.4
	Diff	0.6	-1.4	1.0	-0.3	-1.1	0.7	0.1	-0.9	0.4	-0.6	-1.1	0.5	0.0	-0.1	0.1
Rectum (139)	All (mean=9.9)	0.7	2.8	2.8	0.0	2.4	2.8	-0.2	2.3	2.5	5.0	1.9	2.9	-0.1	0.4	0.4
	first 3	1.4	4.4	2.1	-0.1	3.7	2.1	0.2	3.2	2.0	5.9	3.2	2.5	-0.1	0.5	0.4
	Diff	-0.6	-1.7	0.7	0.1	-1.3	0.6	-0.4	-0.9	0.4	-0.9	-1.4	0.5	0.0	-0.1	0.0
Anal canal (34)	All (mean=13.1)	0.7	3.1	3.3	0.2	2.1	2.5	0.7	2.2	2.7	5.4	1.6	2.8	0.0	0.3	0.4
	first 3	1.1	4.0	2.3	0.3	2.1	1.6	0.9	3.3	1.8	5.1	2.5	2.0	0.1	0.5	0.3
	Diff	-0.5	-0.9	1.0	-0.1	0.0	0.8	-0.2	-1.1	0.8	0.3	-0.9	0.8	-0.1	-0.2	0.1

Abbreviations: M = mean systematic error (mean of the means); Σ = systematic error (SD of the means); σ = random error (root mean square of the SDs); AP = antero-posterior; LL = latero-lateral; SI= supero-inferior.

C022

AN ADAPTIVE STRATEGY FOR EXTERNAL BEAM RADIOTHERAPY IN PROSTATE CANCER AND MANAGEMENT OF THE GEOMETRICAL UNCERTAINTIES WITH ROBUST OPTIMIZATION

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Aims: To develop a new adaptive treatment method for

prostate cancer (PCa) radiotherapy (RT), using an off-line strategy to design a patient-specific ITV based on the study of organ motion obtained by serial Cone-Beam CT (CBCT) images and management of the geometrical uncertainties with min-max robust optimization.

Methods: 20 patients (pts) with intermediate-high PCa treated with radical RT were enrolled in this study. The prescribed dose was 78 Gy to prostate (CTV1) and 60 Gy to prostate plus seminal vesicles (CTV2) delivering 2 Gy/fraction (fr). The CBCTs were acquired according to our IGRT protocol during the first 5 frs, then once a week for the remaining of the treatment. The CBCTs were imported in the Raystation treatment planning system (TPS) and co-registered with the planning CT using the on-line match rigid transformations provided by the OBI system on the treatment unit (Varian Trilogy TX). Then the deformable image registration (DIR) algorithm ANACONDA was applied to propagate the CTV1 and CTV2 volumes from the reference planning CT to the first 5 CBCTs. The reliability of the DIR mapped ROIs was assessed by a radiation oncologist and the contours were used to generate the ITV used to adapt the plan. The original plan was re-optimized using a min-max robust algorithm based on the worst scenario optimization assuming an isotropic 5 mm maximum setup error. Then CTV coverage and OAR sparing achieved with the robust plan (RP) were analyzed and compared with the original standard plan (SP) calculating the dose distributions on the residual CBCTs.

Results: Based on 10 pts preliminary data analysis, our adaptive strategy and RP showed to achieve optimal coverage of CTV also in the worst scenario (geometric error up to 5 mm) with D99>95% of prescribed dose and significant less dose to rectum and bladder. The analysis on all the residual CBCT acquired during the treatment showed that CTV coverage of RP was optimal and not significantly different from SP. Statistically (Wilcoxon test), significant dose reduction was noted for rectum ($p<0.001$) and for empty bladder ($p<0.01$). Moreover, RP appeared to be less sensitive to bladder and rectal filling and to decrease the integral dose.

Conclusions: Robust optimization is a feasible and safe approach in prostate treatment. It may be successfully used to adapt the treatment with better target coverage and OAR sparing than standard PTV based planning during the treatment course.

C023

DAILY WORKLOAD OF BREAST IMAGE-GUIDED RADIOTHERAPY DELIVERED WITH TOMOTHERAPY

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Aims: To analyze treatment times of the Tomotherapy system (Accuray Incorporated, Sunnyvale, CA) used in Direct and Helical modality for the adjuvant treatment of breast cancer patients (pts).

Methods: From May 2017, we are closely monitoring the timing of radiotherapy (RT) procedures of breast cancer pts treated with daily image-guided Tomotherapy. Two treatment protocols are examined: whole breast (WB) irradiation with simultaneous integrated boost (SIB) to the tumour bed (TB) incorporated into a hypofractionated regimen delivered in Direct modality (40.05 Gy and 48 Gy are delivered to WB and TB in 15 fr (2.67/fr and 3.2Gy/fr) or 45 Gy and 50 Gy are delivered to the WB and TB in 29 fr (2.25 Gy/fr and 2.5Gy/fr)) and locoregional irradiation delivered in Helical modality (40.05 Gy are delivered to the chest wall and regional nodes in 15 fr (2.67/fr)). The overall treatment time (door to door: from the patient entrance in the treatment room to the exit) was separately analyzed in terms of (i) patient setup time (from treatment room entrance to the start of megavoltage computed tomography (MVCT) imaging), (ii) MVCT acquisition time, (iii) image registration evaluation time, (iv) treatment delivery time and (v) patient exit time (from the end of the treatment to the exit from treatment room).

Table 1. Treatment parameters and times recorded for 21 patients: 14 patients were treated with SIB protocol in Direct modality and 7 patients had chest wall and regional nodes irradiated in Helical modality. Important treatment parameters affecting treatment time are enlisted and include principally Field width, pitch and modulation factor. The field width is defined as the axial thickness of the fan beam; treatment pitch defines the amount of gantry rotations per unit length of couch translation; modulation factor is defined as the maximum leaf opening time divided by the average (non-zero) leaf opening time and it is an estimate of plan complexity. All statistics are shown as median (range).

		SIB irradiation (Direct modality)	Locoregional irradiation (Helical modality)
Treatment Parameters			
Planning	Field width [cm]	2.5	2.5
	Pitch	0.25	0.43 (6 pts) 0.287 (1 pts)
	Modulation Factor	1.905 (1.67-2.027)	1.632 (1.545-1.861)
	N° fields	3 (2 pts) 4 (12 pts)	-
	Planned field width [cm]	-	11.6 (10.2-11.9)
	Gantry rotations	-	24.9 (21.3-37.1)
	Gantry period [sec]	-	33.6 (17-37.7)
	Couch travel [cm]	-	26.7 (23-27.5)
MVCT	N° acquired slices	10 (6-32)	29 (21-48)
	Acquisition modality	Coarse	Coarse
Treatment Times			
	Overall treatment time [min]	14.0 (11.2-20.2)	23.2 (6.3-40.5)
	Setup time [min]	1.9 (1.3-4.5)	2.2 (1.3-4.2)
	MVCT acquisition time [min]	1.4 (1.0-3.7)	3.0 (2.3-5.6)
	Registration evaluation time [min]	1.5 (0.4-3.2)	1.7 (1.0-14.9)
	Treatment delivery time [min]	8.1 (5.1-9.9)	15 (8.3-18.0)
	Patient exit time [min]	1.2 (0.7-3.1)	1.3 (0.9-2.6)

Results: The study includes data of 21 pts treated in May 2017 at the European Institute of Oncology (Milan, Italy): 14 pts were treated in Direct modality (11 pts with 15 fr and 3 pts with 20 fr) and 7 locoregional RT pts were treated in Helical modality. Analysis was performed on 134 fr (88 and 46 fr for Direct and Helical pts, respectively). SIB plans consists of 2 fields

directed to the WB and 1 or 2 fields directed to the TB. Median expected time necessary to treat WB and TB were 3.2 min (1.9-4.5) and 0.4 min (0.2-0.7) respectively. During the 1st treatment fr, MVCT were performed for the whole planning target volume (PTV) (N° of MVCT slices acquired in 1st fraction were 27 (21-32) and 45 (24-48) for Direct and Helical respectively) in the following fr a portion of PTV is imaged

Comprehensive data of treatment parameters and times collected are in Table 1.

Conclusions: Important treatment parameters affect treatment time and a comprehensive analysis of timing procedure could improve the efficiency of breast image-guided Tomotherapy. Moreover, the effect of the RT time might have significant impact on the organ motion and should be a subject of a separate analysis.

C024

IN- ROOM CT-ON-RAILS FOR ADAPTIVE PROTONTHERAPY: WORKFLOW EXPERIENCE OF THE TRENTO PROTON THERAPY CENTER

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Aims: A 64-slice CT-on-rails (CTR) fully integrated into the proton therapy (PT) system/gantry room has been recently installed at the Trento Proton Therapy Center. It makes possible to incorporate plan verification into the process, using high quality imaging to evaluate the dose distribution based on regular images to assess whether the treatment planning is still valid with regard to anatomical changes within the patient that are critical for PT and adjust the planning if necessary. Our aim is to propose an adaptive PT workflow using CTR.

Methods: The workflow was tested retrospectively for 20 consecutive patients (pts). The patient cohort included a variety of tumor sizes, locations, histologies, total doses and fractionation shedules. Site of tumors was base of skull (3 pts), head and neck (10 pts), spine (3 pts), chest wall (1 pt), pelvis-proximal leg (1 pt), rectum (1 pt), retroperitoneum (1 pt).

Results: All pts underwent active beam scanning PT using 2-3 fields with single field optimization (SFO) technique. Median total dose was 66 GyRBE (range 50.4-78) in a median fractionation schedule of 35 sessions. Treatment was composed by one volume in 9 pts, two volumes in 6 pts and three volumes in 5 pts, in six cases simultaneous integrated boost technique was used. Eighty-six CTR images were performed with a median of three CTR (range 2-8) during the treatment course. The CT-on-rail scan was first rigidly aligned to the planning CT (pCT) by the physician. The Ray Station ANACONDA algorithm for hybrid deformable image registration (DIR) was subsequently applied to register the pCT scan to the CTR scan, afterwards physicians verified and corrected the mapped contours on the new CTR. Finally physicists performed dosimetric recalculation of the plan. Acquisition of the new CT, validation of the contours and plan recalculation requested about 1-2 hours of work. Two of the 20 pts needed replanning, in both cases for weight loss that determined a worsening in the coverage of the target. The re-optimization process took an average of one hour but moreover specific Quality Assurance procedures were necessary.

Conclusions: Adapting PT still needs to be performed offline. Research is working towards the ultimate goal: integrating quick indicators of target and dose precision that would allow online reassessment and adaptation before every fraction to obtain an optimal result. The use of in room CT-on-rails could be useful for this purpose.

C025

RADIATION THERAPY OF LOCALLY ADVANCED CERVICAL CANCER: INTEGRATIVE ANALYSIS OF RADIOMICS AND EMATOCHEMICAL PARAMETERS

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Aims: The present study was designed to evaluate MRI texture analysis (TA) and clinical and blood tests in predicting the outcome of patients with locally-advanced cervical cancer undergoing radical treatment.

Methods: We performed a retrospective analysis on forty-two patients with locally advanced cervical cancer (T2b-T4, N0-N1) undergone definitive radiotherapy, between January 2008 and December 2015. The gross tumor volume (GTV) was evaluated at baseline by MRI and contoured on T2 sequences, and multiple derivative parameters evaluated by means of a LifeX Software. We collected clinical informations (age, sex, weight, BMI, use of induction chemotherapy) and blood tests (neutrophil, lymphocytes and platelet counts, hemoglobin, neutrophil to lymphocytes ratio:NLR). By performing univariate analysis and a multivariate analysis (logistic regression), the TA parameters were then correlated with patients' outcome.

Results: A total of 42 patients were included in the analysis (mean age 59 years, mean 63 years, range 32-76 years). Twenty patients (47.6%) developed recurrence (loco-regional or distant), whereas 8 patients (19%) died. Parameters significantly correlated with recurrence included diabetes (p:0.024), platelet count (p:0.022), hemoglobin (p:0.034), T2-GLCM Homogeneity (p:0.012, see Table for description of TA parameters), T2-SRE (p:0.010), T2-RP (p:0.034), whereas parameters that resulted significantly correlated with overall survival included diabetes (p:0.049), T2-HGZE (p:0.036). AUC for recurrence was 0.834 (95% CI 0.689-0.934), whereas AUC for overall survival was

0.725 (95% CI 0.578-0.834).

Conclusions: Our results suggest that TA, toghether with blood tests and clinical parameters have a significant predictive and prognostic value and may lead to the selection of patients that may benefit from different approaches (such as adjuvant chemotherapy, early surgery after CHT-RT or intensive follow up).

Table 1. Texture analysis parameters calculated with Lifex Software, and corresponding description.

Type of TA Feature	TA Feature Name	Description
Co-occurrence Matrix (GLCM): takes into account the arrangements of pairs of voxels to extract textural indices.	Homogeneity	Homogeneity of gray-level voxel pairs
	Energy	Uniformity of gray-level voxel pairs.
	Correlation	Linear dependency of gray-levels in GLCM.
	Contrast	Local variations in the GLCM.
	Entropy	Randomness of gray-level voxel pairs.
	Dissimilarity	Variation of gray-level voxel pairs.
Gray-Level Run Length Matrix (GLRLM): gives the size of homogenous runs for each gray-level.	SRE (short-run emphasis)	Distribution of the short homogeneous runs in an image.
	LRE (long-run emphasis)	Distribution of the long homogeneous runs in an image.
	LGRE (low gray-level run emphasis)	Distribution of the low gray-level runs.
	HGRE (high gray-level run emphasis)	Distribution of the high gray-level runs.
	SRLGE (short-run low gray-level emphasis)	Distribution of the short homogenous runs with low gray-levels.
	SRHGE (short-run high gray-level emphasis)	Distribution of the short homogenous runs with high gray-levels.
	LRLGE (long-run low gray-level Emphasis)	Distribution of the long homogeneous runs with low gray-levels
	LRHGE (long-run high gray-level emphasis)	Distribution of the long homogeneous runs with high gray-levels
	GLNUr (gray-level non-uniformity for run)	Non-uniformity of the gray-levels of the homogeneous runs.
	RLNU (run-length non-uniformity)	Length of the homogeneous runs
	RP (run percentage)	Homogeneity of the homogeneous runs
Neighbourhood Gray-Level Different Matrix (NGLDM): corresponds to the difference of gray-level between one voxel and its 26 neighbourhoods in 3 dimensions.	Coarseness	Level of spatial rate of change in intensity.
	Contrast	Intensity difference between neighbouring regions.
	Busyness	Spatial frequency of changes in intensity.
Gray-Level Zone Length Matrix (GLZLM): provides information on the size of homogenous zones for each gray-level in 3 dimensions.	SZE (short-zone emphasis)	Distribution of the short homogeneous zones in an image.
	LZE (long-zone emphasis)	Distribution of the long homogeneous zones in an image.
	LGZE (low gray-level zone emphasis)	Distribution of the low gray-level zones.
	HGZE (high gray-level zone emphasis)	Distribution of the high gray-level zones.
	SZLGE (short-zone low gray-level emphasis)	Distribution of the short homogenous zones with low gray-levels
	SZHGE (short-zone high gray-level emphasis)	Distribution of the short homogenous zones with high gray-levels
	LZLGE (long-zone low gray-level emphasis)	Distribution of the long homogeneous zones with low gray-levels
	LZHGE (long-zone high gray-level emphasis)	Distribution of the long homogeneous zones with high gray-levels
	GLNUz (gray-level non-uniformity for zone)	Non-uniformity of the gray-levels of the homogeneous zones
	RLNU (zone length non-uniformity)	Length of the homogeneous runs
	ZP (zone percentage)	Homogeneity of the homogeneous zones
Indices from Sphericity	Sphericity	Measures how spherical a Volume of Interest is.
	Compacity	Measures the degree to which the Volume of Interest is compact
Indices from Histogram: provides informations derived from global histogram analysis	Skewness	measures the asymmetry of the gray-level distribution in the histogram.
	Kurtosis	measures whether the gray-level distribution is peaked or flat relative to a normal distribution.
	Entropy	mesures the randomness of the distribution
	Energy	measures the uniformity of the distribution

C026

THE PROGNOSTIC IMPACT OF FDG PET-CT (EARLY -PET) IN LOCALLY ADVANCED CERVICAL CARCINOMA PATIENTS (LACC): PRELIMINARY RESULTS

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Aims: To evaluate in patients with LACC the prognostic impact of FDG PET-CT (early -PET) after exclusive chemoradiotherapy and before intra-uterine brachitherapy

Methods: This study includes 17 patients (range 32-82 years) treated in our centre between 2013 and 2016 with LACC with concomitant chemo-radiotherapy and subsequent brachytherapy. FIGO STAGE: 1/17 was IB1, 10/17 was IIB, 2/17 was IIIB, 1/17 was IIA, 1/17 was IIIA and 2/17 was IVA. 5/17 patients presented regional lymph nodes involvement and one patient had also positive lombo-aortic lymph nodes. Two patients did also a neoadjuvant chemotherapy, while 14/17 underwent radiotherapy and concomitant weekly chemotherapy with Cisplatin 40mg/mq2. 12/17 patients were treated with IMRT tecnique, and 8 of them received IMRT-SIB (2.2 Gy x 28 fractions on GTV-cervix and GTV-LNs PET-positive, 1.8 Gy x 28 fraction on pelvis ± LN lombo-aortics). The total brachitherapy dose was 21 or 28 Gy in 3-4 fractions of 7 Gy for fraction with the aim to achive a total dose (EBRT plus BT) in the range of 85-90 Gy. (4 pz 28 Gy, 1 pz 25 Gy, 12 pz 21 Gy). All patients performed PET-CT with FDG after chemo-radiotherapy and before brachytherapy (early-PET). Images were rated as positive with a SUV greater than 3.

Results: At the end of chemo-radiotherapy and before brachitherapy all patients performed early-PET: 12/17 were negative and 5/17 resulted positive. Two/12 (16%) patients with negative early-PET showed a relapse: 1 pelvic nodal relapse after 15 months and 1 cervical, annexial and nodal relapse after 5 months from the end of brachytherapy. Two/5 patients (40%) with positive early PET-TC had progressive/relapse disease: 1 systemic (lung) progressive disease after 4 months and a nodal, cervical and bone relapse after 18 months from the end of brachytherapy

Conclusions: Our preliminary evaluation showed that early-PET before brachytherapy could have a predictive value in assessing the risk of recurrence / progression in LACC patients. The patients with positive early-PET at the end of chemoradiotherapy may benefit from adjuvant systemic treatment after brachytherapy.

C027

EVALUATION OF DIFFUSION-WEIGHTED MAGNETIC RESONANCE IMAGING DURING BRACHYTHERAPY OF LOCALLY ADVANCED CERVICAL CANCER: PRELIMINARY RESULTS

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Aims: To investigate the change in ADC during BT of cervical cancer tumors and to evaluate its correlation with recurrence and survival rates.

Material and Methods: 17 consecutive patients with locally advanced cervical squamous cell carcinoma (16) and clear cell carcinoma (1) were retrospectively evaluated. All patients were treated,between May 2015 and October 2016, with a combination of Volumetric Modulated Arc Therapy (VMAT) delivered using 6-MV photon beams (with concurrent weekly 40 mg/m^2 CDDP) followed by high-dose rate BT (HDR BT). BT treatment planning was performed on MRI images using 7 Gy per fraction prescribed to high risk clinical target volume (HR-CTV) given in 4 fractions with 192Ir-High dose rate. MRI was acquired at 1.5 T and MRI protocol consisted of T2-weighted imaging (T2WI) obtained in 3 orthogonal planes and DWI. Diffusion-encoding gradients were applied at b values of 0, 50, 400 and 800 s/mm^2. A radiologist with more than 10 years of experience in pelvic MRI, manually outlined a ROI on T2WI and DWI image and the ADC maps of each section was automatically generated by the software.

Results: Preliminary results showed the median percent ADC change between first (BT1) and last BT (BT4) was 21.4% and the ADC change was lower in responder patients (median 0,092, DS 0,117) than in patients with progression or partial response (median 0,395, DS 0,204). Larger DWI volume at the time of BT1 seems to be related with local persistence of disease and a larger volume at the time of BT4 seems to be related with nodal progression.

Conclusions: DWI parameters, measured at each BT fractions, may be useful prognostic biomarkers for clinical outcomes in cervical cancer patients, but data need to be further investigated.

C028

INTENSITY MODULATED RADIATION THERAPY FOLLOWED BY PULSED-DOSE-RATE BRACHYTHERAPY BOOST IN THE CURATIVE TREATMENT OF UTERINE CERVICAL CANCER: UPDATED RESULTS OF THE EUROPEAN INSTITUTE OF ONCOLOGY EXPERIENCE

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Aims: The aim of the study was to evaluate local and distant control, disease progression, overall survival (OS) and toxicity profile for patients (pts) treated with Intensity Modulated Radiation Therapy (IMRT) followed by Pulsed-Dose-Rate Brachytherapy (PDR-BT) for uterine cervical carcinoma. Methods: Between 3/2012 and 2/2014, 43 pts (37 squamous cell carcinoma, 6 adenocarcinoma) were treated with PDR-BT boost after IMRT. Median age at diagnosis was 50.9 years (range 28.2-86.9). Patients in stage FIGO IA, IB, IIA, IIB, IIIA, IIIB and IVB were 2, 12, 2,14, 1, 11 and 1, respectively. Positive lymph nodes were found in 24 pts (55.8%). Concomitant platinum based chemotherapy +/- paclitaxel was administered in 39 pts (90.7%). Radiation treatment consisted of pelvic +/- lomboaortic tract IMRT using RapidArc® to a total dose of 45-50.4 Gy/25-28 fractions, 5fr/week. PDR-BT boost was delivered with a median CTV prescribed dose of 30 Gy (range 24-30 Gy) and after a median time of 15 days (range 1-92 days). The median dose-rate was 0.5 Gy/h (range 0.4-0.6 Gy/h), delivering 1 pulse/h, 24/24h by a cable-driven remote afterloaded Iridium-192 source. Acute and late toxicity were evaluated by Radiation Therapy Oncology Group (RTOG) scoring criteria and Subjective, Objective Management Analytic-Late Effects of Normal Tissues (SOMA-LENT) criteria, respectively. Results: Median follow-up was 37.3 mos (range 3-68). At the end of BT 4 pts (9.3%) referred a grade 1-2 genito-urinary (GU) symptoms. Acute toxicity (within 6 mos) was observed in 23 pts (53.4%) with a grade 1-2 in one or more of the following sites: skin, vagina, mucosae, GU or Gastrointestinal tract (GI). Grade 1-2 GI and GU late toxicity occurred in 9 pts (20.9%), while G3-4 in 9 pts (20.9%): 4 pts developed a G4 rectal complications requiring colostomy and 8 pts had a G3 vaginal stenosis. OS, disease free survival and local control at last follow-up were 90.7% (39/43), 74.4% (32/43), 86.0% (37/43), respectively. Distant metastases (mets) occurred in 20.9% (9/43), pelvic relapse in 13.9% (6/43), both pelvic and distant mets in 13.9%(6/43). Conclusions: Our study confirms that the combination of IMRT and PDR-BT can be considered a safe and effective treatment for cervical cancer. Despite high percentage of locally advanced disease pts, local control was very high (near 90%).Patterns of failure with metastatic dissemination claims for the optimization of the systemic approach.

C029

POTENTIAL ROLE OF STEREOTACTIC BODY RADIOTHERAPY USING VOLUMETRIC MODULATED ARC THERAPY AS AN ALTERNATIVE TO HDR BRACHYTHERAPY IN ENDOMETRIAL CANCER: A DOSIMETRIC ANALYSES

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Aims: To evaluate the role of stereotactic body radiotherapy (SBRT) using VMAT technique as an alternative to high-dose rate brachytherapy (HDR-BRT) in the treatment of vaginal cuff in postoperative endometrial cancer.

Methods: CT scans of 5 patients were used in this study. The CTV was defined as the 0.5 cm tissue around the applicator (then subtracting the applicator). Total dose was 30Gy delivered in 5 fractions. In HDR-BRT, dose was prescribed at a distance of 0.5 cm from the surface applicator. To take into account set-up uncertainties in external VMAT irradiation, a PTV was obtained from CTV by an expansion of 3 mm. Two VMAT plans were generated using a full arc rotation. The first plan was optimized with an anatomy-based optimization module (AB_VMAT) using a 1mm MLC beam margin to enhance dose heterogeneity and dose fallout. The second plan was generated with a full-inverse planning module (FI_VMAT). CTV and PTV coverage in terms of D99%, mean dose (Dmean) and D1% were used for plan comparison. Conformity indexes (CI100 and CI50), gradient index (GI) and homogeneity index

(HI) were calculated. For rectum and bladder, mean dose and doses to 2cc volume were used for evaluation. To account for various dose heterogeneity distributions we calculated the equivalent uniform dose (EUD) using the Niemerko model. The treatment time was also compared between the three techniques.

Results: VMAT plans provided targets coverage comparable with HDR. Dose distribution were more heterogeneous with HDR: Dmean were 144.2% for CTV in HDR and 118.0 and 109.1% for PTV in AB_VMAT and FI_VMAT, respectively. The mean values of EUD for CTV were: HDR 40.9 Gy; AB_VMAT 39.0 Gy; FI_VMAT 33.3 Gy. GI indexes were 2.81, 3.37 and 4.15 for HDR, AB_VMAT and FI_VMAT, respectively. Dmean and maximal doses to 2cc for rectum and bladder were lower in HDR-BRT plans compared to AB_VMAT and FI:VMAT (rectum Dmean: 39.8% vs 47.4% and 53.0%; bladder Dmean: 35.4% vs 40.4% and 46.1%,; rectum D2cc: 104.8% vs 108.0% and 116.2%; bladder D2cc: 86.64% vs 94.0% and 100.0%). The mean treatment time for AB_VMAT was approximately 2.5 min.

Conclusions: HDR-BRT provided superior dose distribution with respect to VMAT. AB_VMAT plans tend to better mimic the HDR dose distribution, providing a fast, safe and reasonable alternative. AB_VMAT plans showed a successful capability of highly conformal dose distribution, EUD values similar to HDR, steep dose-gradient outside PTV and minimal treatment time.

C030

INTENSITY MODULATED RADIATION THERAPY BOOST IN LOCALLY ADVANCED CERVICAL CANCER: IS IT A SAFE AND FEASIBLE ALTERNATIVE WHEN BRACHYTHERAPY IS NOT PRACTICABLE?

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Aims: Standard treatment in locally advanced cervical cancer is External Beam Radiotherapy (EBRT) concomitant to platinum based chemotherapy (CHT), followed by brachytherapy (BRT). We questioned whether an Intensity Modulated Radiation Therapy (IMRT) boost is safe and feasible in patients (pts) clinically or radiologically unfit for a BRT boost.

Methods: We retrospectively analyzed 23 pts with cervical cancer who underwent IMRT boost with BrainLab VERO® between 7/2014 and 12/2016 in our Institution. Toxicity, local control (LC), progression free survival (PFS) and overall survival (OS) were assessed. Acute and late toxicity were evaluated by CTCAE Version 4.1. Pre boost MRI was performed in all but one pts, Clinical Target Volume (CTV) drawn considering the initial extent of the disease and Planning Target Volume (PTV) achieved adding 3-5 mm to CTV. Constraints to organs at risk were borrowed from the BRT ones. Image Guided Radiotherapy (IGRT) was performed at every fraction in all pts.

Results: The median patient age was 54.9 years (range 29.3-81.6). Clinical International Federation of Gynecology and Obstetrics (FIGO) Stages I, II, III, and IV was present in 9%, 30%, 13%, and 48% pts, respectively. All pts underwent EBRT to pelvis ± lombo-aortic nodes with a median dose of 50.4 Gy (range 43.2-50.4), all but one received concomitant CHT. Contraindications to BRT were technical or anatomical limitations or comorbidities. Boost treatment was homogeneously performed to a total dose of 25 Gy in 5 fractions (alternating days). Median follow-up was 21 months (range 4–58.2). According to CTCAE scoring criteria 9 pts experienced gastrointestinal and genitourinary grade 1-2 acute toxicity (within 6 m.) Late grade 2 rectal toxicity requiring laser-coagulation was registered in 2 pts. There were no grade 3 or 4 acute or late toxicities. Local relapse (LR) occurred in 3 pts (13%), 5 pts experienced distant progression (21%) and 2 pts had both (9%). LR occurred in the pts with following FIGO stages: 2pts-IIB, 1 pt-IIIB and 2 pts-IVB. At 2 yrs LC, OS and PFS were 74%, 75% and 53%, respectively. At the time of assessment, 16 pts were alive and 7 died of progressive disease.

Conclusions: Our preliminary data show the safety and feasibility of IMRT boost in terms of acute and late toxicity. LC, OS and PFS are coherent to the cohort of pts (48% of stage IV disease). IMRT boost seems to be a safe and reasonable alternative when BRT is not practicable.

C031

ADJUVANT CHEMORADIOTHERAPY VERSUS RADIOTHERAPY AND CHEMOTHERAPY ALONE IN STAGE III ENDOMETRIAL CANCER

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Aims: Standard treatment for stage III endometrial cancer (EC) is surgery consisting of total hysterectomy and bilateral salpingo-oophorectomy with peritoneal and lymph nodes assessment. Adjuvant strategies to improve locoregional and systemic control after surgery is not

well standardized. The aim of the study was to investigate whether adjuvant chemo-radiotherapy (CRT) compared to radiotherapy (RT) and chemotherapy alone (CT) was associated with a benefit in patients (pts) outcome.

Methods: A retrospective review of pts who received adjuvant treatment after surgery for FIGO stage III EC between 1999 and 2015 was conducted. Statistical analyses were performed using SAS version 9.4. Overall survival (OS) and recurrence free survival (RFS) analysis were estimated with Kaplan-Meier. ANOVA multivariate analyses were used to assess the impact on OS and RFS of the type of adjuvant treatment, controlling for high risk factors.

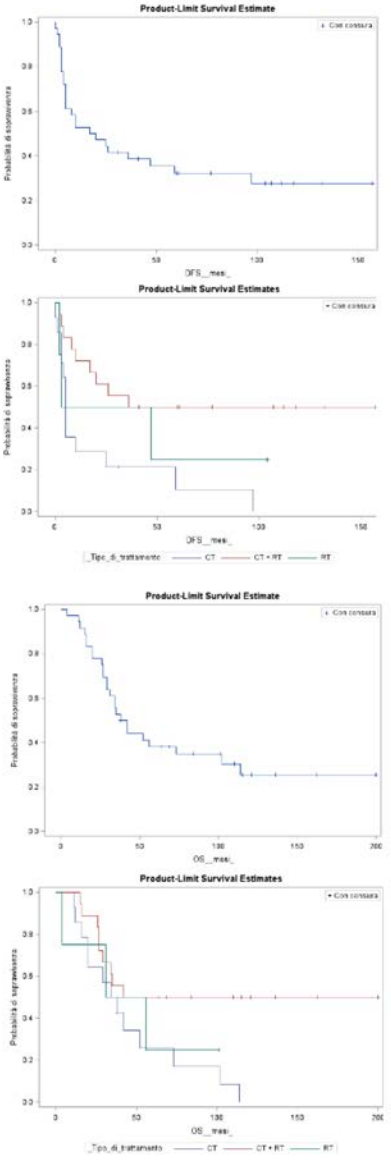

Figure 1.

Results: The study included 36 pts with a median follow-up of 31 months (range 3-195). Median age of the pts was 64 years (range 43-81). All patients underwent radical surgery with lymph nodes assessment in 29 pts. The histological specimen revealed 27 type I (endometrioid tumors) and 9 type II cancers (8 serous and 1 clear cell) staged IIIA, IIIB, IIIC1 and IIIC2 respectively in 9, 3, 17 and 7 pts. After surgery 18 pts were treated with CRT (50% with sandwich approach, 50% with concurrent chemotherapy), 4 pts received RT and 14 had multiagent CT. RT consisted in 45-50.4 Gy/25-28 fr/5w to the pelvis with paraaortic lymph nodes irradiation to 45 Gy in 3 pts. Four pts completed RT with endocavitary brachytherapy for cervical stromal invasion (10Gy in 2 fr to the vaginal cuff). Median recurrence free survival (RFS) and overall survival (OS) for all patients was 18.5 and 38 months. Median RFS for CRT, RT and CT was 38.5, 25 and 5, respectively (p=0.0209). Median OS was 53, 43.5 and 36 (p=0.0835). Compared to RT and CT alone, CRT was associated with a decreased risk of recurrence (p=0.0209) and death (RR= - 0.25). Given the small number of patients, controlling for high risk factors (histologic type, grading, age, LVSI, aneuploidy, lymph nodes involvement, tumor size) and surgery type, the benefit of CRT over CT and RT remains uncertain.

Conclusions: Adjuvant chemoradiotherapy for stage III EC, compared to RT and chemotherapy alone, appears to be associated with a significant decreased risk of recurrence and death.

C032

TOXICITY AND DOSIMETRIC PARAMETERS IN PELVIC INTENSITY-MODULATED RADIOTHERAPY IN GYNAECOLOGICAL CANCER: COMPARISON BETWEEN PRONE VS SUPINE POSITION

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Aims: We compared toxicity and dosimetric parameters between IMRT in supine (SP) or prone position (PP) in 37 uterine cervix and endometrial cancer patients treated in the adjuvant or radical setting.

Methods: 19 patients in SP and 18 in PP underwent a planning CT, with a full bladder and no rectal preparation. For planning target volume (PTV), 1-1.5 cm margin was added to the clinical target volumes uterus, cervix or vaginal cuff and 0.7 cm margin was added for the nodal PTV. The bladder, the rectum and the single small bowel loops were contoured as organs at risk (OARs). 45-50 Gy, standard fractionation was prescribed. 4 to 7 coplanar 15MV fields were used. QUANTEC recommendations for dose constraints at the OARs were followed.

Results: Median follow-up was 25 months for SP and 44 months for PP patients. Chemotherapy was con-

comitantly or sequentially administered in 7 and 16 patients, respectively.

Total PTV volume and PTV coverage were similar in both groups.

No differences were found for bladder parameters. Rectal V40 and V45 were significantly lower in SP (p=0.022, p=0.021, respectively).V10, V20 small bowel volume were lesser in PP (0.021 and 0.048, respectively).

No difference was found for G1-G2 global acute toxicity (100% in PP and 79% SP). No G3-G4 acute pelvic toxicity occurred; 6 patients submitted chemotherapy had G3 haematological acute toxicity.

Small bowel V30 was the only significant parameter linked to the occurrence of acute gastrointestinal toxicity in both groups (p=0.012).

Not different was G1-G2 late pelvic toxicity: 31% in PP and 29% in SP patients. 1IIIB cervical cancer patient, submitted definitive chemo-RT in SP and brachytherapy had G3 late rectal toxicity. No late G4 toxicity occurred.

No significant dosimetric parameters for late toxicity were found. Patient's position, surgery and treatment of pre-sacral nodes were not significant for the occurrence of late toxicity.

Conclusions: Our results are comparable with clinical data showing no differences on acute and late toxicity in gynaecological patients submitted IMRT in PP or SP. However, the limited number of the sample and the differences in clinical and treatment characteristics of the patients don't permit to draw Conclusions: Although IMRT is able to reduce the rate and grade of toxicity, almost all patients experienced acute low-moderate symptoms. Further studies addressing the role of patient's positioning are needed to establish the best treatment position assuring less toxicity

C033

HDAC4 AND HDAC6 SUSTAIN DNA DOUBLE STRAND BREAK REPAIR AND STEM-LIKE PHENOTYPE BY PROMOTING RADIORESISTANCE IN GLIOBLASTOMA CELLS

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Aims: Glioblastoma multiforme (GBM) standard treatment includes a multimodality approach based on the surgical resection combined to concomitant temozolomide (TMZ)-mediated chemotherapy and radiation therapy. GBM, as other many cancers, displays increased expression of histone deacetylases (HDACs) a class of enzymes that remove acetyl groups from an -N-acetyl lysine amino acid on a histone, allowing the histones to wrap the DNA more tightly. Therefore, the aberrant HDACs expression induce a transcriptionally inactive chromatin that results in the downregulation of genes including tumour suppressor. HDACs inhibitors (HDACi) are a heterogeneous group of epigenetic therapeutics, showing promising anti-cancer effects in both pre-clinical and clinical settings. In particular HDACi have shown radiosensitisation effects on several cancer types, when administered in combination with radiotherapy. Among the HDACs, HDAC4 and HDAC6 have been recently shown to sustain GBM onset and progression while their role in radioresistance and as predictive markers of radiation response, are still largely unknown. Herein, HDAC4 and HDAC6 implication in GBM radioresistance was investigated.

Methods: Speciments from 31 GBM patients treated with TMZ+RT and GBM cell lines stable silenced for the HDAC4 or HDA6 expression, were used.

Results: GBM patients showed an abnormally increased HDAC4 and HDAC6 expression in 93.5% and 96.7% of cases, respectively. Retrospective clinical data analysis demonstrated that high-intensity HDAC4 and/or HDAC6 immunostaining was predictive of poor clinical outcome. In vitro experiments revealed that short hairpin RNA-mediated silencing of HDAC4 or HDAC6 radiosensitized U87MG and U251MG GBM cell lines by promoting DNA double-strand break (DSBs) accumulation and by affecting DSBs repair molecular machinery. We found that HDAC6 knockdown predisposes to radiation therapy-induced U251MG apoptosis- and U87MG autophagy-mediated cell death. HDAC4 silencing promoted radiation therapy-induced senescence, independently by the cellular context. Finally, we showed that p53WT expression contributed to the radiotherapy lethal effects and that HDAC4 or HDAC6 sustained GBM stem-like radioresistant phenotype. Conclusion: Altogether, these observations suggest that HDAC4 and HDAC6 are guardians of irradiation-induced DNA damages and stemness, thus promoting radioresistance, and may represent potential prognostic markers and therapeutic targets in GBM.

C034

IMPACT OF GSTP-1 POLYMORPHISM IN GBM PATIETS TREATED WITH RADIO-CHEMOTHERAPY

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Aims: The primary role of glutatione S-transferase P (GSTP-1) proteins is to detoxifity xenobiotics, preventing their interaction with crucial cellular proteins and nucleic acids. Through this activities, glutatione S-transferase P (GSTP-1) proteins play a role in resistance to radio-chemotherapy (RT) in several solid tumors. With these basis, the aim of the present study was to evaluate the impact of GSTP-1 single nucleotide polymorphism

(SNP) rs1695 on Glioblastoma (GBM) patients treated with up front radiotherapy in combination with temozolomide (Stupp protocol).

Methods: Fifty patients with proven diagnosis of GBM, ECOG PS 0-2, age>18 years and treated with RT-CT were enrolled in this retrospective analysis. Polymerase chain reaction amplification was performed using AmpliTaq Gold DNA polymersare (Applied Biosystem, Foster City, CA). Kaplan Meier curves were performed for statistical association with genotypes. The study has been approved by the local Institutional Review Board.

Results: In may 2017, at the data analysis, median progression-free survival (PFS) and median overall survival (OS) were 11 and 20 months, respectively. A relevant finding of our study was the identification of a GSTP-1 genotype that was significantly associated with a better OS: patients harboring the AG or GG genotype had a median OS of 22.9 months, whereas patients with genotype AA 14.3 months (P=0.0187). A trend to statistically significant association with PSF was found, as a matter of fact, median PFS of GSTP-1 AA versus AG+GG were 10.5 months and 12.6 months, respectively.

Conclusions: The GSTP-1 genotype is significantly associated with a different OS in GBM patients treated with radiotherapy and temozolomide. The present, pilot study may represent the stimulus to prospectively investigate the role of GSTP-1 polymorphisms as a predictive pharmacogenetic biomarker or as a target for new drug therapies for GBM patients.

C035

DELTA RADIOMICS FEATURES ANALYSIS FOR THE PREDICTION OF PATIENTS OUTCOMES IN GLIOBLASTOMA MULTIFOME: A PROSPECTIVE, MULTICENTRIC STUDY - GLI.F.A. PROJECT

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Aims: Despite decades of research Glioblastoma multiforme (GBM) remains the most lethal primary brain tumors in adults. As a result, recent investigations have focused on the GBM's heterogenous features to develop an individualized patient management. In this context the use of medical imaging technologies has also greatly expanded as a quantitative tool. To performed a comprehensive analysis of GBM's heterogeneity, a multi-institutional study, the GLI.F.A. (Glioblastoma: advanced Imaging Features Analysis) Project, was performed. The aim of the study is to analyze the imaging features to create a multidimensional map for predictive models (PM) and decision support systems (DSS) in GBM.

Methods: The DSS are the practical and helpful (softwares, apps, nomograms, etc) results of one or more previous PM creation; the PM demands a standardization of data collection. Therefore the project provide for a feasibility and an operative phase. The primary endpoints of feasibility phase are: 1) the implementation of a standardized data collection for brain cancer, through the creation of the ontology; 2) the development of platform for sharing and combining multiple datasets; 3) the development of software system for the conversion of images into mineable data. The primary endpoint of the operative phase is the high-throughput extraction of quantitative features and the subsequent analysis of these data for DSS creation; this practice is termed radiomics. Therefore imaging features are extracted from magnetic resonance imaging (MRI) carried out at baseline, within 72 hours after surgery, before radiotherapy, at 45 days after the end of radiotherapy, during adjuvant chemotherapy and follow-up according to international guidelines, in adult patient with newly diagnosed glioblastoma, that undergo to surgery and standard chemo-radiotherapy according to EORTC 26981-22981-NCIC trial.

Results: The preliminary feasibility phase was conducted; an ontology to collect, standardize and organize features of glioblastoma was created. An acquisition protocol for MRI studies was defined and the MODDICOM software was developed and tested for the extraxtion of imaging features of MRI studies, resulting feasible.

Conclusions: The preliminary phase of GLI.F.A. Project allowed to implement a platform for a standardized data collection and confirmed the feasibility of MRI features extraction. We are going on with the patients enrollment.

C036

DEVELOPMENT OF A FEASIBLE IMMUNO-HISTOCHEMICAL APPROACH FOR SUBTYPING GLIOBLASTOMAS FOR LARGE SCALE CLINICAL APPLICATIONS

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Aims: It is now currently accepted that Glioblastomas (GBMs) can be classified according to their transcriptional profile in 3 major molecular subtypes: Classic (CL), Proneural (PN) and Mesenchymal (MES), each associated with different gene signature, molecular alte-

rations and different prognosis. However, molecular approach is not routinely feasible. Goal of our study has been to investigate the possibility of classifying GBMs based on immunohistochemical (IHC) approach. We extended our work with clinical correlations, with particular attention to adjuvant treatment (RT+CHT).

Material and Methods: from a large cohort of GBMs (n=151) we evaluated by IHC the expression of a wide panel of biomarkers recognized as subgroup specific gene classifiers: EGFR, P53, IDH1, ASCL1, OLIG2, PDGFR , PTEN, MET and YKL40. Cluster analysis were performed in order to identify different expression profiles possibly correlated to the different GBM molecular subtypes. Data were validated at molecular level (RNA-sequencing technology, RNAseq) in 26 selected cases. For clinical correlations, we retrospectively collect clinical data from 104 patients.

Results: Based on the combination of the different biomarkers we were able to recognize GBM subtypes in about 97% of cases. Validation of the IHC approach by RNAseq on representative GBM samples showed a strong correlation between the subgroups assigned by IHC and the transcriptional profile. Median OS of the whole group was 11.2 months. The median age at diagnosis was 58 yrs, with younger patients over-represented in the PN and MES subtypes. Survival analysis showed shorter survival for patients with MES GBM (OS= 10.5 months) as compared to the other two subgroups (CL=11.2 months and PN=12 months). In addition, we examined the effect of more intensive adjuvant treatment on survival. While aggressive treatment significantly reduced mortality in CL (p=0.006) and MES (p=0.003) subtypes, it did not alter survival in the PN (p=0.4) subtype. Interestingly, the benefit of aggressive treatment in MES and CL subtypes seems to be related to the radiation dose (BED>144Gy) rather than TMZ.

Conclusions: Our results indicate that using a restricted panel of highly sensitive biomarkers we can identify GBM subgroups with protein expression profiles strongly related to the transcriptional profile. The assessment of a simple method for classifying GBMs is highly required, particularly for the development of personalized therapeutic strategies.

C037

TARGET VOLUME DEFINITION WITH 18F-DOPA PET IMAGING IN RE-IRRADIATION WITH PROTON THERAPY OF RECURRENT GLIOBLASTOMA

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Aims: To investigate the impact of 18F-DOPA on target volume contouring in recurrent glioblastoma (rGBM) patients (pts) undergoing re-irradiation with proton therapy (PT).

Methods: We investigated the differences in volume and relationship of magnetic resonance imaging (MRI)- vs. DOPA PET-derived gross tumor volumes (GTVs) of 20 rGBM pts re-irradiated with PT between January 2016 and February 2017. All pts had been previously treated with photon radiotherapy (60 Gy) with concomitant and adjuvant temozolomide. All the pts received morphological MRI with contrast enhancement medium administration and 18F-DOPA PET-CT study. We used the pathological distribution of 18F-DOPA in brain tissue to identify the so-called Biological Tumor Volume (BTV). Such areas were assessed using a tumor to normal brain ratio > 2. Moreover, any area of contrast enhancement on MRI was used to identify the MRI-based GTV (MRGTV). Definitive GTV included MRGTV plus BTV. Clinical target volume was generated by adding to GTV a 3-mm uniform margin manually corrected in proximity of anatomical barriers. All pts received 36 GyRBE in 18 fractions. Mean values of differently delineated GTVs were compared each other by paired Student's t-test; $p < 0.05$ was considered significant. Moreover, the overlapping (MRGTV BTV) and the composite (MRGTV BTV) volumes were calculated, and a concordance index (CI) was defined as the ratio between the overlap and composite volumes.

Results: MRGTV (mean 13.5 ± 10.6 cc) was larger than BTV (mean 10.8 ± 9 cc) although this difference was not statistically significant ($p = 0.17$). The composite volume (mean 19.1 ± 11.9 cc) was significantly larger than each single volume ($p < 0.00008$). The overlapping volume (mean 5.2 ± 7.2 cc) was quite small compared to each single volume. Accordingly, we recorded also a low CI (mean 0.27 ± 0.2). The PT irradiation of PET-integrated target volumes provided a median progression-free survival (PFS) of 6.3 months; 6-month PFS rate was 60%; median survival after PT was 10.7 months.

Conclusions: Target volume definition for rGBM undergoing re-irradiation may yield significantly differing results depending upon the imaging modality used for target contouring. Overall, our data suggest that 18F-DOPA PET can detect relevant non-enhancing pathological areas outside the conventional MRGTV ultimately yielding to larger volumes to be irradiated. Influence on clinical outcomes deserves further evaluation.

C038

ANALYSIS OF 68GA-DOTATOC PET IMAGING FOR TARGET VOLUME DEFINITION IN PATIENTS WITH BRAIN MENINGIOMA TREATED WITH PROTON THERAPY

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Aims: Target volume definition is of critical relevance when

radiotherapy is delivered and steep dose gradient irradiation techniques, such as proton therapy (PT), are employed. Aim of the study is to investigate the impact of gallium-68-labeled DOTATOC PET (68Ga-DOTATOC) on target volume contouring in brain meningiomas (BM) undergoing PT.

Methods: We investigated the differences in target definition of magnetic resonance imaging (MRI)- vs. 68Ga-DOTATOC PET-derived gross tumor volumes (GTVs) of 18 patients (pts) with BM treated with PT between April 2015 and May 2017. For pts who underwent surgery, 8 had a diagnosis of World Health Organization (WHO) Grade I, 3 of WHO grade II, and 1 of a WHO Grade III. In 6 pts diagnosis was based on the typical imaging appearance of a benign meningioma. All the pts received morphological MRI with contrast enhancement medium administration and 68Ga-DOTATOC PET-CT study within two weeks from the MRI. We used the pathological distribution of 68Ga-DOTATOC in brain tissue to identify the so-called Biological Tumor Volume (BTV). Because no general cutoff value exists for the standardized uptake of 68Ga-DOTATOC, the PET window level was adjusted so that the 68Ga-DOTATOC-avid volume of the main mass was in accordance with the MRI-based GTV (MRGTV), which then served as the basis for delineation of BTV. Moreover, any area of contrast enhancement on MRI was used to identify the MRGTV. Differently delineated GTVs were visually compared.

Results : 68Ga-DOTATOC PET provided valuable information in all pts. The overall volume of BTV of the main mass did not differ from MRGTV. However, PET imaging did help distinguishing between meningeal thickening versus extension of meningiomas (dural tail). In pts who received PT after surgical resection or in meningiomas infiltrating bony and soft tissue, PET scan improved discrimination between tumor and normal or scar tissue. Moreover, in 5 pts PET imaging was able to identify new areas of tumor involvement not detected at MRI, ultimately yielding a significant change in planning decision.

Conclusions: 68Ga-DOTATOC PET imaging adds valuable information for target volume definition in pts with BM. Influence on clinical outcomes deserves further evaluation at longer follow-up.

C039

STAGING OF THE INTRACRANIAL DISEASE IN PATIENTS WITH BRAIN METASTASES: DETECTION OF ADDITIONAL LESIONS WITH A PROPER SEQUENCE OF BRAIN MRI BEFORE GAMMA KNIFE RADIOSURGERY

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Background: The number of brain metastases impacts radiation therapy approach, prognosis and treatment toxicity: thus, assessment of the precise number of brain metastases is a key-factor in the decision-making process for the appropriate treatment. The diagnostic efficacy in the detection of additional brain metastases of a thin-slice, double dose contrast three-dimensional, T1-Weighted Gradient-Echo Imaging was evaluated.

Materials and Methods: On the day of the treatment, patients underwent a brain magnetic resonance imaging (MRI) scan to be used during the treatment planning in order to contour the targets . All the patients underwent a post-contrast study with T1-weighted, 3D Magnetization- Prepared Rapid Acquisition Gradient Echo (MPRAGE) sequence. We used a double dose of gadobenate dimeglumine and slice thickness of 0.9 mm.

Results: We included in this analysis 148 patients with brain metastases treated with Gamma Knife radiosurgery (GKRS). On the diagnostic MRI, the patients had a number of lesions ranging from 1 to 4. The most common primary site of metastases was NSCLC cancer (63,5%). Median time interval between diagnostic MRI scan and the day of GKRS was 17 days (range 5- 30). A total of 143 additional lesions were detected on MR imaging performed in the same day of the GKRS in fifty-one patients out of 148 (33.8%). A median number of 2 additional lesions were detected (range 1-13). Among these 51 patients only 27 patients had a number of lesions ≤4 on the day of treatment. Patients with a total number of lesions ≤10 were treated with GKRS, whereas patients with a total number of lesions > 10 were treated with whole brain radiotherapy.

Conclusions: Detection of additional metastases at the time of SRS planning occurred in almost 35% of the cases, suggesting a need for more accurate imaging in this group of patients. Since the detection of the real number of lesions may potentially change either the risk of treatment failure or the appropriateness of RS, a double-contrast study with T1-weighted, thin-slice, volumetric MPRAGE sequence should be recommended in all the patients with newly diagnosed brain metastases.

C040

PRELIMINARY RESULTS OF PROSPECTIVE PHASE II STUDY OF HYPOFRACTIONATED STEREOTACTIC RADIOTHERAPY FOR PATIENTS WITH RECURRENT HIGH GRADE GLIOMA

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Aims: The aim of this study was to evaluate outcomes of hypofractionated stereotactic radiation therapy (HSRT) for patients with recurrent high-grade glioma (HGG).

Methods: Patients with recurrent HGG were re-irradiated. The total dose and fractionation schedule were

accorded with the aim to obtain a BED10 ≥ 60 Gy and BED2 ≤ 180 Gy. The total dose was 25 Gy in single fraction for lesions ≤ 2 cm of maximum diameter, 37.5 Gy in 5 fractions for lesions between 2.1 and 3 cm and 49.5 Gy in 15 fractions for lesions ≥ 3.1 cm or located in eloquent area or near to critical structures (optic chiasma, optical nerve). Inclusion criteria were: Karnosky performance status (KPS) ≥70, histopathologically confirmed grade III or IV glioma according to WHO (2007), estimated survival of ≥ 3 months, unifocal tumor and interval time from previous radiotherapy ≥ 6 months. Patients were evaluated every 3 months after treatment with physical and neurological examination, brain MRI scan, MET-PET scan and neuropsychological evaluation. Local Control was evaluated according to RANO criteria.

Results: From January 2015 to April 2017, 87 patients were enrolled. Twenty-one patients underwent radiation therapy alone, while 66 underwent combined treatment with surgery and/or chemotherapy. The median follow-up was 16 months. The median and 1 year progression-free survival (PFS) were 12 months and 74%, respectively. The median and 1 year overall survival (OS) were 14 months and 78%, respectively. No severe toxicity was recorded. In univariate and multivariate analysis extent of resection at diagnosis significantly influenced PFS and OS ($p < 0.01$). Patients treated on smaller recurrent tumor volume had better local control and survival. Indeed, for volume ≤ 50 cm3 the 1-year PFS was 45% versus 15% (p=0.1) and the 1-year OS was 60% versus 31%, respectively (p=0.26).

Conclusions: According to our results, HSRT could be considered a safe and feasible approach for recurrent high grade glioma, also for large tumors. Multidisciplinary evaluation is mandatory to assure the best treatment where local therapy is part of multimodal management.

C041

THE PREDICTION OF THE TREATMENT RESPONSE OF CERVICAL NODES USING INTRAVOXEL INCOHERENT MOTION DIFFUSION-WEIGHTED IMAGING

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Aims: To investigate the predictive role of Intravoxel Incoherent Motion Diffusion-Weighted Imaging (IVIM-DWI) parameters on cervical nodal response to chemo-radiotherapy (CRT) of head and neck squamous cell carcinoma (HNSCC).

Materials and Methods: Patients with pathologically confirmed HNSCC were included in the present prospective study, having at least one positive cervical lymph node (LN). They received concomitant CRT and underwent three serial IVIM-DWI investigations: before, at mid-treatment and after treatment completion. Tissue diffusion coefficient D, perfusion-related diffusion coefficient D* and perfusion fraction f were calculated by a bi-exponential fit. The two-sided Mann–Whitney rank test was used to compare the imaging parameters of patients with regional failure (RF) and regional control (RC). A p value lower than 0.05 was considered to be statistically significant.

Results: Thirty-four patients were accrued. Twenty-four out of 34 LN (70.6%) showed persistent RC after a median follow-up time of 27.6 months (range: 12.0-50.2 months), while ten cases of RF (29.4%) were confirmed with a median time of 6.8 months (range: 1.5-19.5 months). Patients with RC showed significantly lower pre-treatment D values compared to the RF patients (p=0.038). At mid-treatment, the patients with RF showed significantly higher D values (p=0.025), and exhibited larger percent reductions in f and the product D* f from the baseline (p=0.008 and <0.001, respectively). No additional information was provided by the examination at the end of treatment.

Conclusions: Pre-treatment and mid-treatment IVIM-DWI showed potential for prediction of treatment response of cervical LN in HNSCC patients.

C042

ROLE OF BASELINE 18F-FDG PET/CT PARAMETERS IN PREDICTING OUTCOME FOR NON-ENDEMIC EBV-DNA RELATED NASOPHARYNGEAL CANCER PATIENTS UNDERGOING CURATIVE IMRT AND CHT

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Aims: To evaluate the prognostic role of baseline 18F-fluorodeoxyglucose Positron Emission Tomography (18F-FDG PET/CT) parameters in non-endemic Epstein-Barr Virus (EBV-DNA)-related locally advan-

ced nasopharyngeal cancer (NPC) patients and to assess a potentially interactive role between 18F-FDG PET/CT indices and stage and biormarker factors.

Methods: Since 2004, 160 consecutive non-metastatic NPC patients have received IMRT with or without chemotherapy at our Institution. Patients that underwent whole body 18F-FDG PET/CT for disease staging with a minimum follow-up of 12 months (mos) were included in this retrospective study. The following parameters were considered: maximum and mean standardized uptake value (SUVmax and SUVmean, respectively), metabolic tumour volume (MTV) and total lesion glycolysis (TLG) of primary tumour (T) and cervical nodes (N), age, disease stage, EBV-DNA plasma load (copies/ml), gross tumor volume (GTV) of T and N. The prognostic value of these parameters on overall survival (OS) and disease-free survival (DFS) was assessed through Kaplan-Meier actuarial curves and log-rank test. Continuous features were dichotomized according to the third quartile of their distribution. Univariable Cox regression analysis was performed to estimate the hazard ratio associated with dichotomized and continuous variables.

Results: Overall, 49 patients were analyzed. Median follow-up was 55 mos. Two- and 5-year OS were 95.8% and 90.5%, respectively, while DFS was 83.4% at both time points. SUVmax-T ≥18.8 g/ml, and TLG-T ≥203.1 g and age >57 years were significant prognostic factors of worse OS, while SUVmean-N ≥13.3 g/ml, a stage IVB, or EBV-DNA load ≥3493 copies/ml were significantly associated with lower DFS. No correlation was found between PET parameters and clinical stage, GTVs and EBV-DNA plasma load.

Conclusions: Even in a limited series, our data confirm that SUV-T and TLG-T can predict a poor outcome in NPC patients putting forward their use for refinement of prognostication also in non-endemic areas and personalized treatment.

C043

RADIOMIC FEATURES KINETICS IN HEAD AND NECK CANCER PATIENTS TREATED WITH IMAGE-GUIDED RADIATION THERAPY: A TOOL FOR PREDICTING TUMOR RESPONSE?

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Aims: The prediction of tumor response during radiotherapy (RT) could open doors to further treatment individualization. We used radiomics texture analysis for quantifying changes in tumoral structure in a cohort of head and neck cancer (HNC) patients (pts).

Methods: HNC pts undergoing image-guided RT were included. Primary tumor response at the end of RT per RECIST 1.1 was retrieved. 155 in treatment CT scans at days 1, 5, 10 and 15 were reclaimed. Primary gross tumor volumes were contoured. A total of 145 radiomic features were selected from the categories: intensity direct, neighborhood intensity difference, grey-level co-occurrence matrix (GLCM), grey-level run length and shape, and analyzed using IBEX. Spearman correlation after adjusting for dose was used to reduce the 145 features to 7. Features were: 5-7 Correlation, 11-7 Correlation, 9-7 Correlation from GLCM3 category, 90-7 Correlation from GLCM2.5 category, Skewness from GradientOrientHistogram category and Orientation from 'Shape' category. These were used to build 3 types of models 1)using only the baseline (BL) value of the feature, 2)the ratio between the mid-treatment value of the feature to its value at BL and 3)a functional principal component analysis model leveraging the structure of the temporal trajectory of the feature from BL to mid-treatment.

Results: 39 predominately male pts, mean age 54. 61.5% had a diagnosis of oropharyngeal cancer (OPC), 38.5% of non-OPC; 1 pt was stage II, 4 were III, and 34 were IV per AJCC 7. 38 received chemotherapy; 1 pt had RT alone. Mean RT dose was 69.68 Gy. 24 pts (61.5%) underwent complete response (CR) on the primary tumor, 15 (38.5%) partial response (PR), per RECIST 1.1. The corresponding areas under the curve (AUCs) and confidence intervals (CI) for the prediction of tumor PR vs CR, according to the 3 models were: 0.473 [95% C.I.: 0.27-0.67], 0.6 [95% C.I.: 0.4-0.8] and 0.69 [95% C.I.: 0.51-0.87], respectively (Figure 1). This suggests the functional approach yields a superior predictive power in the evaluation of tumor response compared to either the baseline radiomic features or the delta ratio between the final and mid-time points.

Conclusions: Textural kinetic trajectories from sequential in-treatment CT scans can be correlated

with tumor response. Radiomics may convey additional clinical information from routine imaging studies towards adaptive RT. Further studies and larger cohorts are warranted to validate this approach in clinical practice.

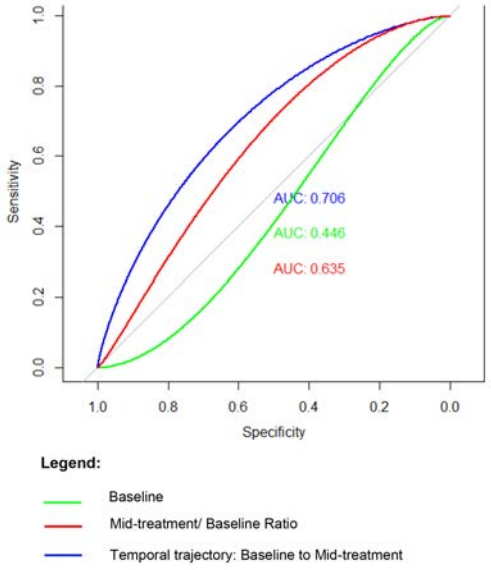

Figure 1. ROC (receiver operating characteristic curve) for radiomic features kinetics across treatment time.

C044

HOW DOES THE PRESENCE OF AN EXPERT RADIOLOGIST IMPACT ON THE THERAPEUTIC DECISIONAL PROCESS OF A HEAD AND NECK MULTIDISCIPLINARY TUMOR BOARD?

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Aims: Head and neck (HN) cancers are heterogeneous malignancies for which different treatment options can be offered. The precise definition of tumor extension is fundamental for clinical staging and treatment strategy. This analysis evaluates the impact, on the therapeutic decision process, of the radiologic images revision performed by an expert in field radiologist (LP) in a contest of a HN multidisciplinary team (MDT).

Methods: We retrospectively analyzed all records of HN cancer patients referred to a MDT evaluation at the European Institute of Oncology of Milan from April 2016 to April 2017. For the present analysis we selected only the clinical cases for which a radiologic images (Computed Tomography and Magnetic Resonance) revision was required. Results in terms of therapeutic decision based on the radiologic revision were classified as follows: 1) modification of the radiologic staging 2) final therapeutic decision (among different options at baseline) defined according to the radiologic revision 3) minor therapeutic changes (changes of the baseline therapeutic proposal but remaining within the same therapeutic strategy, p.e different types of surgical approaches) 4) major therapeutic changes (changes of the baseline therapeutic proposal p.e. from surgery to non-surgical treatment and vice versa). Moreover, the images revision of patients during the follow-up period was also analyzed.

Results: Fifty-five multidisciplinary meetings were performed on a weekly basis in the considered period. A total of 971 clinical cases (mean 18 cases/meeting) were discussed. Among these, images revision was required for 337 (35%) cases. Results of the radiologic revision are summarized in Table 1.

Conclusions: Our results showed that the revision of radiologic images has a relevant impact on the HN cancer patients management, in particular on the final therapeutic decision (changed in one out of two cases). The presence of an expert head and neck radiologist during the multidisciplinary discussion should be therefore strongly encouraged.

Table 1.

Results of radiologic revision	Number of cases (%)
Modification of the radiologic staging	25 (7%)
Final therapeutic decision among different option at baseline	176 (52%)
Minor therapeutic changes	15 (4%)
Major therapeutic changes	17 (5%)
Any changes in the follow up strategy	18 (4%)

C045

PROGNOSTIC SIGNIFICANCE OF IMMUNE MICROENVIRONMENTAL FACTORS IN UNDIFFERENTIATED NASOPHARYNGEAL CARCINOMA PATIENTS TREATED WITH CHEMORADIOTHERAPY

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Purpose. Our primary aim was to retrospectively assess the significance of immunosuppression in the EBV-associated Undifferenciated NasoPharyngeal Carcinoma (UNPC) microenvironment as prognostic biomarker of treatment failure in a non-endemic area population. As secondary aim we investigated the immunogenic effects of chemoradiotherapy (CRT) monitoring the variation of EBV-specific immunity before and after treatment.

Materials and Methods: We reviewed 87 consecutive patients (pts) with EBV-associated stage II-IVB UNPC undergoing radical CRT. Our policy was of administering concurrent CRT in pts with stage II disease, and sequential therapy in pts with advanced stages. The number of relapsed pts was 13 (cases), while 74 pts (controls) were free from treatment failure at a minimum follow-up of 2 years. DNA and RNA were extracted from tumor (T) and healthy (H, tonsil) frozen biopsies at diagnosis. We verified the expression of EBV-derived Barf1 gene in T versus H samples. We investigated the expression of the immune-related genes PD-L1, CD8, FoxP3 and IFN- in T and H tissues by quantitative RealTime PCR. We applied ANOVA test to compare data obtained from cases versus controls. Ten pts (cases n=7, controls n=3) resulted evaluable for the monitoring of peripheral blood cellular immunity against EBV and Barf1 before and after CRT, through IFN- -ELISPOT assay and flow cytometry.

Results: The higher expression of Barf1 ($p<0.001$) in T versus H tissues confirmed the adequacy of UNPC samples for the analyses. Cases showed higher levels of the immunosuppressive marker PD-L1 ($p<0.05$, 9.2E05 vs 6.6E05 molecules/µg RNA) and of Barf1 ($p<0.001$) with respect to controls, conversely controls had higher T cell activity in terms of CD8 ($p<0.001$, 3.2E05 vs 3.9E04) and IFN- ($p<0.002$) amounts. Overall, when comparing T samples with H tissues, we observed increased expression of IFN- ($p<0.001$), but also higher levels of the immunosuppression hallmark FoxP3 ($p<0.001$). With respect to the secondary aim we noticed EBV-specific immunity in all pts investigated at baseline, and, 7/10 pts achieved boosted immune responses against Barf1 after CRT.

Conclusions: In our series, the higher level of immunosuppression (high PD-L1, low CD8) in UNPC microenvironment predicts treatment failure after CRT. The increased immune response against Barf1 after treatment supports the immunogenic effects of radiation. These analyses may identify pts who would more likely benefit from immunotherapy.

C046

PATTERN OF LATE DYSPHAGIA AND ASPIRATION AFTER SWALLOWING-SPARING INTENSITY MODULATED RADIOTHERAPY (SWOARS-SPARING IMRT) OF HEAD AND NECK CANCERS: RESULTS OF A MONO-INSTITUTIONAL PROSPECTIVE STUDY

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Aims: A prospective instrumental assessment of late dysphagia and aspiration using SWOARs-sparing IMRT.

Materials and Methods: Eligibility criteria included all patients affected by nasopharynx and oropharynx cancers (Stage II-IVA) candidates for a non-surgical RT based treatment with curative intent and requiring bilateral neck irradiation. 8 swallowing related structures (SWOARs) were outlined according to Christianen et al. guidelines and included in the IMRT plan objective function as secondary organs at risk: superior, middle and inferior constrictor muscles (SPCM, MPCM and IPCM), supraglottic (SL), glottis larynx (GL), cricopharyngeal muscle (CPM) and cervical esophagus (EC). Objective instrumental assessment included Fiberoptic Endoscopic Evaluation of Swallowing (FEES) and Videofluoroscopy (VFS) at baseline, at 6 and 12 months after treatment. FEES assessed the pharyngeal residue according to the Farneti pooling score (P-score). This score is based on the endoscopic evaluation of the site, the amount and the management of retention as the number of dry swallows required to clear pooling (<2; 2-5;>5) and it comprises 4 levels. A P-score of 4-5 (minimum score) indicated no dysphagia; a score of 6-7 (low score) mild dysphagia; a score of 8-9 (middle score) moderate dysphagia; 10-11 (high score) severe dysphagia. Also, 3 different consistencies were used to test the P-score: 10mL of water marked with blue methylene (L=liquid), 10mL of marmalade (SS=semisolid) and 1/2 of cracker (S=solid). VFS was specifically used to assess the pattern of penetration and aspiration based on the Penetration Aspiration Scale (PAS) and was also simplified by dividing it into 3 categories (1:normal; 2–5:penetration; 6–8:aspiration). 2

different consistencies of bolus were used to test the PAS score: 10mL of thin liquid barium (L=liquid) and 10 mL of paste barium (S=solid).

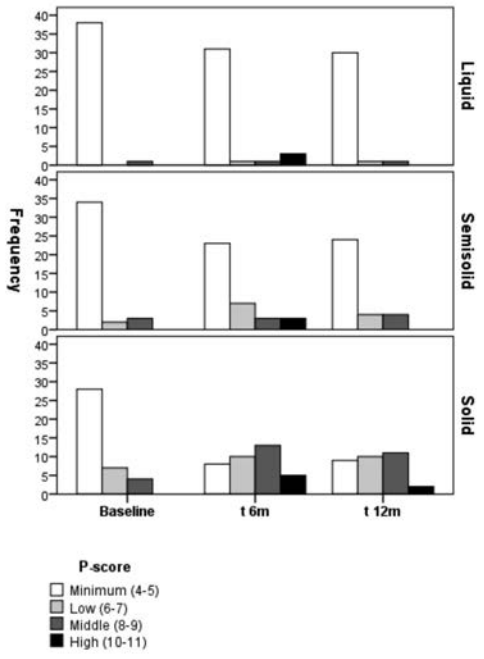

Figure 1. The distribution of P-score at the 3 different times interval for the 3 different consistencies of the bolus.

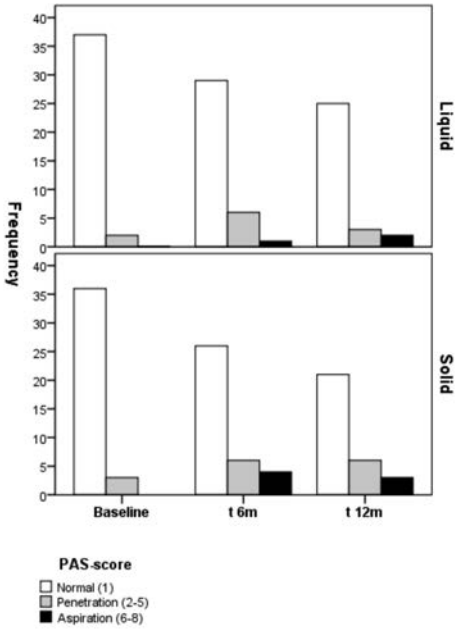

Figure 2. The distribution of PAS score at the 3 different times interval for the 2 different consistencies of the bolus.

Results: 38 patients were evaluable. There was a significant worsening of the P-score at 6 months both for SS (p=0,015) and S (p<0,001) which persisted only for S at 12 months (p<0,0001). Similarly there was a significant worsening of the PAS score at 6 and 12 months (p=0,065 and 0,039, respectively) for S bolus. An overall moderate or severe dysphagia was observed after S bolus in 47% and 37% of patients at 6 and 12 months as well as 3-7% and 10-14% of aspiration after L and S, respectively (Figures 1 and 2).

Conclusions: Promising results are reported using a SWOARs-sparing IMRT technique.

C047

SHORT COURSE ACCELERATED RADIATION THERAPY (SHARON) IN PALLIATIVE TREATMENT OF ADVANCED HEAD AND NECK MALIGNANCIES: A PHASE I-II STUDY

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Aims: To define the maximum tolerated dose (MTD) of a conformal SHort course Accelerated RadiatiON therapy (SHARON) and safety and efficacy of this treatment in patients with symptomatic advanced head and neck cancer.

Methods: A phase I trial in four dose-escalation steps was designed: 14 Gy (3.5 Gy fraction), 16 Gy (4 Gy fraction), 18 Gy (4.5 Gy fraction) and 20 Gy (5 Gy fraction). Treatment was delivered in 2 days with a twice daily fractionation and at least 8 hour interval. The dose limiting toxicity (DLT) was defined as any acute toxicity > Grade 3, according to RTOG scale. Moreover, the MTD was used to plan a phase II trial based on Simon's two-stage design. Pain was recorded using a Visual Analogic Scale (VAS). Impact on Quality

of Life (QoL) was evaluated according to CLAS scales.

Results: A total of 48 patients were treated. The most frequent baseline symptoms were pain (66.6%), pain associated to dysphagia (16.7%), pain associated to bleeding (8.3%), bleeding (4.2%), and dysphagia (4.2%). In the phase I trial the 20 Gy dose level was determined to be the MTD, with 1 out of 6 patients showing Grade 3 acute mucositis. In the phase II trial the palliative response rate (complete plus partial) was 82.7% with a median duration of palliation of 3 months. Complete pain relief was achieved in 33.3% of patients. The overall response rate for pain was 81.5%.

Conclusions: Conformal short course radiotherapy in twice daily fractions and 2 consecutive days is well tolerated up to a total dose of 20 Gy and produces an encouraging rate of symptomatic response. A non-inferiority phase III trial has been planned to compare this regimen with a standard palliative regimen (30 Gy in 10 daily fractions).

C048

THYROID COBRA: THE INTERDISCIPLINARY STANDARDIZED IMAGE AND DATA COLLECTION SYSTEM OF THE ITALIAN METABOLIC RADIOTHERAPY WORKING GROUP (ASSOCIAZIONE ITALIANA DI RADIOTERAPIA ONCOLOGICA - AIRO)

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Aims: Main objective of the Thyroid COBRA (COnsortium for BRachytherapy data Analysis) Project is the creation of a multicenter national working group and of a standardized web image and data collection system.

Methods: The Associazione Italiana di Radioterapia Oncologica (AIRO) Metabolic Radiotherapy Working Group developed the project and endorsed the setup of a consortium for thyroid cancer management and clinical image and data acquisition and storage. The agreement conditions, the ontology of the collected data and the related software services were defined by a multicenter ad hoc working-group (WG).

Results: Six centers from Italy developed and signed the Thyroid COBRA consortium agreement and its ontology has been approved by the WG. The consortium identified three data set tiers: Registry (oriented to epidemiology), Procedures (predictive modeling and DSS) and Research (radiomics). The COBRA-Storage System (C-SS) appeared to be not time-consuming and able to fully respect patient's privacy through the extraction of data directly from single center's storage systems using a secured encrypted connection. Automatic images data archiving (staging images, dose distributions and therapy volumes) through a direct link with the PACS and a Treatment Planning Software is also possible and the C-SS architecture will allow a "distributed learning" approach for predictive model definition and for the development of decision making support tools.

Conclusions: The creation of the Thyroid C-SS through a multicenter consortium approach appeared to be a feasible tool in the definition of complex and privacy saving image and data sharing systems oriented to the multidisciplinary management of thyroid tumors.

C049

68-GA PSMA PET/CT AS A NEW TOOL IN THE DECISION-MAKING STRATEGY OF PROSTATE CANCER PATIENTS WITH LOW-LEVEL OF PSA AFTER RADICAL PROSTATECTOMY

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Aims: Currently, Choline PET/CT is under definitive assessment for staging of prostate cancer (PC) patients with Prostatic Specific Antigen (PSA) failure level up to 1.5-3 ng/mL. At lower level of PSA relapse, its accuracy is dramatically reduced. Thus, in this setting a reliable tool to detect PC recurrences is advocated. Aim

of the study is to evaluate the impact of 68-Ga Prostate Specific Membrane Antigen (PSMA)-PET/CT in decision-making strategy of patients with prostate cancer (PC) who underwent radical prostatectomy (PR).

Methods: From June 2016 to April 2017 forty consecutive patients, previously submitted to PR with a PSA value detectable in the range between 0.1 ng/mL and 2 ng/mL were recruited for 68-Ga PSMA-PET/CT restaging. Therapeutic strategy based on the 68-Ga PSMA-PET/CT evaluation was compared with the strategy that would have been proposed in case of PET not available and/or not strictly indicated.

Results: In twenty six out of 40 patients (65%), 68-Ga PSMA-PET/CT was considered positive for disease recurrence. Considering the site of recurrence, lymph nodes metastases were found in 20 cases, prostatic bed relapse in 5 cases, bone in 8 cases. More specifically, multiple sites of recurrence were shown in 5 cases: in 4 cases bone and lymph nodes and in one case prostatic bed and lymph nodes. Accordingly to 68-Ga PSMA-PET/CT findings, the decision making strategy was changed as follows: radiation therapy was proposed in 22 out of 40 cases (55%) while systemic therapy was suggested or modified, when compared to the previous, in 6 out of 40 patients (15%). In details, in 3 (7%) patients was administered a complete androgenic blockade, in a patient (2%) a manipulation of the androgen deprivation therapy, in a single case zoledronic acid was prescribed (2%) and finally a patient (2%) received an androgen-receptor–signaling inhibitor (Enzalutamide).

Conclusions: In conclusion, therapeutic strategy based on the 68-Ga PSMA-PET/CT was changed in the 65% of patients analyzed compared to the strategy that would have been proposed in case of PET not available and/or not strictly indicated. Thus, 68-Ga PSMA-PET/CT seems to be a promising diagnostic tool in patients with PC who underwent PR with PSA relapse values in the window between undetectability and 2 ng/mL. Looking at the present results, further studies investigating the reliability in terms of accuracy of 68-Ga PSMA-PET/CT are needed in this scenario.

C050

RADIOTHERAPY EXCLUSIVE IN INTERMEDIATE - HIGH RISK PROSTATE CANCER. FOLLOW UP WITH CHOLINE PET/CT. OUR EXPERIENCE

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Aims: Radiation therapy(RT), radical prostatectomy, and hormone therapy(HT) (i.e. androgen deprivation therapy) are the three main treatments for prostate tumor. In intermediate-high risk prostate cancer the standard treatment, according guidelines NCCN, is the HT combined with RT. Our treatment provides radical radiotherapy without HT and the follow up provides PSA value and Choline PET/CT. Aim of this study is to evaluate feasibility and RFS in pts treated with exclusive radiotherapy and the role of Choline PET/CT.

Methods: From 2011 to 2016, we have treated a total of 439 patients(pts) with prostate cancer. The 55% of these pts (241 pts) were treated with radical radiotherapy (80 Gy/ 40 fractions over 8 weeks) by means step-and-shoot IMRT technique. 218 of these pts (90,4%) had intermediate or high risk prostate cancer (according to WHO 2016). Aged between 52 and 84, cTNM T2b to T3a, PSA value range 10 - 20 ng/mL, a Gleason Grade Group of 2 to 5 and a Gleason Score between 7 (3+4) and 9-10. All patients were subjected to at least 12 biopsy samples and they had never been undergone to HT before. Additional criteria were a good expected pts survival, a ECOG perfomance status <2 and no previous local treatments for prostate cancer. We evaluated PSA value, digital rectal examinations(DREs), biopsy, CT and/or MRI scans to exclude metastatic disease, and all pts submitted to [11C]-Choline Positron Emission Tomography/Computerized Tomography(PET/CT) that showed the positivity at level of the prostate gland with or without pelvic lymph node metastases at the time of recruitment(T0). Follow up provided, every 3-6 months and one year after the end of the treatment PSA value, and 11C-Choline PET/CT. Target volume was determined as the whole prostate gland and lower part of seminal gland. During radiotherapy were performed Cone-Beam CT to verify the correct positioning of the pts.

Results: 218 pts were treated with radical radiotherapy. The median follow-up was 36 months. All pts were subjected to PSA level measurement after 3 months from the end of the radiotherapy showing a clear reduction in its value. After 6 months, a Choline-PET/CT has been carried out that shows a negativity in 196 pts(90%), RFS were respectively 84% (183pts), 79%(172pts) and 72% (156pts) after 12, 24 and 36 months. No pts interrupted the treatment for toxicity and/or progression of disease.

Conclusions: In this study we can say that exclusive radiotherapy without hormonotherapy in pts with intermediate-high risk is a safe, feasible and curative treatment, with a good local control of disease. 11C-Choline PET/CT has a crucial role to detect early progression disease and/or local recurrence.

C051

PELVIC MULTIPARAMETRIC MAGNETIC RESONANCE IMAGING (MPMRI) FOR LOCALIZED OR LOCALLY ADVANCED PROSTATE CANCER (PCA) PATIENTS (PTS): DOES IT REALLY IMPACT MANAGEMENT AND RADIOTHERAPY (RT) PLANNING?

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Aims: Prostate mpMRI is an emerging imaging modality for diagnosis, staging and treatment planning of localized and locally advanced PCa. Aim of this study is to retrospectively evaluate how this non-invasive technique has improved tumor staging and even RT treatment planning of PCa pts treated at our Department.

Methods: From 2008 to 2017,115 pts with histologically proven PCa were staged using standard or mpMRI before being submitted to radical RT (alone or in association to total androgen deprivation –ADT). At time of diagnosis mean and median age was 72 years (range 57-81),ECOG Performance Status for all pts was 0-1. Furthermore all pts were staged with clinical exam, digital rectal exploration and transrectal ultrasound before being referred to our Department. At time of diagnosis, 60 pts (52.2%) had cT1, 43(37.4%) cT2, 7(6.1%) cT3a, 5 (4.4%) cT3b. All pts were clinically and radiologically N0 (according to TNM classification). Pts were also divided in different risk classes according to V1.2017 NCCN guidelines: seven pts (6.1%) were low risk, 64(55.6%) intermediate and 44(38.3%) high risk.All pts were submitted to pelvic MRI to complete the staging before proceeding with RT treatment planning.

Results: After MRI, 71 pts (62.1%) were "upstaged": particularly 26 pts moved from T1 to T2, 23 from T1 to T3, 1 from T2a to T2b, 20 from T2 to T3 and 1 from T3a to T3b; just 1 pt was "downstaged" having moved from T2c to T2a. Finally, clinically significant pelvic nodes (cN+) were found in 5 pts. Consequently, MRI changed also clinical risk stratification in 31pts (26.9%): 2 moved from low to intermediate risk, 3 from low to high, 26 from intermediate to high risk. These findings have led to changes in RT volumes in 28 pts (24%). Particularly, the target volume of RT treatment encompassed only the prostate in16 pts, prostate and seminal vesicles in 47 and even pelvic nodes in 52 pts. Regarding RT dose, 20 pts were treated with conventional fractionation (range 74-78Gy, median dose (MD) 76,7Gy), while 95 pts with moderately Hypofractionated RT (range 54.3-75,9Gy, MD 69,6Gy). The use of ADT has been modified in 27 pts being added to RT or changed from short (6 months) to long term (24-36 months) due to a change in risk class.

Conclusions: Nowadays pelvic mpMRI is a very promising non-invasive diagnostic tool with the potential to provide more accurate staging before RT and consequentially to better define the most appropriate therapeutic strategy and RT target volumes.

C052

DETECTING BIOLOGICAL TARGET VOLUME (BTV) BY MEANS OF 18FCH-PET/TC IN PATIENTS WITH BIOCHEMICAL PROGRESSION TREATED WITH HIGH DOSE SALVAGE RADIOTHERAPY: FEASIBILITY STUDY IN 155 PATIENTS

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Purpose: biochemical recurrence after radical prostatectomy occurs in 15-50% of operated patients. Site of recurrence is generally unknown, and radiotherapy is generally adopted as salvage treatment with 60-66 Gy delivered to prostatic fossa. Dynamic 18F-Choline PET/CT could identify biological target volume (BTV), thus to ameliorate radiotherapy target definition and results.

Materials and Methods: data on 155 patients with biochemical progression after radical prostatectomy between January 2009 and December 2015 were reviewed. All patients at time of diagnosis of biochemical recurrence underwent to dynamic 18F-Choline PET/CT, which revealed in all cases a local recurrence. High-dose salvage radiotherapy (HD-SRT) was accordingly delivered up to total dose of 80 Gy to BTV. Toxicity was recorded according to CTC vers. 4.0 scale.

Results: The mean value of PSA before radiotherapy was 1.21 ng/mL. Treatment was generally well tolerated: 143 patients (92%) completed treatment without any interruption. Acute toxicity was: Gastro-intestinal (GI) in 62 patients (40%); Genito-urinary (GU) in 31 patients (20%). No grade > 3 acute toxicity was recorded. Late toxicity was: 16 events (10.3%) of grade 1 GU toxicity and 9 patients (5.8%) with grade 1 GI. Three patients (1.9%) experienced grade 2 toxicity (two gastro-intestinal and one genito-urinary toxicity). With a mean follow-up of 48 months 38/155 (24.5%) experienced a biochemical recurrence.

Conclusions: dynamic 18F-Choline PET/CT could identify BTV in biochemical relapsed patients. HD-SRT delivered according to PET/CT data is safe and could validate ex-adiuvantibus the role of functional data overcoming the definition of biochemical recurrence.

C053

STEREOTACTIC BODY RADIOTHERAPY FOR LOW AND INTERMEDIATE RISK PROSTATE CANCER. TOXICITY RESULTS OF PHASE II STUDY

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Aims: We conducted a phase II prospective trial in prostate cancer patients treated with stereotactic body radiotherapy (SBRT). Primary end-point was late gastro-intestinal (GI) toxicity; secondary end-points were biochemical relapse-free survival and genito-urinary (GU) toxicity.

Methods: Inclusion criteria were the following: low/intermediate risk prostate cancer, MRI staging, and lymph node involvement risk<15% according to the Roach Index. SBRT was delivered using volumetric IMRT, to a nominal dose of 42 Gy in 7 fractions, so that the 95% of the dose would cover the 95% of the PTV. CTV included the prostate and the proximal 1/3 of seminal vesicles; a 5 mm isotropic margin was used to define the PTV. Image guidance was performed by daily cone-beam CT with the use of intra-prostatic fiducial markers. Acute and late toxicity was recorded using the RTOG/EORTC scale. Biochemical failure was determined using the Phoenix definition. We hypothesized that SBRT could lead to late Grade 2 GI toxicity not higher than 5%.

Table 1. Acute and late toxicity

Toxicity	G1	G2	G3-G4	Total
Acute GI	0	0	0	0
Acute GU	8 (19)	3 (7)	0	11 (26)
Late GI	6 (14)	0	0	6 (14)
Late GU	13 (31)	2 (6)	0	15 (37)

GI, gastrointestinal; GU, genitourinary. Data presented as number of patients, with percentages in parentheses.

Results: 42 patients were enrolled in the present study. The median follow-up was 30 months (range, 24-46 months). Median age was 74 years (range, 57–80 years). Eighteen patients received hormonal therapy. Main tumor characteristics were: Gleason Score (GS) = 6 in 82%, and GS=7 in 18% of the cases; T1 in 73% and T2a-b in 27% of the cases. This is a positive trial: no late Grade ≥2 GI toxicity was documented. Other acute and late toxicities are summarized in Table 1. Biochemical free-survival at 4 years was 98%. Only one patient developed distant failure.

Conclusions: SBRT for low/intermediate risk prostate cancer to a total dose of 42 Gy in 7 fractions is safe; no late grade ≥2 GI toxicity was documented. Longer follow-up is needed to assess its efficacy.

C054

"GIVE ME FIVE" EXTREME HYPOFRACTIONATED RADIOTHERAPY (RT) FOR LOCALIZED PROSTATE CANCER (PCA): SAFETY WITHOUT LOSING EFFICACY UPDATE OF CLINICAL AND TOXICITY PATIENTS' RECORDS

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Aims: Extreme Hypofractionated RT is given over a shorter time with larger doses per treatment in patients (pts) with localized PCa. The use of Hypofractionation is supported both from the radiobiological point of view (the low a/b-ratio in PCa and dose escalation) and from the raising number of clinical evidences. The aim of this study is to review our data regarding oncological outcomes, acute and long term toxicities in patients treated with a short course of RT.

Methods. We retrospectively reviewed pts with clinically localized PCa treated primarily with extreme hypofractionated RT. All pts were stratified following NCCN risk groups classification and all categories were included in the analysis. Data on acute and late-term toxicities were collected according to RTOG/EORTC grading system. Biochemical progression free survival (b-PFS) and Overall Survival (OS) were also assessed. A Cox proportional hazards model was used to identify independent predictors of biochemical recurrence/survival, with adjustment for relevant covariates.

Results. We identified 194 treated in our Institute from 2012 to 2016 with RT to total doses of 35 Gy or 32.5 Gy (in 25 selected pts: elderly or significant comorbidity) in 5 fractions on alternate days. All risk groups were as follow: 65 (33.5%), 101 (52%), and 28 (14.5%) representing low-, intermediate- and high-risk group, respectively. Median age, pre-RT PSA and GS were 74 yrs (range 51-89), 6 ng/mL (range 2-40 ng/ml), 6 (range 4-9). With a median follow-up time of 28.7 months (range 5-50.2 mos) at the time of the analysis: 175 pts (93.2%) are alive with no evidence of disease, biochemical recurrence was observed in 14 pts (7.2%), 5 pts died, 3 for not related cancer death, 2 for unknown reasons. Neither acute or late grade 3 or higher genito-

urinary or rectal toxicity was observed. We assessed the associations of risk categories and prescribed RT dose with b-DFS: Log-rank test found significant differences by low vs high risk (p value = 0.03) and by 35 Gy vs 32.5 Gy (p value = 0.03).

Conclusions: The toxicity of hypofractionated RT in a large clinical cohort of PCa pts was tolerable confirmed that this treatment is safe and offers excellent tumor control. Moreover the hypofractionated RT allows to delivery the whole RT over 10 days with a sensible impact in patients' quality of life.

C055

POSTOPERATIVE HYPOFRACTIONATED RADIATION THERAPY IN PROSTATE CARCINOMA: A SYSTEMATIC REVIEW

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Aims: While several randomized studies tested hypofractionated radiotherapy (HFRT) as exclusive treatment of prostate cancer (PCa), high level evidences on safety and efficacy of HFRT in postoperative setting are lacking. Therefore, a systematic review on acute and late toxicity after postoperative HFRT was performed. Even outcome data in terms of local control (LC), overall survival (OS), and biochemical relapse-free survival (bRFS) were analyzed.

Methods: A systematic search based on PRISMA methodology was performed using PubMed. Only studies published in English reporting clinical results (toxicity and outcome) after adjuvant or salvage HFRT were included.

Results: A total of 1081 patients from 16 eligible studies were included. These retrospective (6) or prospective (10) studies had heterogeneous characteristics in terms of dose, fractionation, target definition, and combination with hormonal therapy. Median follow-up ranged between 11.5 and 111 months (median: 28.7 months). No case of grade ≥ 3 acute gastrointestinal (GI) toxicity was recorded. Grade ≥ 3 acute genitourinary (GU) toxicity ranged between 0% and 3.0% (median: 0%). Crude rates of Grade ≥ 2 late GI toxicity was 0%-9.0% (median: 1.5%) and crude rate of Grade ≥ 2 late GU toxicity was 0%-66.0% (median: 11.5%). LC was reported only in two studies: 93.7% crude rate, and 54.0% 10-year LC, respectively. Crude rate of OS ranged between 96.4% and 100% (median: 98.5%). Crude rate of bRFS was 83.0% and 100% in two studies, respectively. Two studies reported 67.0% and 75.0% 4-year bRFS, respectively.

Conclusions: Acute toxicity does not seem to be increased in patients with PCa receiving HFRT after radical prostatectomy (RP). Results in terms of late GU toxicity are conflicting and therefore further prospective studies are needed to clarify this issue before including postoperative HFRT in clinical practice.

C056

IMAGE-GUIDED IMRT FOR HIGH AND VERY HIGH-RISK PROSTATE CANCER PATIENTS

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Aims: To report clinical outcomes in high and very-high risk prostate cancer (HRPCa) patients treated with Image-Guided IMRT delivered with TomoTherapy® (Hi Art II, Accuray, USA).

Methods and Materials: From April 2006-December 2014, 184 HRPCa patients, with a median age of 74,7 (52,7-90) years, were treated with Image-Guided hypofractionated IMRT (IG-IMRT) in our department. Median GS was 8 (7-10), and median initial PSA 12.00 (1.68-826.0) ng/ml. A total dose of 51.8 Gy/ 28 fractions was prescribed on pelvic lymph-nodes (WPRT), with a simultaneous integrated boost(SIB) on prostate and seminal vesicles up to 74.2 Gy (2.65 Gy/fraction). Nine patients had a lower prescription, of 71.4 Gy (2.55 Gy/fraction) on prostate and seminal vesicles and eight pts were treated without WPRT because of comorbidities. On the overlap PTV-rectum the dose prescription was 65.8 Gy. Androgen deprivation (AD) was prescribed for 90% of patients for a median time of 24.5 (0-119) months. Daily Megavoltage CT was performed every day with an active evacuation protocol for rectal dilatation and empty bladder filling.

Results: With a median follow up of 54 (1.8- 148.7) months after the end of radiotherapy the median overall survival from diagnosis was 62.7 (9.8-215.0) months.

Biochemical relapse was 13.6% and 9.2% of patients presented a systemic relapse. Seven patients died for prostate cancer progression (3.8%), 11 (6%) for second tumors, 20 (10.9%) for other causes, and in 3 patients (1.6%) the cause of death was unknown. Acute toxicities were: genito-urinary(GU): G1= 25.0%, G2= 5.4%; G3= 1.1%; rectal: G1= 12.5%, G2= 2.7%; bowel: G1=34.8%, G2=7.0%, G3= 0.6%. Late toxicities were: GU: G1=31.5%, G2= 12.5%, G3= 7.1%, gastro-intestinal (GI): G1= 13%, G2= 9.3%, G3=4.9%, but were followed by spontaneous and therapeutic resolution in most cases, thus late toxicity rate at the last follow up was: GU: G1= 20.7%, G2= 5.4%, G3= 3.2%, and GI: G1= 5.4%, G2= 2.7%, G3= 2.2%.

Conclusions: Image-Guided IMRT, in high and very high-risk prostate cancer patients, ensured a very precise treatment delivery and, despite the high 2 Gy dose equivalent to the prostate (EQD2=88Gy) and extended pelvic irradiation GI toxicity was low. Late GU toxicity was acceptable and the biochemical control rate was excellent.

C057

SELF-REPORTED ACUTE INTESTINAL TOXICTY FROM IMRT-WPRT IN THE RADIATION TREATMENT OF PROSTATE CANCER. RESULTS OF AN OBSERVATIONAL STUDY ON 313 PATIENTS

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Aims: The ongoing multicenter observational study IHU WPRT TOX (AIRC IG14603, NCT02803086) assesses the Intestinal, Hematologic and Urinary toxicity from WPRT in the radical, adjuvant or salvage RT treatment of prostate cancer. The Inflammatory Bowel Disease Questionnaire (IBDQ) is used to evaluate RT-induced Intestinal Toxicity (IT): it explores 10 Bowel symptoms and their possible detrimental effect on Emotional, Social and Systemic Domains. The responses are scored from 7 (best function) to 1 (worst). This analysis focuses on acute IT.

Methods: pts treated with conventional fractionation or moderate hypofractionation were included. Static-field (SS) IMRT, Tomotherapy (TOMO) and VMAT were allowed. IBDQ was completed at baseline, at RT mid-point and end. For this analysis a worsening in single bowel symptoms ≥3 points was set as endpoint for IT definition. This worsening corresponds to 50% of the total possible score, which could be of interest from a clinical perspective. The largest IBDQ worsening between mid/end RT was considered. Associations between IT and patient/treatment related factors were evaluated through logistic regression (LR). Further analyses were performed to identify the symptoms more tightly associated with detriment in Social, Emotional and Systemic domains.

Table 1a.

Bowel symptoms – evaluation during/end of RT			
Symptom	*No. Patients without moderate/severe worsening*	*No. Patients with moderate/severe worsening*	*% Patients with moderate/severe worsening*
Frequent bowel symptom	141	151	51.2
Loose bowel movement	193	98	33.7
Abdominal cramp	260	32	11.0
Abdominal pain	258	33	11.4
Gas passage	225	61	21.3
Abdominal bloating	238	48	16.8
Rectal bleeding	258	27	9.5
Urge to defecate	227	63	21.7
Accidental soiling	266	25	8.6
Nausea & Feeling sick	270	22	7.5
Quality of Life Domains			
Domain	*No. Patients without moderate/severe detriment*	*No. Patients with moderate/severe detriment*	*% Patients with moderate/severe detriment*
Emotional	267	7	2.6
Social	257	20	7.2
Systemic	278	10	3.5

Results: 313 pts having the complete set of IBDQs and were considered. 8% received SS-IMRT, 42% TOMO and 50% VMAT. The median EQDQ2 (=3Gy) dose to the prostate/prostatic bed was 72.58Gy, that to PLN/PLNA 50Gy. Rates of large worsening for each symptom are reported in Table 1a. SS-IMRT was associated to an increased risk (OR≈0.3, p=0.01÷0.05, as compared to VMAT/TOMO) of abdominal pain, cramps, rectal bleeding and nausea&feeling sick. In addition the volume of lymph-nodal PTV (median 1020cc, range 338-1606) was associated with an increased risk of abdominal pain and cramps (OR≈1.2 for 100cc, p=0.01÷0.05). The results of multivariable analysis pertaining to QoL domains are reported in Table 1b.

Table 1b.

DETRIMENT in SOCIAL domain		
Variable frequent bowel symptom loose bowel movement	*Odds Ratio*	*p-value*
	1.5	0.007
	1.5	0.007
DETRIMENT in EMOTIONAL domain		
Variable rectal bleeding	*Odds Ratio*	*p-value*
	1.8	<0.001
DETRIMENT in SYSTEMIC domain		
Variable abdominal pain nausea&feeling seek	*Odds Ratio*	*p-value*
	2.0	0.001
	1.4	0.05

Conclusions: Even in the era of modern IMRT, WPRT-induced IT is non-negligible, symptoms rates ranging 9-50%. Extended WPRT fields are related to increased abdominal pain/cramps, while RT technique

impacts abdominal pain, cramps, rectal bleeding and nausea, as a possible consequence of the reduced ability of SS-IMRT in sparing bowel volumes receiving 40-50Gy. Social domain is highly influenced by frequent bowel movements and loose stool, while rectal bleeding impacts Emotional wellbeing.

C058

HOW TO SELECT PATIENTS WITH UNEXPECTED URINARY TOXICITY PROFILES AFTER RADIOTHERAPY FOR PROSTATE CANCER

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Aims: Predictive models of acute urinary toxicities for patients (pts) treated with radiotherapy (RT) for prostate cancer (PC) have been recently developed. They include clinical and dose variables, but do not consider patient genetic characteristics. Before going through very expensive genetic analyses it is important to select patients who showed unexpected toxicity profiles. In this work we show a method to select these patients.

Methods: We considered the DUE01 patients treated with radical RT for PC with conventional or moderated hypo-fractionation (2.2-2.7 Gy/fr). A multivariable logistic model predicting severe worsening of at least 10 points (delta IPSS>=10) in the International Prostate Symptom Scores (IPSS) at the end of RT was considered and applied to this population.[1] For each patient, we calculated the predicted toxicity risk starting from 8 variables: neoadjuvant hormone, planning target volume, absolute weekly DSH at 8.5 Gy and its interaction with cardiovascular drugs, age, hypertension, BMI and use of 5-alpha-reductase inhibitors. The distribution of residuals (observed toxicities – predicted toxicity probabilities) was used to select patients whose toxicities were not correctly predicted by the model. That is, patients who showed toxicity but had very low predicted probabilities or, vice versa.

Results: 392 pts were considered and in Figure 1 we show the histogram of their residuals. The model accurately predicts the patients who did not show toxicity. Indeed 289/392 (74%) pts did not show toxicity (observed toxicity = 0) but had a low predicted risk of toxicity (<30%), see central part of Figure 1. In addition, there were no patients without toxicity and a high predicted risk (>50%), see the empty left part of Figure 1. However, the model seems to fail in predicting a group of 39/392 (10%) radiosensitive patients who had toxicity after RT (observed toxicity = 1) but had a very low predicted risk (<20%).

Conclusions. A model with clinical and dose variables for predicting acute worsening of urinary symptoms was considered. We showed that it accurately predicts radioresistant patients but it underestimates the radiosensitive ones. Probably, this might be due to the missing of some important factors in the model that can be related with the patient genetic component. The radiosensitive patients who had very low predicted risk will be the first ones to be selected for future genetic investigations.

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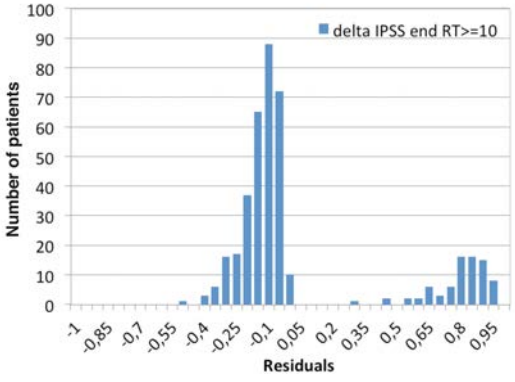

Figure 1.

Reference

F. Palorini et al. 2016

C059

ABITUDE: A PROSPECTIVE REAL LIFE STUDY EVALUATING ABIRATERONE ACETATE PLUS PREDNISONE (AAP) FOR METASTATIC CASTRATION RESISTANT PROSTATE CANCER (MCRPC)

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Background. Due to the heterogeneity of the mCRPC population, we aimed to describe the transferability of pivotal trials outcomes in routine clinical practice.

Methods: ABItude is a prospective observational study conducted in 50 centres of oncology, urology and radiotherapy in Italy. Patients are consecutively enrolled at the start of AAP therapy and followed up for 3 years. The main objective is to describe the effectiveness of AAP for the treatment of mCRPC post-ADT patients in clinical practice (i.e. proportion of patients with ≥ 50% PSA decline, progression-free survival, and duration of clinical benefit). Secondary objectives include: AAP safety profile, quality of life (EuroQol-5D and Functional Assessment of Cancer Therapy–Prostate (FACT-P) questionnaires), pain (Brief Pain Inventory (BPI) and opioid use, treatment adherence, overall survival.

Results: Baseline characteristics of the first 220 enrolled patients are here described. Median age was 77 years (range 56-92), 38% had ≥80 years. 51% had Gleason score ≥ 8; ECOG PS was 0 in 56% of patients, ECOG 1 in 37.3% and ECOG 2 in 4%. At enrolment, 67% of patients presented with comorbidities: cardiovascular disorders were diagnosed in 57% of patients with hypertension (50%) the most common. Other relevant comorbidities were hypercholesterolemia (12%), diabetes (11%), CNS disorders (6%), and chronic renal failure (4.1%). Median PSA at enrolment was 10.5 ng/ml (range 0-2793). Metastases localization was bone (66%), lymphnodes (53%), and viscera (5.5%). Among patients receiving ADT as a manipulation prior to AAP in mCRPC setting, 52% of them had received only 1 ADT line. Only 20% of patients started treatment due to biochemical progression, 67% due to radiographic progression, only a minority started abiraterone due to clinical progression (5.4%) or all of the above (7%). Median BPI worst pain over last 24 hours was 2 (0-10). Median EuroQol VisualAnalogScale was 60 (0-100).

Conclusions. Post-ADT mCRPC patients treated with abiraterone acetate plus prednisone mirror the main characteristic of advanced prostate cancer patients in real life. An heterogeneous population with multiple comorbidities has been enrolled. The ABITUDE study will describe prospectively the outcomes of AAP treatment in a real-world non selected population.

Funding: The study was sponsored by Janssen-Cilag

C060

TRIMODALITY TREATRMENT (TMT) IN NON METASTATIC MUSCLE INVASIVE BLADDER CANCER (MIBC): DO WE NEED MORE EVIDENCE FOR CONTINUING NOT TO OFFER AN ALTERNATIVE TO CYSTECTOMY? THE GROWING EXPERIENCE AT IEO

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Aims: Despite the lack of randomized trials, the TMT approach in MIBC represents a valid and effective alternative for highly selected patients (pts) who refuse cystectomy and decide to preserve their bladder and its functionality, obtaining similar oncological outcomes in terms of progression free survival and overall survival compared to surgery. The aim of this study is to update our data regarding the feasibility, toxicity profile, and tumor outcomes of a bladder preservation curative treatment in non-metastatic MIBC.

Methods: A retrospective analysis was conducted on pts affected by transitional bladder cancer staged T2c N0 M0, who refused cystectomy and were treated with a curative approach in our Institute from 2006 to 2016. All cases were discussed at multidisciplinary urologic tumor board. The standard bladder preservation scheme included maximal transurethral resection of bladder tumor (TURBT) and combination of radiotherapy (RT) and platinum-based chemotherapy (CT), followed by endoscopic evaluation, urine cytology, and instrumental evaluation. Gastrointestinal (GI) and genitourinary (GU) toxicity were assessed according to RTOG/EORTC grading score.

Results: Eighteen pts fulfilled the inclusion criteria. The average age was 65 (range 42-80 yrs). Seventeen patients completed the whole therapeutic program (a bimodal treatment for one patient, unfit for CT). The RT included the bladder (with a median dose of 56 Gy), pelvic lymph nodes (with a median dose of 49 Gy) and a boost on the site of previous tumor (with a median dose of 62 Gy) with a concomitant administration of a weekly platinum-based CT (cisplatin 20 mg/m^2 or carboplatin). Median follow-up is 16 months (range 6-101 mos). At the updated time of analysis 14 pts (78%) are alive with no evidence of disease and with a bladder intact disease free-survival of 100% among them , two patients (11%) died for other causes, and 2 patients had

persistent/recurrence local disease. Only one patient underwent salvage cystectomy after recurrence. None of the pts developed severe urinary or intestinal acute toxicity. All pts have a follow-up > 6 mos and no cases of severe late toxicity were reported (No grade 2 GU or GI). Even hematological CT-related toxicity was acceptable in all the pts with no need to interrupt the treatment.

Conclusions: Based on our data TMT approach, including a combination of maximal TURBT, radiotherapy and chemotherapy for MIBC, is well-tolerated and might be considered a valid and feasible option in fit patients who refuse radical cystectomy (80% intact-bladder disease-free survival at 5 years). Patients selection and a multidisciplinary discussion involving urologists, medical and radiation oncologists remain fundamental elements for proposing this kind of approach.

C061

LOCALLY ADVANCED NON-SMALL LUNG CANCER (NSCLC): THE USE OF SINGLE PHOTON EMISSION COMPUTED TOMOGRAPHY (SPECT) LUNG PERFUSION SCANS IN RADIOTHERAPY PLANNING

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Aims: Radiochemotherapy is the standard of care of locally advanced non-small lung cancer (NSCLC). Radiation-induced normal tissue toxicity is a dose-limiting complication. The incidence of radiation pneumonitis (RP) is dose and volume dependent, and it is related to mean lung dose (MLD). Single Photon Emission Computed Tomography (SPECT) lung perfusion scan, that provides us information regarding lung function, can be useful in the evaluation of more tailored radiotherapy (RT) treatments and lung toxicity, reducing the volume of Functional Lung (FL) irradiated. Methods: We selected 11 patients (7 males, 4 females, median age 69) affected by NSCLC (adenocarcinoma, squamous cell carcinoma); one patient underwent concomitant radiotherapy, 10 sequential chemo-radiotherapy. All patients underwent planning computerized tomography (CT) and lung perfusion SPECT. RT volumes were delineated on the CT scan; FL was defined using co-registered SPECT images. The CT and SPECT scans were co-registered to generate 2 plans, one based only on CT images alone and one with co-registered SPECT scans. For each RT plan we evaluated the MLD and the V20/30 constraints using 2 reference volumes: Total Lung less PTV, planning the treatment on CT images, and FL, using SPECT-CT co-registered images for planning. Results: Four patients were treated with Intensity Modulated Radiation Therapy (IMRT) and 7 patients underwent three-dimensional conformal radiation therapy (3-DCRT). All patients received RT with a median dose of 57,6 Gy in 2 Gy per fraction, range 50-60 Gy. SPECT guided RT planning provides superior lung sparing of both anatomical and functional volumes as compared to the conventional-anatomic planning: we observed a reduction of 2.5 Gy of MLD in FL volume compared to Total Lung less PTV volume; in addition, the volume of lungs receiving 20 Gy was reduced by 348 cc in FL volume vs Total Lung less PTV volume. Our follow up is too short for statistic analysis in terms of late toxicity: 6 patients performed a 3 months follow up, 2 patients were evaluated after 6 months. In 4 patients the results of lung perfusion SPECT performed during follow-up were nearly similar to the basal ones. Clinically, to date only 3 patients presented G2 RP according to RTOG at 3 months after the end of RT. Conclusions: Functional parameters may be useful to guide RT planning in order to provide a more tailored to lung functionality planning and to reduce the risk of late radiation-induced toxicity

C062

DO EGFR, KRAS AND ALK MUTATIONS IMPACT THE RESPONSE TO RADIOSURGERY IN PATIENTS WITH 1-3 BRAIN METASTASES FROM LUNG CANCER ADENOCARCINOMA (ADK)? A MONOINSTITUTIONAL RETROSPECTIVE ANALYSIS

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Aims: Aim of the study was to evaluate outcomes and correlation to molecular status of exclusive radiosurgery (SRS) using IG-IMRT with Tomotherapy® with a non invasive approach in patients (pts) with brain oligometastases (O-MTS) from lung cancer adenocarcinoma.

Methods: Between 2008 and 2016 68 pts with brain O-MTS from lung Adk underwent SRS.Thirty-nine pts were male, while 29 female. Mean age was 65. Fourteen pts were in RPA class 1,54 pts were in RPA class 2. Primary tumor was histologically-confirmed for all pts before being submitted to SRS. Molecular assessment (KRAS, EGFR,ALK status) was available in all pts. At time of SRS brain was the only site involved in 46pts, while 22 had also extracranial disease. Pre-SRS MRI showed supratentorial lesions in 51pts, 11 had subtentorial disease while 6 pts had both. Forty-eight pts had only 1 brain lesion, 14 had 2 and 6 had three. All pts underwent single fraction SRS using Tomotherapy®, median dose delivered was 20 Gy (ICRU83).

Results: After a mean follow up of 14.4 months, 17 pts were alive, whereas 51 pts had died.Complete

response was demonstrated in 4 pts, partial response in 38, stable disease in 11 and progression of disease in 11 cases (in 4 pts it was impossible to evaluate response to treatment due to a fast worsening of the general conditions). Overall response rate was 78%. One and two-years overall survival (OS) was 46.1% (±6,2%ES) and 29.9% (±5.9%ES), respectively. At the same interval local control was 54.3% (ES±7.4) and 33.1%(ES±8.0) and progression-free survival was 26.4% (ES±5,5) and 13.7% (ES±4,5%). Thirty-three pts showed intracranial relapse while 76.4% pts experienced extracranial progression. Worse outcomes in terms of OS were observed for those pts with K-ras mutation, while KRAS wild-type pts seem to show a better 1 year LC compared to those expressing genetic mutation (53% Vs 31) Four pts developed symptomatic radionecrosis.

Conclusions: SRS using IG-IMRT with Tomotherapy® proved to be a feasible "non invasive" approach for pts with brain O-MTS from lung Adk and a good prognostic score. Molecular assessment may allow a better selection of pts who may benefit from treatment with targeted therapy even in a concurrent setting.

C063

EFFICACY AND SAFETY OF STEREOTACTIC RADIOTHERAPY (SRT) IN ONCOGENE ADDICTED ADENOCARCINOMA CONCURRENTLY TREATED WITH TYROSINE-KINASE INHIBITORS (TKIS)

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Aims: Fifteen-twenty percent of stage IV lung adenocarcinoma are treated with targeted therapies. In natural history of stage IV disease, radiotherapy is required and SRT is more and more useful to control small lesions. The aim of our retrospective study is to evaluate outcomes and toxicity in EGFR-mutated and ALK-rearranged patients who underwent SRT associated with systemic treatment with Tyrosine Kinase Inhibitors (TKIs). Progression free survival (PFS) and acute toxicity were the primary endpoints, while Overall Survival (OS) was the secondary one.

Methods: Twenty-seven stage IV oncogene-addicted lung adenocarcinoma were treated with SRT between 2013 and 2016 in our department. For the aim of the study, we considered only patients on TKIs treated with SRT with thirty days as maximum interval between the two treatments. Median age at SRT start was 67 years (range: 45-77). Eleven patients were male and 16 female. Sixteen patients (59%) had EGFR mutation (deletion of exon 19 was the most frequent) and 5 (19%) patients had ALK rearrangement. Six (22%) patients, that were treated with Erlotinib apart from EGFR mutational status, were considered exclusively in the analysis of toxicity profile. Median TKIs treatment duration was 17 months. Main indications to RT were oligoprogression in 24 patients (89%) and palliation after poliprogression in 3 cases (11%). Lung was the main site for SRT (41%), followed by central nervous system (33%).

Results: Median follow-up was 18 months (range: 2-41). SRT was well-tolerated with only grade 1/2 acute toxicity reported for 3 cases (G2 asthenia in 2 patients and G1 dyspnea in 1 patient). No severe G3 acute toxicities were described. In the subgroup of the 21 patients with EGFR mutation or ALK rearrangement, 1-year PFS was 43% and 1-year OS was 67%.

Conclusions: SRT appears to be a safe and efficacious therapy for patients with metastatic lung adenocarcinoma systemically treated with TKIs. Despite variable doses and fractionations applied for various sites, our preliminary analysis in terms of PFS was satisfactory with acceptable toxicity profile.

C064

RETROSPECTIVE EVALUATION OF CYBERKNIFE® IN THE TREATMENT OF LUNG LESIONS: CLINICAL OUTCOME AND TOXICITY PROFILE – UPDATED RESULTS

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Aims: LOT (lung optimized treatment) is an evolution in Cyberknife® technology which allows treatment of lung cancer without invasive fiducial implantation procedures. The aim of this analysis was to evaluate the technical feasibility, toxicity profile and clinical outcome.

Methods: Between 1/2014 and 10/2016 115 patients (pts) (M/F 79/36) were treated with Cyberknife® using LOT at European Institute of Oncology. The median patient age was 72.6 years (range 31.8-90.3). Treated lesions were 123, 57 with histopathological confirmation (49 primitive pulmonary cancer, 8 pulmonary mets), 68 were untyped tumor. A total of 105 pts treated a single lesion, while 10 pts treated multiple target lesions. For 5 pts (6 lesions) treatment using LOT was a re-irradiation for a recurrence in field. Concomitant therapy was administered in 7 pts. Three tracking methods were used: 0-View tracking method (treats an ITV using Xsight Spine tracking for patient alignment) in 68 pts, 1-View tracking method (tracks targets that are visible in only one X-ray image) in 33 pts, 2-View tracking method (tracks targets visible in two X-ray images) in 22 pts. The treatment was performed by a median dose/fraction of 15 Gy (range 4-18), with a

median isodose of 80% (range 50-85). The median PTV was 24.5 cc (range 2.3-195.2). Toxicity was evaluated by RTOG/EORTC and CTCAE Version 4.1. Tumor response was evaluated with RECIST V1.1 guideline.

Results: Preliminary results in a sample of 53 pts are as follows; median follow up was 5.1 months (range 1- 15.4). Acute toxicity (within 6 m.) was observed in 21 of 44 pts with follow-up (47.7%): according to RTOG/EORTC scoring criteria was observed only G1 and G2 grade toxicity, no G3 and G4; in CTCAE Version 4.1 were also observed two cases of G3 grade toxicity. Late toxicity (after 6 m.) was observed in 10 of 19 pts with follow-up (52.6%): according to RTOG/EORTC scoring criteria was observed only G1 and G2 grade toxicity, no G3 and G4; in CTCAE Version 4.1 was also observed one case of G3 grade toxicity. According to RECIST V1.1 guideline complete response, partial response, stable disease and progressive disease was observed in 23.9%, 26%, 43.5% and 4.3% respectively. The study is still ongoing and final results are expected soon.

Conclusions: This first analysis demonstrated high feasibility and minimal toxicity of LOT in lung cancers. Promising response rates have been registered. Further studies are necessary in order to confirm our Results:

C065

USEFULLNESS OF STEREOTACTIC RADIATION THERAPY FOR THE TREATMENT OF REMNANT DISEASE AFTER 3D CONFORMAL RADIATION THERAPY IN PATIENTS WITH PULMONARY CARCINOMA

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Aims: to evaluate local control of disease and toxicity of stereotactic body radiation therapy (SBRT) after 3D conformal RT (3D-CRT) in patients affected by residual disease from pulmonary carcinoma (PC).

Methods: We reviewed patients treated for non small cell lung cancer in our Department. We evaluated acute and late toxicities (primary end-point) and local control disease (secondary end –point).

Results: Nine consecutive patients (8 M and 1 F, mean age 67.6 ± 12.6 years, range 43 - 86) with PCs [8 non-small cell lung carcinomas (NSCLCs) and 1 SCLC] involving right lung (4 pts) and left lung (5 pts), underwent SBRT for remnant disease after 3D-CRT due to PCs from 2012 to 2017 at our University Hospital with a median dose of 21 Gy in 3 fractions delivered with linear accelerator equipped with robotic arm. Previous treatment consisted in 3D-CRT at the therapeutic dose of 60-66 Gy in 30-33 fractions. Four patients underwent CHT in association with RT, 1 discontinued CHT because of haematological toxicity and the remaining 4 received only RT (1/4 because of impaired renal function). Patients were followed-up with Computed Tomography (CT) examinations every three months after SBRT. RECIST criteria 1.1 were used to assess response. In cases of equivocal findings, response was evaluated with 18F-fluorodeoxyglucose (18F-FDG) Positron Emission Tomography/Computed Tomography (PET/CT) was used to evaluate response. Patients were followed-up for a median of 24 months. 7/9 patients reached at least 2-year follow-up. Among them who reached two-year follow-up, 5 patients were alive and 2 died because of progressive disease: 2/5 showed partial response (PR), 2/5 stable disease (SD) and 1/5 progression of disease (PD) due to brain metastases. At three-year follow-up, 2 patient developed PD. Mean overall survival was 29.4 months. Only 1 female patient, alive after five years, had pulmonary fibrosis. No other additional toxicities were found in our patients.

Conclusions: Our study has demonstrated that in patients undergoing SBRT for residual disease after 3D-CRT, SBRT is well tolerated with a significant local control of disease. Further studies are warranted and SBRT should be considered in this set of patients.

C066

RADIATION THERAPY IN LOCALLY ADVANCED LUNG CANCER PATIENTS: CAN ACUTE RADIATION PNEUMONIA EVENTS CAUSE EARLY STOPPED TREATMENTS?

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Aims: To assess the rate and degree of observed acute pulmonary toxicity in locally advanced lung cancer patients, treated with or without concurrent chemotherapy.

Methods: Locally advanced lung cancer patients underwent concomitant radio-chemotherapy or, according to patients' performance status, exclusive radiotherapy. During treatment, weekly CT scans and clinical evaluations were performed and, if occurred, radiation pneumonitis was graded according to the National Cancer Institute Common Toxicity Criteria (vers. 4.02).

Results: Between January 2015 and December 2016, 126 patients [93 male (73.8%), 33 female (26.2%); median age 66 years (range 43-85); histologically 55 adenocarcinoma (43.7%), 45 squamous cell (35.7%), 23 small-cell lung cancers (18.2%), 2 pulmonary sarcoma (1.6%), 1 without histological diagnosis (0.8%)] underwent concomitant radio-chemotherapy (91%) or exclusive radiotherapy (9%). Mean radiotherapy dose delivered was 52,53 Gy. In particular, 48 patients (38%) were treated with 3D-CRT technique, 27 patients (21.5%) with VMAT technique, 50 patients

(39.7%) with Hybrid 3D-VMAT technique, 1 patient (0.8%) with Hybrid 3D-IMRT technique. Acute pulmonary toxicity (CTCAE scale G ≥2) was reported in 9 patients (7%): in particular 6 grade 2 acute pulmonary toxicities (4.7%) occurred, 1 grade 3 toxicity (0.8%), 2 grade 5 toxicities (1.6%). Acute pulmonary toxicity (CTCAE scale G ≥2) occurred at a mean radiotherapy dose of 41.7 Gy: 7 patients (5.6%) stopped radiation treatment, the other 2 patients underwent continuously radiation therapy.

Conclusions: Concomitant radio-chemotherapy or exclusive radiotherapy in locally advanced lung cancer patients is a well tolerated treatment, that causes a low rate of early stopped treatments, with encouraging clinical Results:

C067

LUNG CANCER RE-IRRADIATION BY SBRT, SINGLE INSTITUTIONAL EXPERIENCE

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Aims: Lung cancer is one of the most prevalent malignancies worldwide. Frequently, after a primary treatment with radiotherapy the tumor can relapse. SBRT is a chance to give a re-irradiation limiting the toxicity. With this technique we have high dose on the target, sparing the surrounding healthy tissues. Aims of this study are to evaluate the benefits in term of Local Control (LC), Progression Free Survival (PFS) and Overall Survival (OS) and the risks in term of toxicity.

Methods: From 2011 to 2016, 14 patients with lung cancer underwent re-irradiation by SBRT. The total of re-irradiation was 16, eleven (69%) of these were performed on the same area of previous PTV, 5 (31%) were re-radiated in the same lung, but in a different area. The medium volume was 19.43cc (range: 3-47 cc). Four lesions (25%) received one fraction of SBRT, three (19%) had a total dose of 30 Gy and one (6%) 23 Gy. Twelve lesions (75%) received FSBRT. Three lesions (19%) received 40 Gy in 5 fractions, 4 lesions (25%) 50 Gy in 5 fractions, 3 lesions (19%) 45 Gy in 3 fractions and 2 lesions (12%) 54 Gy in 3 fractions. For previous treatment, we had 10 patients (71%) treated with SBRT with a medium dose of 44 Gy (range: 30-50 Gy in 1-3 fractions), 4 lesions (29%) with EBRT with a medium dose of 44 Gy (range: 50-60 Gy in 25-30 fractions). The median time from the first and second treatment was 13.5 months (range: 6-47 months). The toxicity was evaluated with CTCAE v4 scale.

Results: The local control was reached in 12 out of 16 lesions re-irradiated (75%). At last follow-up, eight (57%) of 14 patients were free from progression disease. The median interval of PFS was 10 months (range: 1-42 months). At last follow-up, 9 patients (64%) out of 14 were alive. The median interval of overall survival was 15 months (range: 1-69 months). The median time of follow-up for patients alive was 9 months (range: 1-27months). In our study we found acute and late toxicity ≤ Grade 3.

Conclusions: Re-irradiation by SBRT is a chance of treatment in the recurrence of lung cancer, with good results in term of Local Control and low toxicity. More studies with more patients and a longer follow-up are necessary to define the better doses and fractionations.

C068

FDG-PET/CT GUIDED DOSE ESCALATION MODERATELY HYPOFRACTIONATED IMAGE-GUIDED HELICAL IMRT FOR PROGRESSIVE MALIGNANT PLEURAL MESOTHELIOMA IN PATIENTS WITH INTACT LUNGS

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Objectives: NCCN guidelines allow adjuvant IMRT after Pleurectomy/Decortication(P/D), in pts with intact lungs. To present the outcomes of our protocol of moderately hypofractionated Image-Guided helical IMRT (RT) with/without simultaneous integrated boost(SIB) on FDG-PET positive areas(BTV), for pts with progressive Malignant Pleural Mesothelioma after previous treatments(chemotherapy+/- surgery), and intact lungs.

Methods and Materials: From May 2006 to April 2014, 51 pts with median age 68.8(38.6-82.0) years, 41 men and 10 women, were treated. The histology was epithelioid in 43 pts and sarcomatoid in 8, of the left pleura in 25 and right pleura in 26 pts. The initial stage was: I in 11 pts, II in 14 pts, III in 17 pts and IV in 9 pts. Chemotherapy was prescribed for 46 pts: for 33 up to, and for 13 more than, 6 cycles. Eighteen pts had P/D and 33 talc pleurodhesis. A total dose of 56 Gy/ 25 fr was prescribed to the whole pleura for all pts and simultaneous integrated boost up to 62.5 Gy on PET positive volumes was used in 38 pts.

Results: Median survival from diagnosis was 25.8(8.4-99.0) months, and was 5.9(1.2-50.5) months from the beginning of salvage RT for pts treated without SIB and 10.9(1.7-73.5) months with SIB. Only one patient, treated with SIB, was alive at the 05/2017 follow up, 73.5 months after the end of RT. Ten pts died within 3 months of the beginning of RT, 60,8% of pts lived more than 10 months, 31.4% of pts more than 20 months, 11.8% of pts more than 30 months and 5.9% of pts more than 50 months. One patient died three weeks after the end of therapy, with fever and worsening dyspnea, despite the antibiotics and oxygen prescribed by the ambulance doctor. Three other G2 and 1 G3 acute pneumonitis were registered. Only one patient,

with type 2 Diabetes, died with CT evidence of bilateral actinic pneumonia and without progressive disease, 6.9 months after the end of RT. Two other G2 and 7 G3 late pneumonitis were registered, 3 with limited duration of oxygen therapy prescription.

Conclusions: With salvage FDG-PET/CT guided IG- IMRT in pts with progressive MPM similar median survival was obtained to pts treated with extrapleural pneumonectomy or P/D and adjuvant chemotherapy and radiotherapy(Rosenzweig *et al*., Int J Radiat Oncol Biol Phys 2011). G≥3 late pneumonitis rate and fatal toxicities are similar to other recent published series, but longer median survival was obtained with FDG-PET guided dose escalation.

C069

INCORPORATING 18FDG-PET-DEFINED PELVIC ACTIVE BONE MARROW IN THE AUTOMATIC TREATMENT PLANNING PROCESS OF ANAL CANCER PATIENTS UNDERGOING CHEMO-RADIATION

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Aims: To investigate whether the incorporation of 18FDG-PET into the automatic treatment planning process may be able to decrease the dose to active bone marrow (BM) for locally advanced anal cancer patients undergoing concurrent chemo-radiation (CHT-RT).

Methods: Ten patients with locally advanced anal cancer were selected. Bone marrow within the pelvis was outlined as the whole outer contour of pelvic bones or employing 18FDG-PET to identify active BM within osseous structures. Four treatment planning solutions were employed with different automatic optimization approaches toward bone marrow. Plan A used iliac crests for optimization as per RTOG 05-29 trial; plan B accounted for all pelvic BM as outlined by the outer surface of external osseous structures; plan C took into account both active and inactive BM as defined using 18FDG-PET; plan D accounted only for the active BM subregions outlined with 18FDG-PET. Dose received by active bone marrow within the pelvic (ACTPBM) and in different subregions such as lumbar-sacral (ACTLSBM), iliac (ACTIBM) and lower pelvis (ACTLPBM) bone marrow was analyzed.

Results: A significant difference was found for ACTPBM in terms of Dmean (p=0.014) V20 (p=0.015), V25 (p=0.030), V30 (p=0.020), V35 (p=0.010) between Plan A and other plans. With respect to specific subsites, a significant difference was found for ACTLSBM in terms of V30 (p=0.020), V35 (p=0.010), V40 (p=0.050) between Plan A and other solutions. No significant difference was found with respect to the investigated parameters between Plan B,C and D. No significant dosimetric differences were found for ACTLSPBM and ACTIBM and inactive BM subregions within the pelvis between any plan solution.

Conclusions: Accounting for pelvic BM as a whole compared to iliac crests is able to decrease the dose to active bone marrow during the planning process of anal cancer patients treated with intensity-modulated radiotherapy. The same degree of reduction may be achieved optimizing on bone marrow either defined using the outer bone contour or through 18FDG-PET imaging. The subset of patients with a benefit in terms of dose reduction to active BM through the inclusion of 18FDG-PET in the planning process needs further investigation.

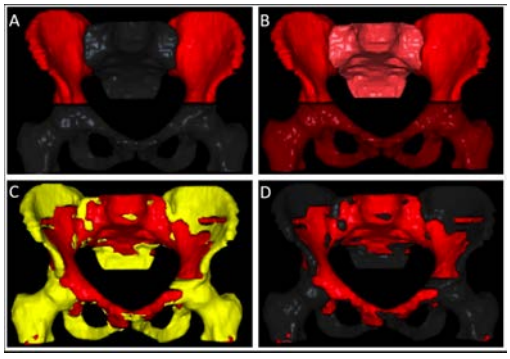

Figure 1.

C070

MARGINAL FAILURES AFTER INTENSITY MODULATED RADIATION THERAPY (IMRT) IN SQUAMOUS CELL ANAL CANCER: NO HIGHER RISK WITH IMRT WHEN COMPARED TO 2D/3D TECHNIQUES

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Aims: Intensity modulated radiotherapy (IMRT) improves tumor control and reduces acute and late toxicities in patients (pts) with anal squamous cancer cell treated with chemoradiation. Nevertheless, an emerging concern is the marginal miss that may occur within the avoided region. The aim of this analysis is to report our records of genital recurrences and marginal recurrences in IMRT treatments and in 2D/3D irradiation.

Methods: Data of pts with anal squamous cancer

cell treated consecutively with IMRT using both dynamic arc (RapidArc®) and Tomotherapy® between 2010 and 2016 at European Institute of Oncology (IEO) were evaluated and compared against data of pts treated from 1999 to 2009 with a 2D/3D technique in the same institution. All pts underwent clinical examination and radiological examination both before and after treatment and during their follow up. The majority of pts underwent concomitant chemotherapy. Tumor response was evaluated with RECIST V1.1 (Response Evaluation Criteria In Solid Tumors) guideline. Pts with marginal misses were identified and analyzed.

Results: Data of 126 pts were evaluated: 68 and 58 pts were treated with IMRT and 2D/3D technique, respectively. In the IMRT group, median dose to tumor and positive lymph nodes, high risk area and low risk area was 56 Gy, 46 Gy and 39.6 Gy respectively. Concomitant chemotherapy was administered in 65 pts. Follow-up was available for 66 pts with a median value of 25 months (range 1-78 months). According to RECIST V1.1 guideline progressive disease (PD) was registered in 11 pts. In particular, in-field recurrence was assessed in 7.4% (5/68) of pts, out-field recurrence in 4.4% (3/68) of pts and concomitant in-field and out-field recurrence in 1.5% (1/68) of pt. Two out of 68 pts (2.9%) had marginal failures, localized at vagina/recto-vaginal septum and left perineal region. In the 2D/3D technique group that was treated following the standard dose 3.4%(2/58) of pts had marginal failures, localized at recto-vaginal septum and perigenital structures. Rate of marginal failures was comparable in IMRT and 2D/3D groups (chi squared test p=0.87).

Conclusions: In this series the use of IMRT for the treatment of anal canal cancer did not increase the rate of marginal failures offering improved dose conformality to the target. However, prospective studies are necessary in order to confirm our Results:

C071

FDG-PET/CT IMAGING FOR TARGET VOLUME DELINEATION IN RECTAL CANCER RADIOTHERAPY: RESULTS OF A PHASE II STUDY

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Aims: The aim of this study is to evaluate if the integration of imaging techniques, such as CT, MRI and PET/CT, can allow the reduction of treatment volumes and avoid the elective nodal irradiation reducing the toxicity without compromising the effectiveness of the treatment.

Methods: Eligible patients had histologically proven locally advanced rectal adenocarcinoma (stage T3 N0-N1, M0) and ECOG performance status 0-1. Staging procedures included CT, MRI and 18F-FDG PET scan. All patients received 3D- conformal radiotherapy, and the CTV included the rectal lesion and the corresponding mesorectum without elective nodal irradiation. The total dose delivered was 50.4 Gy in 1.8 Gy/fx . Toxicity was recorded and scored according to the CTCAE vers 3.0 scale.

Results: Between December 2007 and October 2016, 52 patients (median age 67 years, range 45-85 y) affected by rectal cancer with a II-III stage were enrolled in this trial. The concomitant CT was platinum-based with 5FU/Capecitabine in 32 patients (61,5%) and 5FU/capecitabine in 20 patients (38,5%). The patients showed an excellent compliance to the protocol. Toxicity was evaluated in 50 patients. G1-G2 hematological toxicity was NEU/PLT/HB in 21/14/15 patients (42-28-30%) and G3 anemia in only 2 patients (4%). G3 rectal toxicity/diarrhea occurred in 1 and 3 patients (2%- 6%). Pathological complete response (pT0N0) was in 44% patients with TRG 1 in 48.9% patients. 3y-OS was 89%, 5y-OS 64% with a median survival of 7.5 years and median DFS was 19.6 months.

Conclusions: PET/CT can be an useful tool for target delineation in rectal cancer. This study shows that the reduction of treatment volume, without elective nodal irradiation can lead to a lower toxicity with promising clinical Results:

C072

PERFORMANCE OF DIFFUSION-WEIGHTED MAGNETIC RESONANCE IMAGING AT 3.0T FOR EARLY ASSESSMENT OF TUMOR RESPONSE IN LOCALLY ADVANCED RECTAL CANCER PATIENTS TREATED WITH PREOPERATIVE CHEMORADIATION THERAPY

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Aims: to determine whether changes in apparent diffusion coefficient (ADC) values in locally advanced rectal cancer (LARC) patients, obtained with a MRI performed two weeks after the beginning of chemoradiation therapy (CRT), allow to predict treatment response, and to evaluate if a correlation between those values and tumor histopathologic response exists.

Methods: forty-three patients affected by LARC were treated with CRT and received a 3.0T magnetic resonance imaging with diffusion-weighted sequences before treatment, 2 weeks during and 8 weeks after CRT. ADC values were calculated at each time point and percentage of ADC changes at 2 weeks (ADC during) and after 8 weeks (ADC post) were assessed. All data were correlated to surgical results and histopathologic tumor regression grade (TRG), according to Mandard classification. The ADC values and ADCs of complete responders (CR; TRG1) and non-complete responders (non-CR; TRG 2-5) were compared. A

receiver-operating characteristic curve (ROC) analysis was used to assess the diagnostic accuracy of ADC for differentiating CR from non-CR. The correlation with TRG was investigated using Spearman rank test.

Results: both ADC during and ADC post treatment were significantly higher in CR (33.9% and 57%, respectively) compared to non-CR (13.5% and 2.2%, respectively) group ($p=0.006$ and $p<0.001$, respectively). ROC analysis revealed the following diagnostic performances: ADC during: AUC 0.78 (0.08 standard error), $p=0.004$, cut-off 20.6% (sensitivity 75% and specificity 76.5%); ADC post: AUC 0.94 (0.04 standard error), $p\leq0.001$, cut-off 22% (sensitivity 95% and specificity 82.4%). A significant moderate and good negative correlation was found between ADC during and ADC post and TRG ($r=-0.418$, $p=0.007$; $r=-694$, $p\leq0.001$, respectively).

Conclusions: ADC at 2 weeks after the beginning of CRT is a reliable tool to early assess treatment response, with an appreciable level of sensitivity and specificity.

C073

CONSERVATIVE APPROACH IN LOCALLY ADVANCED RECTAL CANCER: A META-ANALYSIS

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Background: Locally advanced rectal cancer is usually treated with a preoperative approach with radiochemotherapy followed by surgery. Patients obtaining a pathologic complete response have a very favorable long-term prognosis. This study was intended to assess whether major surgery can reduce tumor recurrences and prolong survival of patients with a complete response after radiochemotherapy.

Methods: Computerized literature search was performed to identify relevant articles. Comparative studies reporting the outcomes of non-operative and operative management in patients after neo-adjuvant treatment were reviewed. Data synthesis was performed using Review Manager 5.0 software.

Results: Twelve non-randomized comparative studies with a total of 1812 patients were suitable for analysis. There was no significant difference in overall survival at 3 and 5-year (odds ratio [OR] 1.31; 95%CI 0.64-2.69; $p=0.46$ and 1.48; 95%CI 1.00-2.20; $p=0.50$) and in disease-free survival at 3 and 5 years (odds ratio [OR] 1.20; 95%CI 0.68-2.14; $p=0.53$ and 1.22; 95%CI 0.86-1.74; $p=0.26$, respectively) between LARC patients treated with and without operative approach.

Conclusions: Major surgery does not seem to improve prognosis in patients obtaining a complete response after radiochemotherapy. Clinical trials, using new criteria to identify complete response patients, are needed to recommend non operative approach.

C074

THE NATURAL HISTORY OF PULMONARY MICRONODULES EVIDENCED AT INITIAL CT SCAN IN PATIENTS TREATED WITH NEOADJUVANT RTCT FOR LOCALLY ADVANCED RACTAL CANCER (LARC)

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Aims: The nature of pulmonary micronodules detected at diagnosis in patients affected by rectal adenocarcinoma is not currently clear. In this retrospective study, we analyzed the incidence and evolution of pulmonary micronodules identified at CT scan during the initial staging.

Methods: From January 2008 to March 2015, 146 patients affected by LARC were treated with neoadjuvant radiochemotherapy (RTCT) in Pisa University Hospital. All patients underwent staging examinations including chest CT scan with contrast injection. In this retrospective study, we evaluated the percentage of patients with pulmonary micronodules at diagnosis (excluding calcific micronodules), the size of these and their progression to metastatic disease.

Results: Of the 146 patients treated with RTCT in our department (mean age 61 years), 54.8% had at least one pulmonary micronodule at initial chest CT. The maximum diameter of micronodules ranged between 3 and 14 mm; 56% of these were > 5mm. After a follow-up of 54.8 months, of the 80 patients with pulmonary micronodules at diagnosis, 15 (18.7%) developed pulmonary metastasis, 9 (60%) of whom progressed from pre-existing micronodules. Of the 9 patients with micronodules progression, 7 (77.8%) had nodularity > 5mm in maximum diameter. Of the 66 patients without lung micronodularity, only 6 (9%) developed lung metastasis.

Conclusions: In patients affected by LARC, the nature of the pulmonary micronodules detected by initial CT scan is not currently clear. Analyzing our data, we can conclude that 11% of these lesions tend to become metastasis during the natural history of the disease. These data are in line with those reported in other studies conducted on patients with colonrectal cancer. Comparing the percentage of patients with micronodules who developed pulmonary metastasis (18.7%) with the percentage of patients who developed lung metastasis in absence of micronodularity (9%), we could conclude that pulmonary micronodules represent a risk factor for developing metastasis at this level. These data need further analysis to be carried out on larger cohorts of patients.

C075

NOMOGRAMS DEVELOPMENT IN RECTAL CANCER: AN UPDATE OF A POOLED ANALYSIS OF RANDOMIZED PATIENTS

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Aims: In recent years, several predictive models(PMs) for locally advanced rectal cancer(LARC) to predict follow-up(FUP) outcomes have been developed. Our aim was to update the previous PMs[1], developed for local recurrence, distant metastases and overall survival(OS) at 5 years, based on a more copious pooled set(PS) of LARC patients(pts), longer FUP and more elaborate statistical analysis.

Methods: The PMs were developed using the data of the following LARC trials: Accord 12/0405, EORTC 22921, FFCD 9203, CAO/ARO/AIO-94, CAO-ARO-AIO-04, INTERACT, I-CNR-RT and TROG 01.04. Exclusion criteria(ExC) were: neoadjuvant (Nad) and adjuvant oxaliplatin based chemotherapy(CT), no surgery, short-course radiotherapy(RT), incomplete RT and no Nad RT. We used 20% of the data(stratified per trial) as a validation dataset. Due to different trends of the covariates over the period of the study, an accelerated failure time model was used. FUP(2, 3, 5 and 10 years) for local control(LC), distant control(DC) and OS were used as the model outcome. The variables used in the analysis were age, clinical tumour stage, Nad CT, pathological tumoral stage, pathological nodal involvement, adiuvant CT, surgical procedure, sex and RT dose. Variable selection was performed using a stepwise feature selection, which used Akaike's information criterion(AIC) to determine the optimal subset of covariates. Finally we used nomograms as a visual representation of the PMs developed. The PMs' performance was evaluated using the Area under the Receiver Operating Curve(AUC) as a measure of discrimination on the traning and validation sets and the brier score as a measure of accuracy.

Results: Following ExC, 3609 pts out of 7612 were included in this analysis. The AUC and the Brier scores for each PMs(LC, DC and OS at 2, 3, 5 and 10 years) ranged between 0.69-0.77 and 0.06-0.26 respectively. Nomograms for each outcome(LC, DC and OS) at 2, 3, 5 and 10 years were generated. Furthermore we have reported as an example the nomograms for OS in Figure 1.

Conclusions: Updated models show higher performance (AUC range values between 0.69-0.77) than the models developed in the previous work[1] (AUC range values between 0.68-0.73). Differently to the previous nomograms, developed at a specific timepoint, the new nomograms on LC, DC and OS developed at different timepoints may best fit pts with different characteristics to adapt the therapeutic strategy.

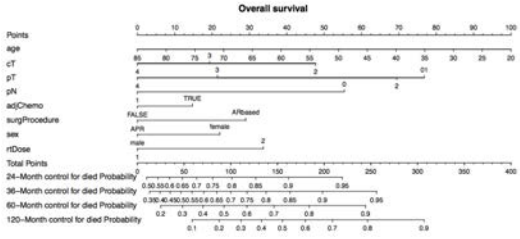

Figure 1.

Reference

1. V. Valentini et al; Journal Clinical Oncology;2011

C076

INFLUENCE OF MAGNETIC RESONANCE IMAGING (MRI) ON THE INTER-OBSERVER VARIABILITY OF GROSS TUMOR VOLUME (GTV) DELINEATION IN PANCREATIC CANCER. PROJECT BY THE AIRO STUDY GROUP FOR GASTROINTESTINAL CANCERS

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Aims: Currently, computed tomography (CT) is the standard for contouring pancreatic tumors for radiation treatment planning. A previous multi-institutional contouring dummy-run study was conducted to evaluate inter-observer variability of Clinical Target Volume (CTV) delineations of two different cases of pancreatic cancer treated by postoperative and preoperative radiotherapy on CT scan. Greater variability was observed for Boost CTV (Gross Tumor Volume, GTV, plus margins) rather than the Elective CTV, in both setting, suggesting that the promotion of contouring guidelines might help to reduce the observational variability. Magnetic Resonance Imaging (MRI) could lead to a better delineation of local tumor extension of pancreatic cancer compared with CT due to its improved soft tissue resolution, improved targeting of the gross tumor volume (GTV), such as other disease sites as prostate, cervix and spinal cord. Since recommendations for contouring of pancreatic cancer using MRI have been recently provided, based on these considerations a new contouring dummy-run study was proposed to evaluate inter-observer variability of GTV delineation using MRI imaging for pancreatic cancer.

Methods: Radiation Italian centers were invited to participate to the proposed study. Two clinical cases about locally advanced and borderline resectable pancreatic cancer were selected by two expert radiologists and two radiation oncologists. MRI scanning was performed on a 3 T. T1 and T2- weighted MRI and CT scan sequences, with or without contrast enhancement, were send to the adherent centers for the GTV and two critical organs at risk (stomach and duodenum) delineation. Recent recommendations for contouring of pancreatic cancer using MRI were also provided.

Results: At the moment, 36 radiation Italian centers joined the study showing interest in it. The study is still ongoing regarding the delineation of required volumes ad inter-observer variability analysis.

Conclusions: The large number of centers that joined to the study confirmed the interest in MRI for GTV delineation in pancreatic cancer. The results are expected to define the impact of MRI inter-observer variability in contouring compared to CT scan.

C077

SBRT FOR LOCALLY ADVANCED PANCREATIC CANCER: RISK-ADAPTED DOSE PRESCRIPTION AND IMAGE-GUIDED DELIVERY

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Introduction: As stated by ASCO 2016 guidelines, Stereotactic Body Radiation Therapy (SBRT) for locally advanced pancreatic cancer (LAPC) represents a treatment option. An accurate treatment planning with risk-adapted dose prescription and the identification of specific constraints for organs at risk (OARs), daily Cone Beam CT (CBCT) as image-guidance, could allow an effective and safe treatment delivery. Here, feasibility and efficacy of SBRT in LAPC treated in our Cancer Care Center are reported.

Table 1. Summary of patient characteristics.

Patients number	**32**
Mean age (range) [years]	66 (39-84)
Gender (M:F)	18:14
Initial T stage (number of patients)	
T2	5
T3	12
T4	15
Tumor location (number of patients)	
Head	24
Body	8
Mean diameter (range) [cm]	4 (2-5)
Mean volume (range) [cm^3]	
CTV	35 (4-98)
PTV	60 (13-142)
Performance Status-ECOG score (number of patients)	
0	15
1	9
2	4
3	4
MRI or PET-CT preRT (Yes:Not)	22:10
Dose: 42-45Gy or 36Gy (number of patients)	16:16

Methods: Between 08/2014 and 01/2017, 32 unresectable LAPC patients underwent SBRT. All patients received Gemcitabine-based chemotherapy before radiation treatment. The clinical target volume (CTV) was identified on CT scan with contrast enhancement as the gross disease and, when available, fusion-image with MRI or PET-CT was used to optimize tissue delineation. An additional margin of 3-5 mm was added for the planning target volume (PTV). The OARs were stomach, duodenum, kidneys, liver and spinal cord. The dose-volume constraints for duodenum and stomach were D1cc <36Gy and D3cc<36Gy, respectively. In order to respect OARs dose-constraints a risk-adapted dose prescription strategy was adopted, choosing between the following schedules: 42Gy or 45Gy in 6 daily fractions (f) with biologically effective dose (BED) >70Gy and 36Gy/6f (BED 57.6Gy), according to ICRU83. SBRT was delivered with volumetric

modulated arc technique (VMAT) using RapidArc and flattening filter-free (FFF) mode. Image guidance was performed by means of CBCT before every treatment session. The patients were evaluated at the end of treatment for acute toxicity and at 3, 6 and 12 months for late toxicity and treatment response.

Results: The main clinical characteristic of patients are summarized in Table 1. At median follow up of 12 months (range 3-31), 18 out of 32 (56%) patients are alive. Although all patients were previously judged as unresectable, 6 out of 32 (19%) underwent surgery after SBRT; all of them received 42-45Gy. Local control at 3, 6 and 12 months was 87%, 62% and 19%, respectively. A total of 12 patients (37%) had an extra-pancreatic progression, 4 cases at 3 months and 8 at 6 months. No cases of ≥G3 acute and late toxicity were reported.

Conclusions: Risk-adapted dose prescription and image-guided SBRT is an effective and safe option for unresectable LAPC: optimal rates of local control and interesting rate of resectability were reported. Further clinical evaluations are warranted.

C078

STEREOTACTIC RADIOTHERAPY IN PANCREATIC CANCER: SYSTEMATIC REVIEW ON PAIN RELIEF

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Aims: Locally advanced pancreatic carcinoma (LAPC) are not amenable to surgery. Radiotherapy (RT) has been reported to reduce pain and stereotactic radiotherapy (SBRT) is considered an emerging RT technique, able to achieve high local control rates with acceptable toxicity. Aim of this paper was to review the impact on pain relief of SBRT in LAPC patients

Methods: A literature search was performed on Pubmed (2000-2017) including prospective and retrospective articles published in English and reporting pain control. A total of 14 studies bearing data on pain control by SBRT in LAPC were found to be suitable for our review. Details on study characteristics, inclusion criteria and treatment are shown in Table 1.

Results: SBRT was delivered with both standard and/or robotic linacs. The delivered SBRT dose ranged from 12 to 45 Gy (median: 31.5 Gy), while the number of fractions ranged from 1 to 6 (median: 3). Twelve of the 14 studies reported various rates of pain relief with 2 studies reporting 48.4% and 81.3% CR rates, respectively. Median overall response rate (CR + PR) was 68% (range: 44%-100%). One study reported no significant pain reduction, while another study reported a significant worsening of pain 2 weeks after SBRT. All studies reported toxicity data. Acute and late toxicity (grade ≥ 3) rates were: 3.3-18.0% and 6.0-8.2% respectively. Reported gastrointestinal symptoms were: duodenal obstruction/ulcer, small bowel obstruction, duodenal bleeding, mucositis, hemorrhage and gastric perforation. Details on treatment outcomes are reported in Table 1.

Conclusions: Further prospective studies on the palliative role of SBRT in LAPC seems justified. These trials should be able to define the optimal dose/fractionation and the best modality of integration with systemic therapies to reduce toxicity and improve palliative outcome. Finally, given the high mortality rate in patients with LAPC, quality of life and particularly pain control should be considered as an end point in future trials on this emerging treatment technique.

C079

AN ATLAS FOR CLINICAL TARGET VOLUME DEFINITION INCLUDING ELECTIVE NODAL IRRADIATION IN DEFINITIVE RADIOTHERAPY OF BILIARY CANCERS

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Aims: Radiotherapy (RT) is a treatment option for advanced biliary tumors, generally combined with sequential and/or concurrent chemotherapy. The use of modern RT techniques requires accurate definition of the Clinical Target Volume (CTV). We recently proposed guidelines to define the nodal CTV in these neoplasms (Marinelli I, et al, 2017). Aim of this study was to propose a CT atlas for CTV definition of biliary tumors candidates to exclusive RT.

Methods: Based on a literature review we defined the margins to be added to the Gross Tumor Volume to include subclinical and microscopic disease. These primary tumor CTV was merged to the nodal CTV, as defined in our previous analysis, to define the final CTV.

Results: An atlas showing the defined CTV was generated on reference CT images illustrating the CTV for intra-hepatic, extra-hepatic, and gallbladder cancers.

Conclusions: This atlas can be used as an aid for CTV definition of biliary tumors and to design prospective studies on RT in these neoplasms.

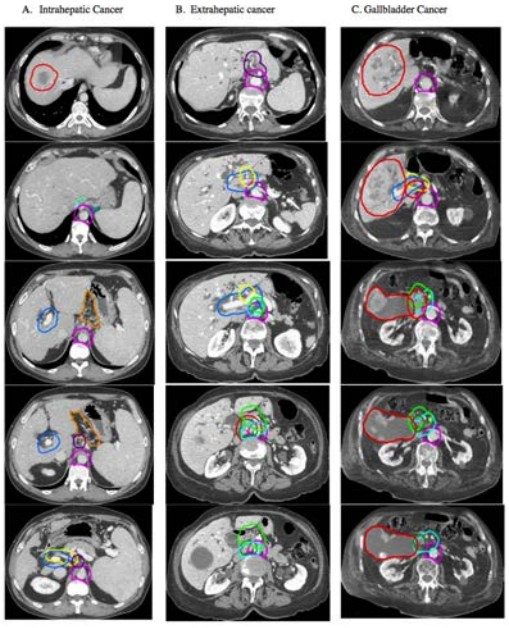

Figure 1. CTV definition for Intrahepatic , Extrahepatic, and Gall Bladder cancer.

C080

PRELIMINARY RESULTS IN PATIENTS WITH ESOPHAGEAL OR ESOPHAGEAL GASTRIC JUNCTION CANCER TREATED WITH NEOADJUVANT CHEMORADIOTHERAPY AND IG-IMRT PET BASED

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Aims: To report our experience in patients (pts) with esophageal (EC) or esophageal gastric junction (EGJ) cancer treated with IG-IMRT PET based.

Methods: pts with histologically proven EC or EGJ were treated according to CROSS study. All pts underwent c-e CT and PET simulation, repeated for restaging. Radiotherapy (RT) consisted in 41.4 Gy in 23 fractions combined to chemotherapy (ChT) with carboplatin and paclitaxel.

Results: From April 2014 to November 2016, 40 pts were treated (F: 8; M: 32), median age at diagnosis: 61 years (45-78), median KPS: 90. Twenty- three pts had adenocarcinoma (57.5%), 16 pts had squamous cell carcinoma (40%), 1 pt had adeno-squamous carcinoma (2.5%). Clinical stage was: T2 (11 pts), T3 (27 pts), T4 (2 pts), N0 (8 pts), N+ (33 pts). The site of tumor was proximal/middle third in 3 pts, middle/middle-distal third in 15 pts, distal third/distal-EGJ/ EGJ in 31 pts. Median tumor length was 4.5 cm (1-15). RT was delivered by Tomotherapy in 24 pts and by VMAT in 16 pts. All pts completed RT. Median cycles of ChT was 5 (2-6 cycles), 63% pts received a full dose of ChT.

The G3 acute haemathological toxicity was: neutropenia in 5% (2pts), lymphopenia in 70% (28 pts). G3 Gastrointestinal toxicity occurred in 12.5% (5 pts). Three pts (7.5%) had bacterial pneumonia (1 pt G5).

Responses: 39/40 pts were available (1 pt early lost). Median time to restaging was 42 days (14-87). CT/PET showed local RP, SD, RC in 17, 17, 15 pts respectively and PD in 7 pts. Median time from CT/RT to surgery was 69 days (15-148). Thirty one pts (77.5%) underwent surgery (8 excluded: 5 for PD, 2 for worsening clinical condition, 1 died; 1 lost) . One pt underwent urgent surgery 15 days after CT/RT because of aorto-esophageal fistula. Post-surgery stage was T0: 3pts, T1: 8 pts, T2: 8 pts, T3: 11 pts, T4: 1 pt; N0: 15 pts, N+: 16 pts. 29/ 31 pts (93.5%) had R0. Mandard TRG was: TRG1: 3 pts (10%), TRG2: 5 pts (16%), TRG3: 19 pts (61%), TRG4: 4 pts (13%). Median OS was 13.9 months. 20/31pts (64.5%) are free from disease at a median follow up of 14.4 months (5.7-33.9). 3 pts had local progression and 8 pts had distant progression at a median time to progression of 10.7 months.

Conclusions: Our data seems to be comparable to CROSS data in term of R0 and toxicity profile. Using IG-IMRT the lymphopenia was the major cause of not

optimal tolerability of ChT and could explain the onset of pneumonia and the difference between TRG responses.

C081

FMECA PROSPECTIVE APPROACH TO INTRAOPERATIVE ELECTRON BEAM RADIOTHERAPY (IOERT) EVALUATION: THE EXPERIENCE OF TRIESTE

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Aims: Failure Mode Effects and Criticalities Analysis (FMECA) represents a prospective method for risk assessment in complex medical practices. Our objective was to describe the application of FMECA approach to intraoperative electron beam radiotherapy (IOERT), delivered using a mobile Linear Accelerator, for the treatment of early-breast cancer as an anticipated boost.

Methods: A multidisciplinary Working Group, including several different professional profiles, was created before the beginning of clinical practice in 2012, with the purpose of writing the Flow Chart and applying the FMECA methodology to IOERT procedure. Several criticalities were identified a priori in the different steps of the procedure and a list of all potential failure modes (FM) was drafted and ranked using the risk priority number (RPN) scoring system, based on the product of three parameters: severity, occurrence and detectability (score between 1 and 5). The actions aimed at reducing the risk were then defined by the Working Group and the risk analysis was repeated in 2014 and in 2016, in order to assess the improvement achieved.

Results: Our activity with IOERT as an anticipated boost started in June 2012. Ninety-four cases have been treated up to May 2016 (46 by the end of 2014 and an additional 40 by the end of 2016). The first FMECA analysis was performed before the start of clinical activity; the risk analysis was then repeated at the end of 2014 and again at the end of 2016. Fifty-one failure modes were identified, which represented the issues prospectively investigated according to the FMECA methodology. Considering a set threshold of 30, the evaluated RPNs show that 33 out of 51 failure modes are critical; 6 are included in the moderate risk class (RPN: 31-40); 16 in the intermediate risk class (RPN: 41-50) and 11 in the high risk class (RPN: > 50). The most critical step concerned the misalignment of the shielding disk, used to protect the normal tissues underneath the target volume, such as the lung and the heart (for the left breast). The introduction of the corrective actions into the clinical practice achieved the reduction of the RPNs in the re-analysis of the FMECA worksheet after two and four years, respectively.

Conclusions: FMECA proved to be a useful tool for prospective evaluation of potential failures in IOERT and contributed to optimize patient safety. Its use, still rather limited in the evaluation of IOERT procedure, should be strongly encouraged.

C082

HIGH DOSE RATE BRACHYTHERAPY FOR CHILDHOOD SOFT TISSUE SARCOMA

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Aims. To evaluate the efficacy of HDR-BT in children undergoing combined modality treatment for STS.

Methods: From September 1998 to December 2016, 58 children (median age 7 years, range 1 to 18) with non-metastatic STS received HDR-BT as part of locoregional treatment at Radiation Oncology Dpt of Veneto Institute of Oncology of Padua. There were 25 males and 33 females, near all (55) had primary lesions, embryonal rhabdomyosarcoma (27) was the most common histological type and extremities were most commonly involved site (19); 10 children had lesions greater than 5 cm in maximum diameter. Surgical margins where positive in 23. Twenty three children have been treated according to the Italian-German cooperative protocol RMS 96 and 35 according to the European EpSSG protocol RMS & NRSTS 2005. Treatment included wide local excision and HDR-BT with or without EBRT. All patients were treated using iridium-192, by Nucletron Microselectron V3 Afterloader. Treatment was started on the fifth day after dosimetry. Fifty three patients have been treated with radical HDR-BT alone, while 5 received a combination of HDR-BT and EBRT. HDR-BT dose has been 36 Gy, in 12 fractions, twice per day, with a minimum interfraction interval of 6 hours, with a 2 day split after the 6th application. All children receiving EBRT have been enrolled in the RMS 96 protocol, therefore they underwent irradiation up to a total dose of 32 Gy in 20 fractions of 1.60 Gy, twice per day, after a HDR-BT boost up to 18 Gy in 6 fractions twice per day. CT simulation has supplanted orthogonal films in BT planning. MRI has been used to delineate differences in soft tissues not readily seen on CT scan. Normal tissues and target volumes have been modeled using contouring on CT-MRI fused images.

Results After a median follow up of 7 years, 52 patients are alive in first CR and 2 are alive after amputation. Two have LR and after developed lung metastasis, 2 have developed nodal and lung metastasis without LR; all of them had died for tumor progression. Patients have tolerated the HDR-BT procedure well and there has been no major acute complications directly related to the procedures.

Conclusions. HDR-BT is an effective modality in

the conservative management of STS in children. The high local control and acceptable toxicity is encouraging. Treatments must be executed carefully, because the short treatment times do not allow any time for correction of errors, and mistakes can result in harm to patients.

C083

LONG-TERM RESULTS OF LOW-DOSE-RATE BRACHYTHERAPY AS MONOTHERAPY FOR EARLY STAGE LOCALIZED PROSTATE CANCER. 10-YEAR OUTCOMES FROM A SINGLE INSTITUTION EXPERIENCE

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Aims: To present survival and toxicities results after a long-term follow up (FU) of a large mono-institutional series of patients treated with Low-dose-rate (LDR) brachytherapy for early localized prostate cancer (PCa).

Methods: from February 2005 to November 2015, 592 cases were retrospectively recruited, but only 430 patients (pts) (from 2005 to 2012) were considered for survival analysis (clinical variables did not differ in the whole series and in the subgroup, Table 1). Based on transrectal ultrasound planning, a I-125 permanent intra-prostatic seeds implantation was performed, delivering 145 Gy total target dose. Post-implant CT-based dosimetry and post-procedure clinical evaluation were checked 1 month after seeds implantation. Subsequently, all pts underwent 3-month/6-month/1-year then annual FU. Toxicities were recorded according to CT-CAE classification v4.0.

Results: Median age 71 years (range 47-81), low- and intermediate-risk PCa (D'Amico Risk classification) 69.3% and 27.4%, respectively. Neoadjuvant androgen deprivation therapy (ADT) was prescribed in 54.1% pts. After a median 71.1 months FU, 8.1% pts relapsed: we recorded 19 biochemical failures (PSA nadir +2 ng/mL), 12 clinical recurrences, 4 distant metastases. 5- and 10-year Progression Free Survival (PFS) was 93.7% and 84.3%. 5- and 10-year Overall Survival (OS) was 92.8% and 85%. 5- and 10-year Disease Specific Survival (DSS) was 99.5% and DSS 97.5%. Univariate analysis showed better DSS and PFS for low-risk PCa (p=0.012 and p=0.009). Mean PSA decreased over time in patients with no evidence of disease (always to ≤1 ng/mL), PFS was better in case of PSA nadir <0.164 ng/mL. Acute urinary symptoms were mostly G1, G2 in 25.9%, G3-4 in 7%. Late urinary toxicity was mostly G1, G2 in 32.6%, G3 in 4.9%. Rectal toxicity: acute G1, 32.4%; G2, 3.9%, G3, 0.2%; late: G1, 22.8%, G2, 2.7%; G3, 0.7%. Neither acute nor late rectal G4 cases were observed.

Conclusions: LDR brachytherapy is a very effective, well tolerated treatment option for early stage PCa. Further dosimetric correlations are granted, along with the evaluation of its role in very low risk cases (data not shown) and in combination with external beam radiation therapy or long-term ADT (intermediate- and high-risk PCa).

C084

INTRACAVITARY APPLICATOR GEOMETRY DURING HDR BRACHYTHERAPY IN CERVICAL CANCER: VARIATIONS AND RELATIONS.

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Aims: Brachytherapy is not an option for cervical carcinoma treatment. Many studies have shown that there are significant day to day variations in applicator positions. This study focuses on variability in HDR intracavitary brachytherapy (ICBT) basing on anatomical parameters and analyzes the relation of applicator geometric variability with age, body mass index (BMI), stage of disease, toxicity, target coverage and doses at organs at risk (OARs).

Methods: From April 2014 to March 2017, sixteen patients (aged 40-82, median 58) with cervical cancer (FIGO stages, IIA-IVA) were treated with curative radiotherapy. They underwent concurrent chemoradiation (CRT), followed by ICBT (5-6Gy x 5, weekly). Eighty ICBT implants were evaluated on DVHs. CRT toxicity was scored by use of CTCAE. Variations of a Fletcher-style applicator were compared basing on an Anatomical Repere (AR), given by the point of intersection of the line joining the S1-S2 vertebrae and the pubic synphysis with the line joining the highest points on the right and left acetabulae. So it was possible to measure the distance (ARD) between the tip end of the intrauterine tube of applicator and the above said AR. According to GEC-ESTRO guidelines and EMBRACE protocol, D90 and D100 fortarget coverage and D2cc of bladder and rectum were evaluated at DVH. Data were analyzed with R statistical program. Since ARD is not normally distributed, non-parametric tests were performed.

Results: Relevant differences, in terms of geometrical variations, were found: ARD median and range were 0.6 and 1.97 cm, respectively. A significant difference was found among each fraction. We found highly significant relations between ARD and BMI (Spearman's rank correlation, P=0.01), clinical stage (Kruskal-Wallis, P=0.03), CRT toxicity (P=0.04) and D100/D90 (Spearman's rank correlation, P=0.01 and 0.02, respectively). No significant relation was found between ARD and age or D2cc for OARs.

Conclusions: Day to day variations of applicator geometry and its movements were observed in patients undergoing multiple ICBT. The higher are BMI, stage

and CRT toxicity, the higher is ARD. In turn, the applicator geometry plays an important role in dose distribution, regarding target coverage. Doses to OARs do not depend on applicator position. Compatibly with BMI and stage, this work suggests to keep ARD as low as possible. Furthermore, attention should be paid to limit CRT toxicity in order to improve implant quality and target coverage.

C085

RISK OF SUBCLINICAL VASCULAR TOXICITY IN SURVIVORS OF HODGKIN LYMPHOMA TREATED WITH CHEMOTHERAPY AND RADIOTHERAPY

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Aims: Radiotherapy (RT) is part of the treatment of Hodgkin Lymphoma (HD). Sovra-diaphragmatic RT volumes often involve major blood vessels. No data are published about the relation between RT dose to vessels and arterial stiffness/pulse-wave velocity (PWV)/thickening (IMT) and plaques. This study aims to ascertain and quantify the presence of long-term vascular damage in relation with the vessels doses.

Methods: A retrospective cohort study among 206 survivors of Hodgkin lymphoma was performed. All patients were treated between 1995 and 2012; the pulse wave femoral-carotid velocity (PWV fc) was measured in 162 patients; carotid ultrasound was obtained in 174 patients. PWV alterations and IMT incidence rates in the HD cohort were compared with their incidence in the general population; the biologically equivalent doses (BED) to the artery wall (carotid artery, aortic arch, thoracic and abdominal aorta) were analyzed and related with vascular damage. General linear model was used to compare means; multivariable regression was adopted to study treatment related factors and other risk factors. All statistical tests were two-sided.

Results: After a median follow-up of 8.5 years, 29 arterial stiffness cases (17.9%, median age 53 years); 131 of thickening (75.2%, median age 47 years) and 69 of plaques (39.6%, median age 57 years) were detected. The incidence of subclinical vascular alterations is higher than in a comparable sample of the general population, after substantial follow-up. Dose > 36 Gy to neck and mediastinum was an independent risk factor for vascular wall damage. All the alteration identified were asymptomatic. Treatment with chemotherapy was not associated with an increased risk. Hypertension, diabetes mellitus, and hypercholesterolemia resulted to be important co-factors in the pathogenesis of subclinical vascular damage, whereas smoking and overweight were not. Even if this is a retrospective study, at each interval of follow up considered (up to >10 years), patients treated on volumes including large vessels have an higher incidence of IMT and plaques.

Conclusions: These preliminary data show that patients treated with doses >36 Gy on neck and mediastinum have an increased risk of subclinical large vessels damage. Already known risk factors for vascular alterations are confirmed as important co-factors inducing the analyzed toxicity. Long term personalized follow up of each patient is critical to predict and prevent late vascular toxicity.

C086

INTENSITY MODULATED TOTAL LYMPHOID IRRADIATION WITH HELICAL TOMOTHERAPY PLUS MELPHALAN AS ABLATIVE TREATMENT FOLLOWED BY AUTOLOGOUS STEM CELL TRANSPLANTATION FOR LYMPHOID MALIGNANCES. ACUTE AND LATE EFFECTS FROM A PILOT STUDY

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Aims: High-dose chemotherapy and autologous stem cell transplantation (ASCT) is the treatment of choice for relapsed or refractory lymphoma patients. Combinations with multiple agents are frequently used, but adverse events are common and can prolong the hospitalization time and influence the outcomes. The purpose is to evaluate Total Lymphoid Irradiation (TLI) with Helical Tomotherapy (HT) in combination with single agent high dose melphalan (L-PAM) to limit transplantation related toxicity. Feasibility of treatment was the main end point, focusing on set-up reproducibility and dose distribution analysis. Secondary end point was to assess late toxicity and patient's outcomes.

Methods: Between February 2011 and March 2012, 6 HD and 4 NHL underwent to HT-TLI with 12Gy in 3 daily fractions followed after 2 days rest by L-PAM 140 mg/m2. Median age was 41 (range 20-60). Two patients with FDG-PET residual bulky disease received a SIB up to 18Gy. The CTV covered all the major lymphatic stations, from the neck to the inguinal region. Set-up was performed with 3 thermoplastic masks for head, thorax and feet. Whole target MVCTs defined the daily right position. GafChromic® films and MOSFET dosimeters were placed on the skin for in-vivo dosimetry. For all patients a 3D-CRT plan was generated and compared with HT. For secondary end points, acute toxicity was reported following the CTCAE v3.0 and outcomes rates were calculated using the Kaplan-Meyer analysis.

Results: The median PTV volume covered by the 95% of prescribed dose was 96.5% ± 3 for HT and 82.4% ± 2 for 3D-RT. The median Homogeneity Index calculated as (D5-D95)/Dmean was 0.07 and 0.16 respectively for HT and 3D-RT. The median dose to all the organs at risk decreased from 20% to 70% with HT compared to 3D-RT. All patients underwent the conditioning regimen without interruptions. Only mucositis of grade 3 and vomiting of grade 2 were reported in 3 patients. No late toxicity was reported. At a median follow up of 70.9 months the 5 yy OS is 76.9%. The DFS is 53.8% and 43.2% respectively for 3 yy and 5 yy. The subgroup of patients with HD obtained better results, with 5 yy OS of 100% and a DFS of 88.9% at 3 yy and 66.7% at 5 yy.

Conclusions: HT-TLI with L-PAM before ASCT is feasible, reproducible and well tolerated. The good dose distribution allows to better spare healthy tissue than conformal 3D-RT. Registered toxicity was very limited. Small group results on DFS and OS are encouraging the study on HD patients.

C087

LOW DOSE TOTAL SKIN ELECTRON BEAM IRRADIATION FOLLOWED BY MAINTENANCE THERAPY WITH ORAL BEXAROTENE IN PATIENTS WITH MYCOSIS FUNGOIDES TREATED AT THE RADIOTHERAPY DEPARTMENT OF CAREGGI HOSPITAL

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Aims: This study aimed to evaluate the clinical results of Total Skin Electron Beam Irradiation (TSEBI) followed by maintenace oral Bexarotene in a group of Stage Ib-IIb patients with Mycosis Fungoides treated at our Institution.

Methods: We retrospectively reviewed our clinical records and we identified 18 patients treated with low dose TSEBI (dose range 10-12Gy in 6-12 daily fractions); 12 of these patients were prescribed oral Bexarotene (BEX) as "maintenance" therapy after TSEBI and were included in our analysis. 8 patients were male and 4 female, 5 were in Stage Ib and 7 in Stage IIb. All patients had progressed through at least one previous therapy (median 2, range 1-8). BEX was prescribed continuously until toxicity or progression of disease requiring a second line treatment.

Results: All patients completed TSEBI without major toxicity. Median follow-up time after TSEBI was 14,1 months (range 10-22,7). After TSEBI 2 patients were in CR (16,6%), 6 patients in VGPR (50%) and 4 patients in PR (33,3%). At the time of our analysis all patients were alive: 6 patients were still continuing BEX; 2 out of 12 patients had to interrupt BEX for toxicity: one patient for a hypercreatininemia and one patient for hyperamilasemia; 3 patients interrupted BEX for progression of disease and another patient for the diagnosis of another malignancy. 7 out of 12 patients had a cutaneous relapse with a median duration of clinical response of 10,7 months (range 2,8-22,7 months) and an actuarial PFS of 75% at 6 months and of 46% at 12 months. 5 of the 7 relapsing patients eventually stopped BEX and were treated with other therapies (two of these patients relapsed after stopping BEX for toxicity), while the other 2 relapsing patients are still continuing with BEX with minimal presence of disease. Duration of Clinical Benefit (defined as the time from the completion of TSEBI and the need for another treatment other than BEX) was 83% at 6 months and 75% at 12 months.

Conclusions: Low dose TSEBI followed by maintenance therapy with oral Bexarotene seems feasible with low toxicity and is able to obtain durable responses with long clinical benefit in our small cohort of patients. Prospective studies are needed to further investigate this therapeutic approach.

C088

HELICAL TOMOTHERAPY IN PEDIATRIC MEDIASTINAL HODGKIN'S LYMPHOMA

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Aims: To evaluate long-term outcome and toxicity in pediatric patients affected by Hodgkin's lymphoma (HL) with mediastinal disease receiving helical tomotherapy (HT) and to estimate the potential reduction of dose to normal tissue with HT when compared to standard two-dimensional/three-dimensional conformal radiotherapy (2D/3DCRT).

Methods: Between 2005 and 2016, 27 patients (median age 15 years, range 10.4-17.6; 14M/13F) affected by HL with mediastinal disease and enrolled in the AIEOP LH 2004 protocol were treated with first-line post-chemotherapy involved-field radiotherapy in our Institution. Prescribed doses were 14.4Gy/8fr or 25.2Gy/14fr in patients in complete or partial remission, respectively. Patients in partial remission with bulky disease at diagnosis also received a 9Gy/5fr boost

to the residual mediastinal mass. Before 2007, all patients received 2D/3DCRT. After 2007, HT or conventional intensity-modulated radiation therapy (IMRT) were applied. The plans of the patients treated with HT were re-planned for 2D/3DCRT. A dosimetric comparison was performed.

Results: Fifteen patients received HT, eleven 2D/3DCRT, and one IMRT. One patient treated with 3DCRT with boost delivered by HT and the single patient treated with IMRT were excluded. All HT-patients (100%) were in complete remission after a median follow-up of 4.8 years (range 1.1-8.1). Among 2D/3DCRT-patients, eight (80%) were in complete remission and two (20%) died of disease after a median follow-up of 7 years (range 3.7-11.9). In HT-group, no chronic toxicity nor second malignancy occurred. We only had one case of soft tissue recurrent fibromatosis. HT showed superior conformation and homogeneity of the dose to the target and was able to reduce of about 16% the maximum dose to the breasts. No other real dosimetric advantages for normal tissues were observed.

Conclusions: HT is an effective and safe treatment for pediatric mediastinal HL. Our preliminary data on favorable local control support further use of this technique.

C089

BORTEZOMIB AND CONCURRENT EXTERNAL BEAM RADIATION IN PATIENTS WITH MM

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Aims: Radiation therapy (RT) is an important part of multimodal treatment of patients affected with multiple myeloma (MM), but little is known regarding the role and effectiveness of RT in the era of new agents,such as immunomodulatory drugs and proteasome inhibitors. Bortezomib is proteasome inhibitor, with potential radiosensitive effect which is currently used in first line systemic therapy of MM. To evaluate the safety and efficacy of radiotherapy for bone metastases of MM and bortezomib.

Methods: We retrospectively evaluated patients with MM treated at our institute with RT and concomitant bortezomib. Toxicity was recorded according to CTCAE v. 4.02. Pain response was assessed by means of Numerical Rating Pain Scale (NRS) scale. Radiological response was described according to RECIST criteria.

Results: Among 52 evaluable patients with MM treated with radiotherapy from 2010 to 2016, 21 (40%) received RT concurrently with Bortezomib for a total of 24 bone sites treated. The most common indication for RT was palliation of bone pain (n = 13, 54.17%), followed by prevention/treatment of pathological fractures (n =11, 45.83%). Sites treated were as follows: 15 (62.5%) spine, 4 (16.6%) pelvic bone and 5 (20.9%) ribs. Medium NRS score was 3.71 (SD: 3.5) before radiotherapy and 1.38 (SD: 2.5) after radiotherapy (p=<0.001). Median RT delivered dose was 36 Gy (range 8-50). One patient treated for a thoracic spinal compression experienced a grade 1 lung toxicity, while one patient interrupted radiotherapy course due to hematological platelet G3 toxicity. One pathological fracture occurred three months after radiotherapy. Radiologic response was assessed in 14 patients (58.3%) after a median time of 3 months (range 1-6 months).

Conclusions: Bortezomib in association with radiotherapy for the treatment of MM bone metastases is well tolerated. This promising association need to be tested in prospective trials.

C090

SINGLE NUCLEOTIDE POLYMORPHISM OF GLUTATHIONE S-TRANSFERASE PI GENE (GSTP1) AND PATHOLOGICAL COMPLETE RESPONSE IN LOCALLY ADVANCED RECTAL CANCER PATIENTS TREATED WITH NEOADJUVANT CONCOMITANT RADIOCHEMOTHERAPY

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Aims: Standard treatment for locally advanced rectal cancer consists of neoadjuvant radiochemotherapy (N-RCT) and surgery with the aim of cure. Pathological complete response (pCR) after N-RCT has shown to be predictive for better outcome and survival; nevertheless there are no biological or genetic factors predictive for the response to treatment. Glutathione S-transferase pi gene (GSTP1) is a polymorphic gene that plays a key role in the phase II xenobiotic metabolism and it is induced by oxidative stress generated by reactive oxidants and drugs, and X-ray repair cross-complementing 1 (XRCC1) is one of the most important genes of the BER (base excision repair) pathway. We explored the correlation between the single nucleotide polymorphisms (SNPs) GSTP1 (A313G) and XRCC1 (G28152A), and the pCR after N-RCT in locally advanced rectal cancer patients.

Methods: Eighty patients with locally advanced rectal cancer were treated with fluoropyrimidine-based N-RCT. Genotypes GSTP1 (A313G) and XRCC1 (G28152A) were determined in all patients by pyrosequencing technology.

Results: The overall rate of pCR in our study population was 18.75%. Patients homozygous AA for

GSTP1 presented a rate of pCR of 26.6% as compared to 8.5% of the AG+GG population (p 0.0396), suggesting a recessive model for the SNP. The heterozygous comparison (AA vs AG) showed a significant difference in the rate of pCR (26.6% vs 6.8%; p 0.034). No significant correlations were found between XRCC1 (G28152A) and the pathological response.

Conclusions: Our results suggest that GSTP1 (A313G) may predict a higher rate of pCR after N-RCT and should be considered in a more extensive analysis with the aim of personalization of radiation treatment.

C091

NON-MELANOMA SKIN CANCER IN ELDERLY PATIENT: TUMOR RESPONSE AND SYMPTOM RELIEF AFTER HYPOFRACTIONATED RADIOTHERAPY

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Aims: To assess tumor response rate and symptom palliation after hypofractionated radiotherapy (HRT) in elderly patients affected by advanced non-melanoma skin cancer (ANMSC).

Methods: A total of 22 patients affected by ANMSC, treated at our Radiotherapy Department with palliative HRT between 2008 and 2017, were evaluated. Age, gender, tumor histology, grading, location, size, borders, primary/recurrent tumor, speed of growth, presenting symptoms (pain, neurologic symptoms, bleeding), immunosuppression and radiation treatment characteristics were recorded at baseline. Tumor size and tumor-related symptoms were recorded at each fraction and at follow-up visit. Patients were treated with photon or electron beam, and received 6-36 Gy in 1-10 fractions (6 Gy 1 fraction/week; 3 Gy or 4 Gy daily fraction). Tumor response, symptom palliation and local recurrence rates were analyzed. Clinical treatment response (tumor size and symptoms), at least at one follow-up visit or at the time of the last available clinical evaluation, was recorded.

Results: A total of 22 patients with ANMSC (16 recurrent and 6 primary tumors) were treated. Median age was 89 years (range 77-110); 12 patients were men, 10 women. Mean tumor size was 2.2 cm (range 0.5-4.5). Most of tumors were squamous (14), 4 patients had a basal cell histology, while 4 a Kaposi's Sarcoma. One patient presented immunosuppression. 10 tumors occurred in the mask-like area of the face, 7 in scalp/neck/forehead region, 5 tumors occurred on extremities. At presentation, 5 patients referred neurological symptoms, 12 bleeding, 3 presented both neurological symptoms and bleeding. Follow up was evaluable for 21 patients (mean: 16 weeks, range 3-102 weeks). The preferred HRT schedule was 6 Gy once a week for a total dose of 24-36 Gy (16/21 patients). At the end of RT course or at the last follow-up visit, tumor response rate evaluated on 14/21 patients was 78.5% (complete response 5/14; partial response 6/14; progression 2/14; no response 1/14). Two patients experienced in-field local recurrence. Symptomatic response was evaluated on 11/21 patients; presenting symptoms were alleviated in 81.8% (9/11).

Conclusions: Palliative HRT in ANMSC offers symptoms palliation and significant response rates, although the duration of response is not known. Furthermore, being administered once a week, HRT provides a good treatment option considering cost/effective ratio, especially for elderly patients.

C092

IMPACT OF FUNCTIONAL RESPONSE ON LOCAL CONTROL IN EXTRACRANIAL STEREOTACTIC RADIOTHERAPY SETTING: DATA FROM 2 PHASE I CLINICAL TRIALS

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Aims: The tumoral and adjacent peritumoral modifications caused by radiosurgery limit the evaluation of response by anatomic imaging and dimensional criteria alone, such as with RECIST. This suggests that it is of interest to also take into account the functional criteria evaluated with PET-CT than routine imaging and metric evaluation alone. Therefore we were prompt to evaluate the impact of functional response on local control in a large series of patients undergoing extracranial stereotactic radiotherapy (SBRT) in our centre.

Methods: Data of patients with oligometastatic disease (less than 5 visceral and/or bone metastases), undergone 5 fractions SBRT (DESTROY-1 phase I clinical trial) or single fraction stereotactic radiosurgery (SRS-DESTROY-2 phase I clinical trial) as exclusive treatment, retreatment or boost after 3D-CRT, were collected and analyzed. Patients were enrolled from

September 2003 to April 2017, therefore SBRT planning was performed previously by 3D conformal non-coplanar beam arrangement, subsequently by volumetric arc technique. The functional response was evaluated by FDG-PET or PET-Colina 3-6 months after SBRT. Objective response rate (ORR) included complete and partial response. Clinical benefit included ORR and stabilization of disease. The 95% confidence intervals (95% CI) have been provided. Local control (LC) of irradiated lesions was calculated using the Kaplan-Meier method from the date of SBRT to the date of the inside SBRT field relapse/progression of disease or the date last seen.

Results: 427 consecutive patients (M/F: 255/172; median age: 69, range 35-93) with 582 lesions were treated. Of these, 159 were primary or metastatic lung tumours, 49 were liver metastases, 93 were bone metastases, 229 lymph nodal metastases and 52 miscellanea of neoplastic lesions. Dose prescription varied from 8 Gy/single fraction (boost after a previous radiotherapy dose) to 50 Gy/5 fractions to the Planning Target Volume. Median follow-up was 16 months (1-157). ORR based on CT/MRI/PET was 79.9% (CI 95%: 75.8-83.4) with a complete response rate of 57.4% (CI 95%: 52.6-62.9). 12-and 24-months actuarial local control (freedom from progression in the irradiated site) was 86.2% and 76.2%, respectively. Patients with a complete functional response had better 2-year local control than those with the worst response (90.2% versus 56.1%; chi-squared p= 0.0001) (Figure 1).

Conclusions: This data on a large series of oligometastatic patients treated by SBRT point out the usefulness of the functional evaluation of the response that seems to be predictive of encouraging local control at 2 years.

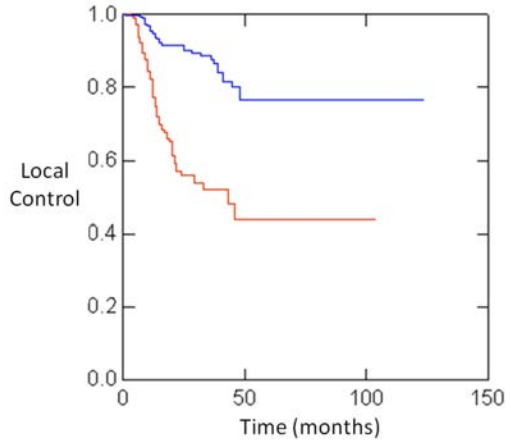

Figure 1.

Poster

P001

ROLE OF CIRCULATING DNA IN GLIOBLASTOMA IDH1 WILD TYPE PATIENTS SUITABLE FOR RADIOTHERAPY

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Aims: Glioblastomas (GBMs) are usually classified on the basis of clinical presentation in two entities with different prognosis, primary or secondary. The most important genetic signature of primary glioblastoma is the lack of IDH1 mutation, which is associated with a short life expectancy. In the present study, through the analyses of circulating tumor DNA (ctDNA), we retrospectively assessed the role of IDH1 mutation in GBM patients IDH1 wild type (wt) assessed on tumor tissue at diagnosis.

Methods: From February 2010 to January 2017 in thirty-one patients referred to the University Hospital of Pisa with diagnosis of GBM, IDH1 wt, the circulating tumor DNA (ctDNA) was analyzed. All patients had KPS greater than 65 and age >18 years; of them 22 patients underwent gross tumor resection and 9 subtotal resection were included in the present analysis. Twenty-six patients received radio-chemotherapy and 5 chemotherapy only. Three ml of plasma were collected at the first radiological evalutation after surgery; ctDNA was extracted using a QIAmp Circulating nucleic acid Kit (Qiagen, Valencia, CA) and analysed for IDH1 p.R132H mutation by digital droplet PCR (ddPCR, BioRad, Hercules, CA). Primary endpoint was Overall Survival (OS), measured from the diagnosis of GBM to last follow-up or patient exitus, stratified using IDH1 mutation detected on ctDNA.

Results: In May 2017, at data analysis, patient median age was 60.1 years (range 50-69). By analyzing ctDNA, 8 patients were carrier of the IDH1 p.R132H mutation whereas 23 were confirmed as IDH1 wt. Median OS recorded in the entire cohort was 40 months (95%CI 1.1-87.4). Stratifyng patients for survival as IDH1 wt vs IDH1 mutant on ctDNA, the OS was 23 vs not reached, respectively, showing a trend of significance of p=0.095.

Conclusions: Among patients with GBM IDH1 wt on tumor tissue, we found a subgroup of patients with IDH1 mutated on ctDNA. The presence of IDH1 mutation on ctDNA were associated with better prognosis and could be considered as a biomarker to be further investigated in a larger series.

P002

LINAC-BASED STEREOTACTIC RADIOTHERAPY FOR BRAIN METASTASES: THE INTRIGUING ISSUE OF HIPPOCAMPUS DOSE.

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Aims: Aim of the present study is to analyze the dose to homolateral and contralateral hippocampus (H-H, C-H, respectively) during Radiosurgery (SRS) or Fractionated Stereotactic Radiotherapy (FSRT) for brain metastases (BM). Secondary endpoint is to evaluate the differences in terms of dose when SRS/SFRT with or without considering hippocampus in optimization phase were performed.

Methods: Patients with BM <5, size ≤30mm, KPS ≥ 80 and a life expectancy>3 months, were considered for

SRS/FSRT. The total dose ranged between 15-30Gy (1-5 fractions). For each BM, a Flattening Filter Free (FFF) Volumetric Modulated Arc Therapy (VMAT) plan was generated with one or two arcs. For primary endpoint, Hippocampi were not considered during optimizations phase. Retrospectively, hippocampi were contoured and evaluated: the Dmedian, Dmean and D0.1cc and the V1Gy, V2Gy, V5Gy and V10Gy were analyzed. Based on primary endpoint results, a subgroup of patients was selected for secondary endpoint. Thus, for each BM, two FFF-VMAT plans were generated: hippocampus was or was not considered during optimizations phase (Planopt vs Planno-opt, respectively). For each plan, hippocampus was evaluated in terms of Dmean, and D0.1cc.

Results: Between 04/2014 to 12/2015, 81 BM were treated with FFF- SRS/FSRT. For the H-H, the average values of Dmedian, Dmean and D0.1cc were 1.5Gy, 1.54Gy and 2.2Gy, while the V1Gy, V2Gy, V5Gy and V10Gy values were 25%, 8.9%, 8.9% and 2.1%. For the C-H, the average Dmedian, Dmean and D0.1cc were 0.7Gy, 0.7Gy, 0.9Gy, while the average values of V1Gy, V2Gy, V5Gy and V10Gy values were 18%, 10.2%, 2.8% and 1.4%. Tumor dimension, tumor crania-caudal length and the distance between BM and H-H correlated to Dmedian, Dmean and D0.1cc. For C-H, only the distance from PTV correlated with a reduction dose. Based on these results, 15 out 81 BM, which were in proximity of hippocampus, were selected for secondary endopoint. Thus, to consider hippocampi in plan optimizations resulted in a significant reduction of dose: the average values of Dmean and D0.1cc were (4,3 + 3) Gy, (5,5 + 5,3) Gy for Planno-opt, while they were (1,8 + 1,7) Gy and (3,2 + 4,3) Gy for Planopt, respectively (p=0,0001 and p=0,0002).

Conclusions: During FFF- SRS/FSRT, hippocampus received a negligible dose, but its clinical significance is still under evaluation. These data confirmed that in patients with a long life expectancy, for whom more SRS/SFRT could be proposed, H-H should be considered as OAR during FFF Linac-based SRT/SFRT.

P003

DOSIMETRIC COMPARISON AND LOCAL CONTROL ANALYSIS OF DIFFERENT PLANNING MODALITIES FOR GAMMAKNIFE RADIOSURGERY OF BRAIN METASTASIS

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Aims: Radiosurgery (RS) is one of the treatment options in selected patients with brain metastasis (BMs).The aim of our study is to analyze if in BMs with a diameter < 10 mm treated with GammaKnife (GK) there is any difference in terms of dosimetric and clinical parameters using one or two isocenters (shots).

Methods: Data of 86 (282 BMs) patients treated with the GK were retrospectively reviewed. Demographic and disease features were collected. Each lesion was treated using one or two shots with a diameter of 4 and/or 8 mm; Coverage, Gradient Index and Selectivity were recorded. Radiological response to the RS treatment was evaluated following RANO criteria with an MRI at 1, 3, 6 and 9 months.

Results: 210 (74.5%) brain metastases were treated with a single isocenter. Mean metastases volume was 103.1 mm^3 (2.4-721). Mean coverage of plans performed with one shot was 99.9% (92-100%) with two shots 99.7% (95-100%), mean selectivity was 0.25 (0.001-0.63) in one isocenter plans and 0.35 (0.07-0.78) in two isocenter plans. We observed a statistically significant better coverage in one shot plans (0.9995 vs 0.9968, p=0.0001), selectivity was significantly better with two shots (0.2494 vs 0.3546, p=0.0001). At one month the majority of BMs were controlled (96.4%); local control decrease with the and it was 95.1% at 9 months. Considering disease and patients characteristics, breast histology correlated with a poorer local control (p=0.0001) at 3 and 6 months, while a GPA > 3 was predictive of local failure (p=0.018) at 9 months. Comparing the local control of the BMs treated with one respect to two shots we found that patients treated with one shot had a better local control at one month (1.0% vs 11.6% p=0.0001) and six months (5.9% vs 20.7%, p=0.026) compared to BMs treated with two shots.

Conclusions: Our study shows that in case of a BM with a diameter < 10mm treated with GK, the use of a single shot results in a better coverage and a better local control at one and three months. This last result is probably due to the higher conformity the steeper dose gradient offered by the GK. GPA score and histology are confirmed important prognostic factors affecting clinical outcome of brain metastases patients.

P004

PSEUDOPROGRESSION IN GLIOMA PATIENTS TREATED WITH CONCURRENT RADIO-CHEMOTHERAPY: CLINICAL, DOSIMETRIC AND BIOMOLECULAR EVALUTATIONS

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Aims: The term pseudoprogression (PsP) is referred to a clinically significant phenomenon that occurs in up to 20% of patients with high grade glioma treated with temozolomide based radio-chemotherapy. Despite the latest improvement in neuroimaging, the diagnosis of PsP is set according to evolutionary criteria: PsP is defined as spontaneous improvement or stabilization of

enhancing lesions without further treatment other than adjuvant therapy. The aim of this study is to investigate the potential association between PsP and clinical, dosimetric and biological factors in patients with glioblastoma (GBM) treated with chemoradiotherapy.

Methods: Between April 2011 and March 2016, 38 patients (pts) with a proven diagnosis of GBM, were treated with radiotherapy and temozolomide at the University Hospital of Pisa. Magnetic Resonance (MR) was performed 6 weeks since the end of RT-CT and then every 3 months until tumor progression. When MR revealed enhancing lesions suggestive for tumor progression inside the radiotherapy field, a new MR was planned after 6-weeks. Lesion shrinking or stability were associated to PsP. Tumor progression was defined according to Mac-Donald's Criteria. In all patients clinical (sex, side, surgery), biological (MGMT promoter methylation, IDH mutation, p53 amplification, EGFR mutation) and dosimetric factors (PTV, PTV/Brain Volume) were analyzed in order to investigated the association with PsP.

Results: At the first MR scan lesion enlargement was evaluated in 22 patients (57.9%), while 16 patients (42.1%) were stable. In the first group, at second MR, 12 pts (31.6%) showed progressive disease whereas 10 pts (26.3%) PsP. The p53overexpression was found to be the most relevant biological predictive factor for the development of PsP (p= 0.042). Small PTV (p=0.044) and low PTV/Brain Volume ratio (p=0.008) were also significantly related with PsP.

Conclusions: p53overexpression, small PTV and low PTV/Brain Volume ratio are significantly associated with PsP in GBM patients treated with radiotherapy and temozolomide schedule.

P005

ENHANCEMENT OF RADIOSENSITIVITY BY THE NOVEL ANTICANCER QUINOLONE DERIVATIVE VOSAROXIN IN PRECLINICAL GLIOBLASTOMA MODELS

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Aims. Glioblastoma multiforme (GBM) is the most aggressive brain tumor which resistance limits radiation therapy efficency.

Methods. The activity of vosaroxin, a first-in-class anticancer quinolone derivative that intercalates DNA and inhibits topoisomerase II, was investigated in GBM preclinical models as a single agent and combined with radiotherapy (RT).

Results. Vosaroxin showed antitumor activity in clonogenic survival assays, with IC50 of 10-100 nM, and demonstrated radiosensitization. Combined treatments exhibited significantly higher H2Ax levels compared with controls. In xenograft models, vosaroxin reduced tumor growth and showed enhanced activity with RT; vosaroxin/RT combined was more effective than temozolomide/RT. Vosaroxin/RT triggered rapid and massive cell death with characteristics of necrosis. A minor proportion of treated cells underwent caspase-dependent apoptosis, in agreement with *in vitro* results. Vosaroxin/RT inhibited RT-induced autophagy, increasing necrosis. This was associated with increased recruitment of granulocytes, monocytes, and undifferentiated bone marrow-derived lymphoid cells. Pharmacokinetic analyses revealed adequate blood-brain penetration of vosaroxin. Vosaroxin/RT increased disease-free survival (DFS) and overall survival (OS) significantly compared with RT, vosaroxin alone, temozolomide, and temozolomide/RT in the U251-luciferase orthotopic model. Cellular, molecular, and antiproliferative effects of vosaroxin alone or combined with RT were evaluated in 13 GBM cell lines. Tumor growth delay was determined in U87MG, U251, and T98G xenograft mouse models. (DFS) and (OS) were assessed in orthotopic intrabrain models using luciferase-transfected U251 cells by bioluminescence and magnetic resonance imaging.

Conclusions: Vosaroxin demonstrated significant activity in vitro and in vivo in GBM models, and showed additive/synergistic activity when combined with RT in O6-methylguanine methyltransferase-negative and -positive cell lines.

P006

SIB VMAT DOSE ESCALATION PLUS TEMOZOLOMIDE IN GLIOBLASTOMA PATIENTS: INTERIM ANALYSIS OF A PHASE I STUDY (ISIDE-BT-2)

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Aims: To determine the maximum tolerated dose (MTD) of Volumetric Modulated Arc Therapy (VMAT) with standard concurrent and sequential-dose temozolomide (TMZ) in patients with resected glioblastoma multiforme.

Methods: Histological proven glioblastoma patients underwent VMAT dose escalation. VMAT was delivered over 5 weeks with the simultaneous integrated boost (SIB) technique to the two planning target volumes (PTVs) defined by adding 5-mm margin to the respective clinical target volumes (CTVs). CTV1 was defined by adding a 10-mm isotropic margin to the tumor bed plus any MR enhancing residual lesion; CTV2 was defined as the CTV1 plus 20-mm isotropic margin. Radiation dose was escalated to the PTV1 with the SIB-VMAT strategy. Four dose levels were planned: Level 1 (PTV2: 45/1.8 Gy; PTV1: 77.5/3.1 Gy), Level 2 (PTV2: 45/1.8 Gy; PTV1: 80/3.2 Gy), Level 3 (PTV2: 45/1.8 Gy; PTV1: 82.5/3.3 Gy) and Level 4 (PTV2: 45/1.8 Gy; PTV1: 85/3.4 Gy). All treatments were delivered in 25 fractions. Patients were treated in cohorts of between three and six per group using a Phase I study design. The recommended dose was exceeded if two of the six patients in a cohort experienced dose-limiting toxicity within 3 months from treatment. Concurrent and sequential TMZ chemotherapy was administered according to Stupp's protocol.

Results: Eleven consecutive glioblastoma patients (male/female: 7/4; median age: 59 years) were treated, 9 of them at first dose level, with none of them experiencing a dose-limiting toxicity (DLT) (grade >3). Being the MTD not exceeded, the PTV1 dose was escalated to the higher planned dose level (80/3.2 Gy) and accrual is actually ongoing. After a median follow-up time of 7 months, no grade >2 late neurological toxicity was recorded.

Conclusions: The SIB-VMAT technique was found to be feasible and safe at the recommended doses of 45Gy to PTV2 and 77.5Gy (biological effective dose – BED- of 157.6 Gy, alpha/beta 3) to PTV1 in the postoperative treatment of patients with glioblastoma.

P007

GAMMAKNIFE RADIOSURGERY IN PATIENTS RECEIVING ANTICANCER IMMUNOTHERAPY: EFFICACY AND SAFETY

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Introduction. In patients with extracranial controlled disease under systemic therapy, radiosurgery is the treatment of choice for brain metastasis (BMs).

Recently, immune checkpoint inhibitors have emerged as a valid therapeutic option in patients with metastatic melanoma, lung and kidney cancer. The aim of the study is to assess the safety and the efficacy of concurrent immune checkpoint inhibitors and GammaKnife Radio Surgery (GKRS) in a retrospective cohort of patients.

Materials Methods: We retrospectively analyzed patients treated with anti CTLA4 and/or anti PDL1 immunotherapy who underwent GKRS from January 2014 to March 2016 for BMs at the University of Florence. Radiosurgery was delivered within 6 months from the last immunotherapy administration. Response to radiosurgery was evaluated according to iRANO criteria by magnetic resonance (MRI) performed at 45 days, 3 and 6 months after procedure.

Results: We analyzed 12 patients (5 melanoma, 6 lung, 1 kidney), for a total number of 61 treated lesions for a median number of 3 (range:1-16) lesions per patient, with a median age of 55 years (32-77) and a median GPA of 2 (1-4). Anti CTLA4 (Ipilimumab) was administered in 3 patients (for a total of 8 lesions), Anti PDL1 (Nivolumab) in 8 patients (37 lesions) and one (16 lesions) patient received both drugs. GKRS was delivered in a single session in all patients for a median dose of 21 Gy (range: 15-24 Gy); median treatment volume was 9.45 cm^3 (range: 1.75-220.35 cm^3). No acute neurotoxicity occurred after GKRS. MRI at 45 days showed complete response, partial response and stable disease in 7 (11.5%), 22 (36.1%) and 32 (52.4%) lesions. MRI at 6 months showed progression of treated lesions in 4 (6.6%) cases; five (41.7%) patients experienced distant brain failure. At statistical analysis, only BRAF mutation was related with local control at 6 months (p=0.029). At a median follow up of 9.6 months (range: 6.3-30.6 months) there was only one death due to brain progression, while 5 patients died for extracranial disease. We registered radionecrosis in one case.

Conclusions: The association of immune checkpoint inhibitors and GKRS is possible and did not result in severe toxicity. Enhanced local control in GKRS treated BRAF mutated melanoma BMs might result from defective DNA-repair or by increased antigen load allowing for stronger immune reaction toward mutant clones. Larger series and translational research is needed.

P008

CYBERKNIFE RADIOTHERAPY FOR ORBITAL METASTASES: A SINGLE CENTER EXPERIENCE ON 24 LESIONS

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Aims: To evaluate the feasibility, in terms of acute toxicity and symptom control, of CyberKnife (Accuray, Sunnyvale, CA)-based stereotactic radiotherapy (CyberKnife-SRT) for metastatic orbital lesions.

Table 1: Volume treated and dose-volume parameters for OARs

Volume	Median (range)
GTV volume (cm^3)	
All lesions	1.50 (0.14 – 17.50)
Intraocular lesions	0.65 (0.14 – 17.50)
Periocular lesions	3.65 (1.20 – 12.30)
Ipsilateral optic nerve D_{max} (Gy)	
All lesions	16.95 (1.55 – 24.00)
Intraocular lesions	15.69 (1.55 – 17.80)
Periocular lesions	17.25 (6.04 – 24.00)
Ipsilateral lens D_{max} (Gy)	
All lesions	3.00 (0.40 – 14.20)
Intraocular lesions	5.85 (2.80 – 10.00)
Periocular lesions	2.35 (0.40 – 14.20)
Ipsilateral lens D_{mean} (Gy)	
All lesions	1.35 (0.30 – 9.00)
Intraocular lesions	3.04 (0.79 – 4.30)
Periocular lesions	1.10 (0.30 – 9.00)
Optic chiasm D_{mean} (Gy)	
All lesions	2.10 (0.50 – 18.00)
Intraocular lesions	1.15 (0.50 – 2.54)
Periocular lesions	3.30 (0.90 – 18.00)
Eye globe D_{max} (Gy)	
All lesions	20.25 (6.90 – 24.00)
Intraocular lesions	24.00 (24.00-24.00)
Periocular lesions	17.85 (6.90 – 21.30)
Eye globe D_{mean} (Gy)	
All lesions	6.25 Gy (1.10 – 13.50)
Intraocular lesions	8.65 Gy (6.00 – 12.80)
Periocular lesions	4.55 Gy (1.10 – 13.50)

Legend: OAR: organ-at-risk; G TV: gross target volume, Dmax: maximum dose, Dmean: mean dose.

Methods: This retrospective study included patients with symptomatic metastases wholly located within the orbit. Palliative radiation treatment was performed using CyberKnife image-guided technology with skull-tracking technique. Gross tumor volume (GTV) was defined on a pre-radiotherapy magnetic resonance imaging (MRI) with Gadolinium. Acute toxicity was recorded according to Radiation Therapy Oncology Group/European Organization for Research and Treatment of Cancer (RTOG/EORTC) Scale.

Results: Between April 2012 and July 2016, 21 patients underwent CyberKnife-SRT for 24 orbital metastases (3 patients were treated bilaterally; 10 metastases were intraocular, 14 periocular) from different primary tumors (breast, lung, kidney, lymphoma, thyroid and leiomyosarcoma in 13, 3, 2, 1, 1 and 1 patients, respectively). The median treatment dose was 18 Gy (range 15-24 Gy) given in a median of 3 fractions (range 2-3 fractions) with a median dose of 6 Gy per fraction (range 5-10 Gy/fraction). At the end of the treatment, grade 1 toxicity was observed in 8 cases. No decrease in visual field or loss of vision was documented. Sixteen lesions underwent post-SRT MRI and, after median follow-up of 5.5 months (range 1.1 – 26.5 months), no local recurrence occurred. All of these patients reported decreasing pre-SRT symptoms and improvement in their quality of life. Longer follow-up with a median time of 13.7 months (range 6 – 26.5 months) is available in 8 lesions, 4 with complete radiological response and 4 with partial radiological response.

Conclusions: In our experience, CyberKnife-SRT is a well-tolerated treatment that offers high local control and symptom relief in patients with intraocular and periocular malignant lesions.

P009

THE POSSIBLE PROGNOSTIC ROLE OF HISTONE DEACETYLASE AND TRANSFORMING GROWTH FACTOR /SMAD SIGNALING IN HIGH GRADE GLIOMAS TREATED BY RADIO-CHEMOTHERAPY: A PRELIMINARY IMMUNOHISTOCHEMICAL STUDY

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Glioblastoma (GBM) is the most common and aggressive tumor of the central nervous system. Unfortunately, patients affected by this disease have a very poor prognosis, due to high level of invasiveness and resistance to standard therapies. Although the molecular profile of GBM has been extensively investigated, the events responsible for its pathogenesis and progression remain largely unk-

nown. Histone Deacetylases (HDAC) dependent epigenetic modifications and transforming growth factor (TGF)-β/Smad pathway seem to play an important role in GBM tumorigenesis, resistance to common therapies and poor clinical outcome. The aim of this study was to evaluate the involvement and the possible interaction between these two molecular cascades in the pathogenesis and prognosis of GBM. Immunohistochemistry (IHC) was performed on microdissected GBM samples, collected from 14 patients (6 men and 8 women) ranging in age from 43 to 74 years. The patients were previously divided, on the basis of their overall survival (OS), into two groups: short and long OS. Patients with poor prognosis showed hyperexpression of HDAC4 and HDAC6, an activation of the TGF-β/Smad pathway, with high levels of IL-13, Smad2, PDGF and MMP3 expression, compared to the long survivors. The short OS group exhibits a decrease in Smad 7 expression and also low levels of p21 immunostaining, which represents a common target of the two pathways. The IHC data was confirmed by quantitative analysis and Immunoblotting. Our preliminary results suggest that both HDAC4 and HDAC6 together with the TGF-β/Smad pathway may be involved in progression of GBM and this cross talking could be a useful prognostic marker in this deadly disease.

P010

HIPPOCAMPUS-SPARING INTENSITY MODULATED WHOLE-BRAIN RADIOTHERAPY WITH SIMULTANEOUS INTEGRATED BOOST TO MULTIPLE BRAIN METASTASES: A DOSIMETRIC AND RADIOBIOLOGICAL ANALYSIS

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Aims: High dose irradiation to hippocampus is critical in determining neurocognitive function (NCF) outcomes. We evaluated the feasibility of intensity-modulated whole-brain radiotherapy (IMRT) and simultaneous integrated boost (SIB) to multiple brain metastases (BMs) to generate hippocampus-sparing plans.

Methods: 5 patients with a total of 16 BMs who previously underwent whole brain radiotherapy with boost to multiple metastases were selected. Radiotherapy was prescribed according to SIB technique with all targets irradiated simultaneously over 10 daily fractions. Doses of 30 Gy and 50Gy were prescribed to PTVWB and PTVM, respectively. Bilateral hippocampi were delineated according to RTOG 0933 trial suggestions, on T1w MRI co-registered planning CT. Clinical standard plans (s-IMRT) were compared with plans aiming to spare hippocampus irradiation. Two plans were re-optimized for hippocampal sparing using two Elekta MLCs: MLCi2 with 10mm leaf width (hs10-IMRT) and Agility with 5 mm leaf widths (hs5-IMRT). All plans were evaluated using target coverage metrics, homogeneity index (HI) and conformity index (CI). Normal tissue complication probabilities (NTCP) for neurocognitive function impairment (NCF) were calculated using a predictive model developed by Gondi et al.

Results: Plans aiming to hippocampus sparing demonstrated comparable planning target volumes coverage and no differences in sparing of other organs at risk (brainstem, optic chiasm, eyes, lens). Significant reductions in hippocampal doses relative to standard plans were achieved in all patients. Mean dose to bilateral hippocampi was reduced from 36.5 Gy (range: 34.7-37.7 Gy) to 17.4 Gy (range: 11.2-24.7 Gy) and 16.4 Gy (range: 11.0-24.1) for hs10-IMRT and hs5-IMRT plans, respectively. D40% was reduced from 36.9 Gy (range: 35.3-37.7 Gy) to 18.2 Gy (range: 11.8-25.2 Gy) and 17.2 Gy (range: 11.5-25.0 Gy) for hs10-IMRT and hs5-IMRT plans, respectively. Mean NTCP values for NCF impairment as predicted by Gondi model decreased from 98.0% (range: 97.7-98.5%) to 62.1% (range: 34.8-83.9%) and to 58.2% (range: 33.4-83.5%) for hs10-IMRT and hs5-IMRT plans, respectively. Dose reductions depended mainly on metastases location and distance from hippocampus.

Conclusions: IMRT plans aiming at sparing bilateral hippocampi can be successfully optimized with SIB-IMRT despite the high-dose irradiation of multiple brain metastases, providing a significant reduction in NTCP for radiation induced NCF decline.

P011

IMAGE-GUIDED INTENSITY MODULATED RADIOTHERAPY (IG-IMRT) IN GLIOBLASTOMA: OUTCOMES OF A MONO-INSTITUTIONAL EXPERIENCE

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Objective: To report outcomes of patients(pts) with

newly diagnosed glioblastoma(GBM) treated with radical/adjuvant Image-Guided Intensity Modulated Radiotherap (IG-IMRT) at a single institution.

Methods: From 02/2013-02/2016, 90 GBM pts and a median age of 60.2(33.0-79.1) years, were treated with IG-IMRT in our institution. One lesion was diagnosed in 78% of pts, while in 22% was multifocal GBM. Surgery was performed in 62.2%, biopsy in 33.3% of pts, respectively; in 4.5% of pts, the diagnosis was based on MRI characteristics. Concomitant and adjuvant chemotherapy(CT) was prescribed in 72% of pts; 62% of pts had an adjuvant IG-IMRT, while 38% a radical IG-IMRT. Median GTV was 48.9(10.2- 340.5) cc. A total dose(TD) of 60 Gy /30 fr was prescribed in 66 pts, and 40 Gy/15 fr(Roa's protocol) in 22 pts; in two pts, the TD prescribed was 50.4 and 53.4 Gy, respectively, because of tumor position and PTV volume. GTV definition was based on contrast-enhanced MRI in all pts. The treatment was delivered with helical IMRT in 59% of pts and with volumetric IMRT in 41% of pts. Image guidance (kVCT/MVCT) was performed daily in all pts.

Results: With a median follow-up of 10.9(0-47.5) months, 7 pts were alive at the last follow-up. Median OS was 17.0(0.9-50.2) months in pts treated with surgery and adjuvant IG-IMRT-CT and 8.1 (1.8-36.8) months in pts treated with radical IG-IMRT. This results compares favorably with those of GBM survival in U.S. and Roa's trial. Median survival was 9.8 months in pts treated with 40 Gy/ 15 fr and 15.9 months in pts treated with 60 Gy/ 30 fr. Pts with only one lesion had a better median survival that pts with multifocal GBM : 15.4 vs 10.2 months. Time to progression was 6.6(1.8-47.5) months in adjuvant treatments and 3.3(0.2-34.1) months in radical treatments. Acute toxicity were: headache:G1=10.0%, G2=2.2%; dizziness: G1=3.3%, G2=2.2%; nausea: G1= 10.0%,G2= 1.1%; hearing loss: G1=3.3%,G2=1.1%; Ophtalmic: G1=10.0%,G2=2.2%; Cognitive(subjective): G1=5.6%,G2=2.2%; Haematologic: G1=4.6%,G2=4.6%,G3=4.6%, G4=1.5%; Alopecia: G1=31%,G2=2.2%. Late toxicities were evaluable in 74 pts and no G3 toxicities were registered. Headache was: G1= 1.1%, G2= 1.1%; dizziness G1= 2,2%; fatigue G1=6.8%,ophthalmic: G1=1.1%;cognitive(subjective):G1=2.2%;G2=1.1%

Conclusions: OS and PFS in GBM pts is enhanced by surgery and concomitant CT. Other prognostic factors for OS in our pts: multifocal lesions and RT TD. IG-IMRT ensured a low acute and late toxicity.

P012

RADIOTHERAPY (RT) AND TEMOZOLAMIDE (TMZ) IN RESECTED PATIENTS WITH GLIOBLASTOMA MULTIFORME (GBM): THE EXPERIENCE OF OUR INSTITUTION

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Aims: GBM is the most frequent neoplasm of central nervous system; surgery followed by cranial irradiation still remains the standard treatment. However, the outcome of patients (Pts) treated with such approach is dismal with most of them having a survival time of less than 2 years. Temozolamide has shown to be effective and manageable when given to Pts with advanced stage of disease.

Methods: To assess efficacy and toxicity of TMZ given as concomitant treatment to 60 Gy and as maintenance therapy after RT in Pts with completely surgically resected GBM. From 1997 to 2016 283 Pts (male 169, female 114) with a median age of 59 years (range 24 – 75) were enrolled in this observational study. All Pts received cranial RT 60 Gy with daily fraction of 2 Gy and concurrent TMZ at dose of 75 mg/m daily. Six weeks after the end of treatment, Pts underwent cranial MRI. The Pts that were still in CR received TMZ at dose off 200 mg/m /daily for 5 days every 4 weeks for 4 courses.

Results: None of Pts enrolled progressed during RT and all received TMZ also al maintenance therapy. 25% Pts had progression disease during the maintenance therapy and died. After a median follow-up of 18 months the overall and progression-free survival rates were 70% and 55% respectively. Four patients had a survival of more than four years without progression of disease. Main toxicities were WHO grade 3 leukopenia and thrombocytopenia recorde in 10% of courses and WHO grade 2 nausea and vomiting occurred in 25% of courses.

Conclusions. TMZ given as concomitant to RT and as maintenance treatment in Pts with GBM has shown to be effective and well tolerated in adjuvant setting. Further follow-up and larger number of Pts will be required to define its concrete advantage on survival

P013

THE POTENTIAL ROLE OF HYPOXIA IMAGING WITH 18F-FAZA PET/CT IN RADIOTHERAPY PLANNING FOR HIGH GRADE GLIOMAS

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Background and Aims: Hypoxia plays a central role in high grade Gliomas development, angiogenesis, growth and resistance to radio and chemotherapy. In hypoxic conditions the expression of transcriptional factors, such as the hypoxia-inducible factor (HIF), is involved in tumor malignant progression, decreasing patient survival. In this study we evaluated how the information about tumor oxygenation status, obtained from18F-FAZA PET/TC, could modify our treatment planning.

Methods and Materials: From April 2016 to April 2017, 10 patients with diagnosis of high grade glioma, underwent a baseline 18F-FAZA-PET/TC in order to define maximum standardized uptake value (SUVmax) and to generate 7 different biological Volumes of Interest (VOIs). The first VOI was manually drawn by an experienced Nuclear Medicine Physician who included the whole uptake area (BTV-1). Starting from BTV-1 three other volumes have been automatically generated as 40%, 50% and 60% of the SUVmax (BTV-40, BTV-50 and BTV60). Further, 3 BTVs have been generated as representative of the Hypoxia regions based on the tissue-to-muscle ratio, respectively with thresholds of 1.2, 1.3 and 1.4. Target delineation was performed using contrast enhanced T1 + T2/FLAIR Magnetic Resonance (MR) sequences, with Dynamic Susceptibility Contrast and Dynamic Contrast Enhanced perfusion, fused with the planning CT. Gross Tumor Volume (GTV) included tumor postcontrast T1 weighted imagies, without peritumoral edema, according to the European Organization for Research and Treatment of Cancer (EORTC), plus regions of abnormal T2/FLAIR MR in case of low grade glioma concomitant areas. Clinical Target Volume (CTV) was generated adding 20 mm to GTV, and Planning Target Volume (PTV) was obtained adding an isotropic margin of 5 mm to CTV. After the contouring, planning MR was matched with FAZA PET/TC imaging.

Results: In every patients, the T1 MR enhanced volume, corresponding to GTV high grade component, included the 7 FAZA-VOIs, validating the hypothesis that hypoxia is strictly correlated with the tumor aggressiveness.

Conclusions: In our experience the biological information from 18F-FAZA PET/CT doesn't modify the target delineation but it could be used to identified hypoxic areas within the tumor mass for dose escalation.

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P014

DIFFUSION MRI FOR DIFFERENTIAL DIAGNOSIS BETWEEN PSEUDOPROGRESSION OR RELAPSE IN GLIOBLASTOMA PATIENTS.

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Aims: Diffusion MRI (DWI) values are directly related to the tumor cellularity. We evaluated a clinical application of DWI for a differential diagnosis between pseudoprogression or relapse after chemo-radiotherapy (CT-RT) in the follow-up of patients (pts) with post-surgery residual glioblastoma (GBM).

Methods: After primary surgery, 16 pts (6 females and 10 males), median age 59 years (range, 65-77), were submitted to CT-RT. The treatment schedule was according to Stupp's protocol. All pts were submitted to conventional MRI and DWI before and after CT-RT. Region of interest (ROI) positioning (range,10-150 cc) was carried out with dedicated software using the axial post-contrast T1-weighed images. The ROI was placed in a hyper intense region of gross tumor volume (GTV) on at least three contiguous slices and reported on the DWI. The MRI and DWI were performed within 2 weeks before, 2 months after CT-RT and then every 2 months until disease progression.

Results: Two months after CT-RT, 6 (37.5%) pts obtained a reduction of the GTV, other 4 (25%) a stabilization of disease; median duration of response was 7 months (range, 3-13). In the remaining 6 (37.5%) pts we observed a progression in-field in four cases and out-field in other two. In pts with a reduction of GTV, a decrease of DWI signal of 18% was registered with respect to pre CT-RT values ($p<0.05$). The DWI signal increased in all 6 cases with tumor relapse. T1-weighed MRI gave a discordant result showing 10 (62.5%) in-field relapse diagnosed by a contrast enhancement increase, which in 4 cases were pseudoprogression documented by cell reduction at DWI. This interpretation was confirmed in the follow up where also MRI showed a contrast enhancement reduction. Furthermore, for 4 pts in progression after an initial response, DWI informations were used for better identify the area with greater cellularity concentration to re-irradiate. 3 lesions were re-irradiated with fractionated stereotactic RT (10 x 3Gy), the other 1 with radiosurgery (15Gy).

Conclusions: Our experience has shown that DWI is useful in the follow-up of pts with GBM to differentiate between pseudoprogression and relapse. In clinical practice DWI could be also used for re-irradiation of areas with greater cellularity concentration.

P015

HIPPOCAMPAL SPARING RADIOTHERAPY AND NEUROCOGNITIVE IMPAIRMENT: A REVIEW

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Aims: Whole brain radiation therapy (WBRT) is an effective therapeutic modality in patient with brain metastases. However, nearly 90 % of patients undergoing WBRT suffer from neuro-cognitive function (NCF) impairment at the diagnosis and up to two-thirds will experience a further decline within 2 to 6 months after WBRT. Focal dose reduction on bilateral hippocampus is thought to improve NCF preservation. Aim of the present study is to present a systematic review of clinical results on NCF after HS-WBRT.

Methods: A systematic review of published literature was performed on PubMed and the Cochrane Library. Only prospective clinical trials reporting NCF outcome of patients treated with hippocampal sparing (HS)-WBRT have been analyzed.

Results: A total of 165 patients from 3 studies were included. The studies are characterized by small sample size and different methods in term of radiotherapy technique, but with similar planning results and NCF assessment tests. No significant changes in NCF (i.e., verbal and non-verbal learning memory, executive functions, and psychomotor speed) between baseline and 4 month-follow-up after RT or only a mean relative decline in delayed recall to 4 months (7%), significantly lower in comparison with historical control (30%), were observed.

Conclusions: HS-WBRT is a feasible technique, able to provide highly conformal and homogenous dose distributions for the whole brain planned target volume with lower doses to organ at risk such as the hippocampus. Considering the safety profile of HS-WBRT and preliminary results on NCF preservation, further studies appear justified in patients undergoing brain irradiation for brain metastases.

P016

STEREOTACTIC RADIOTHERAPY IN PATIENTS WITH RECURRENT GLIOBLASTOMA MULTIFORME: OUR CENTRE EXPERIENCE.

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Aims: Available approaches for glioblastoma multiforme (GBM) include surgery and adjuvant chemoradiation in operable cases. In patients with recurrence of disease, few experiences exist to improve survival. We report our experience with stereotactic radiotherapy (SRT) in patients with recurrent disease after standard chemoradiation or radiation therapy alone.

Methods: 46 patients (25 M and 21F; men age 56.5±12.3 years) with recurrent GBM after surgery and chemoradiation or radiation therapy alone (mainly 60Gy in 30 fractions through external beam radiation therapy) were retrospectively evaluated. They were treated in our centre from 2007 to 2016 with a delivered dose of 15-30 Gy (mean 20 ± 4.7 Gy) thorough fractionated SRT (FSRT, one to five fractions) with a linear accelerator equipped with robotic arm. 31 patients were treated also with temozolomide (TMZ) and two received an association of TMZ and fotemustine and bevacizumab, respectively.

Results: Mean clinical target volume (CTV) was 20 ml. Mean overall survival (OS) from the end of FSRT was 17.3 months; OS at 6 and 12 months was 67.4% and 43.5%, respectively. Interestingly, 11/46 (or 23.9%) patients reached a survival ≥ 18 months: among them, one died 84 months after FSRT delivery and another is alive after 96 months from treatment. In 4/46 (8.7%) patients radionecrosis occurred.

Conclusions: Our study has demonstrated that re-irradiation in patients affected by recurrent GBM is a feasible option and that FSRT delivered with linear accelerator equipped with robotic arm is safe and effective after chemoradiation or radiation therapy alone: this modality allows to obtain a higher OS than standard treatments, also superior to 18 months, with limited toxicity.

P017

RADIOSURGERY AND STEREOTACTIC RADIOTHERAPY WITH CYBERKNIFE® SYSTEM FOR MENINGIOMAS

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Aims: The Aim of our work was to evaluate the impact of radiosurgery (SRS)/stereotactic radiotherapy (SRT) with Cyberknife® system in local control, final clinical outcome and toxicity in patients affected by meningioma, according to location, size and histological grade of

lesion. Methods: From January 2013 to April 2017, 52 patients (pts), 28 female and 24 male, with median age of 62 years, affected by intracranial meningiomas, were treated with Cyberknife® system in in the Department of Radiation Oncology of National Cancer Institute Pascale of Naples. Of these, 24 pts (46%) had undergone prior surgery: 20 (38%) with a gross total resection and 5 (10%) with a subtotal resection. Other 27 (52%) pts did not underwent surgery, and 22 pts (42%) had a diagnosis of recurrence of meningioma. Clinical target volume (CTV) was considered with the same volume of gross tumor volume (GTV); planning target volume (PTV) was the CTV plus a 2-mm margin in all directions. SRS was used to treat lesions smaller than 2 cm, SRT to treat lesions bigger than 2cm or smaller than 2 cm but near to a critical site such as optical chiasm, optic pathway or brainstem. Local Control (LC) and clinical outcome in terms of symptomatic resolution were analyzed. A correlation with progression disease (PD) and fraction scheme was made. Results: 47 pts were evaluated for follow up. Median follow-up was 20 months (range 2-48). Six patients died, two for progression of disease after 5 and 8 moths from RT, 1 patient after 27 months from RT was re-submitted to surgery and died at 31 months from RT for post-surgical sepsis, 3 patient died for heart disease. At follow-up of 12 months we evaluated 28 pts of these 100% are in LC. At follow-up of 24 months we evaluated 19 pts of these 89% are in LC. At follow-up of 36 months we evaluated 9 pts of these 89% are in LC. The tumor volume decreased in 12 pts (23%) at average time of 19 months after end of treatment, while it was unchanged in 27 pts (52%) at average time of 20 months, and in PD in 7 pts (13%) at average time of 18 months. PD not seems to be related to the fractionation of the treatment delivered. At baseline 44/52 pts (85%) were symptomatic with visual disorders in 19 patients (43% of symptomatic patients), motor disorders in 17 pts (39% of symptomatic patients), hearing disorders in 6 pts (14% of symptomatic patients), headache in 10 pts (23% of symptomatic patients) and epilepsy in 6 pts (14% of symptomatic patients). No acute neurological symptoms related to RT were reported. Was observed for visual symptoms an improvement in 6 pts, complete resolution in 3 pts, stability in 10 pts. For motor disorders an improvement in 2 pts, complete resolution in 1 pts, stability in 11 pts, worsening in 3 pts, appearance in 3 pts. For hearing disorders an improvement in 2 pts, resolution in 1 pts, appearance in 3 pts, worsening in 1 pts, stability in 2 pts. An improvement of headache was observed in 1 pts, complete resolution in 4 pts, stability of symptoms in 5 pts, appearance in 2 pts. For epilepsy a complete resolution was observed in 1 pts, improvement in 1 pts, stability in 2 pts, worsening in 2 pts, appearance in 1 pts. Conclusion: Our experience confirm that SRS/FSRT with Cyberknife system allows a good disease control and improves, in a limited number of patients, visual, hearing and motor symptoms.

P018

RADIOLOGICAL RESPONSE MONITORING DURING PROTON IRRADIATION OF A PAEDIATRIC SKULL BASE CHORDOMA: A CASE REPORT.

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Aims: Proton therapy (PT) is considered the gold standard in the treatment of chordoma of the skull base; this tumor is a very rare disease in paediatric patients. Even though this tumor is usually considered a very slowly responding tumor, MRI-based monitoring was applied to evaluate possible morphological changes and/or complications and to evaluate therapeutic response and safety in terms of possible re-planning.

Methods: the 10-year old girl had previously received three surgical interventions with a residual macroscopic bilateral disease on the dens of the epistropheus and a left nodular lesion in the lateral medullary-spine junction with compression and shifting of the spinal cord. She was treated with PT at the Trento Proton Therapy Centre (the first pediatric patient treated with PT in Italy). The treatment was performed after the comparison of the proton plan with an IMRT photon plan developed at Università Cattolica del Sacro Cuore, Rome. The proton plan was calculated from acquired CT(TPS Elekta XIO, Pencil Beam algorithm calculation) images fused with MRI. The total irradiation dose of 73.8 Gy (1.8 Gy RBE per fraction, 5 times a week) was delivered with three fields (one posterior and two anterior-oblique). Four MRI examinations were performed (without contrast, with T2weighted sequence) during the course of the treatment at the dose of 32.4 , 54, 64.8, and 73.8 Gy RBE, respectively.

Results: The bony lesion around the dens of the epistropheus did not change in volume or morphology whereas the nodule component showed a progressive volume reduction from 4.336 cm3 at the beginning of the treatment course to 2.829 cm3 (32.4 Gy RBE); 2.051 cm3 (54 Gy RBE); 1.045 cm3 (at 64.8 Gy RBE and 73.4 Gy RBE) for a total decrease of 76%. This reduction entailed the decompression of the spinal cord.

Conclusions: The monitoring of the evolution of chordoma during PT can permit to observe change in volume and morphology of the lesion in a disease usually considered to be a stable tumor during irradiation. This procedure can also allow to control the safety of a treatment delivering very high doses in proximity to critical organs at risk. It could also be used as a tool for re-planning of the treatment, if indicated.

P019

EVALUATION OF THE RESPONSE AND SURVIVAL IN PATIENTS WITH 1-4 BRAIN METASTASES TREATED WITH FRACTIONATED STEREOTACTIC RADIOTHERAPY (FSRT): A MONO-INSTITUTIONAL EXPERIENCE

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Aims: Evaluation of the response and survival in patients with 1-4 brain metastases (BM) treated with fractionated stereotactic radiotherapy (FSRT).

Methods: We prospectively observed 35 patients with BM from different primary tumors (breast, lung, colorectal), treated with FSRT from 2015 to 2017. Patients presenting 1-4 BM, age <70 years and Karnofsky Performance Status > 70%. Patients were treated with VMAT (Volumetric Modulated Arc Therapy) radiotherapy technique, using 2 different schedules: 20 Gy in 4 fractions (5 Gy/day) or 24 Gy in 3 fractions (8 Gy/day). For all patients a baseline MRI performed before starting FSRT was co-register with planning-TC using a rigid algorithm; to evaluate treatment response MRI was acquired 3 months after the end of FSRT, every 3 months during first year of follow up than every 6 months. Response to treatment was evaluated considering changes both in the larger tumor diameter according to RECIST criteria and 2 larger diameters according to WHO criteria, measured at each MRI control on T1 sequences.

Results: To date 25/35 patients were evaluable for tumor response at least at 3 months after the end of FSRT; evaluation of response to treatment showed an agree between WHO and RECIST criteria for all patients evaluated at 3 months; this correlation appears to remain in subsequent MRI. Treatment response observed at 3 months consisted in: 3 complete responses (CR) (12%); 7 partial responses (PR) (28%); 8 stable disease (SD) (32%); 7 progressions (PD) (28%). At a follow-up of 6 months, 15 patients could be evaluated: 3 CR (20%); 1 PR (6,7%); 8 SD (53.3%); 3 PD (20%). At 9 months, on 10 evaluable patients, we observed: 1 CR (10%); 8 SD (80%); 1 PD (10%). Only 4 patients were evaluable at 12 months: 3 SD (75%) and 1 PD (25%). 7 patients died between 3 and 6 months of follow-up, no patients died between the 6 and 12 months; one patient died after 12 months follow-up. Living patients at 6, 9 and 12 months is respectively 15, 10 and 4, corresponding to survival rate of 65.2%, 43.5%, 17.3%.

Conclusions: Although the sample size is still small, FSRT seems efficacy in terms of local control and survival. The obtained results correlate to prognostic factors as reported by literature data and used for our analysis; a longer follow-up will confirm this trend.

P020

PATIENTS AFFECTED BY UNMETHYLATED O(6)-METHYLGUANINE-DNA METHYLTRANSFERASE (MGMT) GLIOBLASTOMA UNDERGOING RADIO-CHEMOTHERAPY MAY BENEFIT FROM MODERATELY DOSE-ESCALATED RADIOTHERAPY.

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Aims: To compare the therapeutic results of two radiotherapy (RT) dose schedules in combined Temozolomide (TMZ)-RT treatment in newly diagnosed glioblastoma (GB), according to the MGMT methylation status.

Methods: Patients with newly diagnosed GB received either standard (60 Gy) or moderately escalated dose (70 Gy) radiation therapy (RT) with concomitant and adjuvant TMZ between June 2006 and October 2013. We retrospectively evaluated the therapeutic effectiveness of the latter RT schedule in terms of Overall Survival (OS) and Progression-Disease Free Survival (PDFS) in suitable cases with univariate and multivariate analysis, after analyzing the MGMT methylation status.

Results: One hundred and seventeen patients were selected for the present analysis on the grounds of suitable criteria (unifocal GB, limited volume RT, KPS >70) out of 222 total treated patients accrued. Seventy-two out of the selected cases received the standard RT-TMZ course (SDRT-TMZ) whereas the remaining 45 underwent the escalated schedule (HDRT-TMZ). Median OS and PDFS were comparable between these groups (13 months and 7 months in the former and 14 months and 10 months in the latter, respectively). The analysis according to the MGMT promoter methylation status showed instead that, in unmethylated-MGMT GB patients, HDRT-TMZ and SDRT-TMZ groups had different median OS (p=0.01) and PDFS (p=0.007), that is, 8 months and 5 months for the SDRT-TMZ group, and 14 months and 9 months for the HDRT-TMZ group, respectively. No difference in survival outcomes was found in methylated-MGMT GB patients according to the two RT schedules (p=ns)

Conclusions: In our experience, unmethylated-MGMT GB patients benefited from a moderately escalated dose of RT plus TMZ. The therapeutic approach adopted in the present study for this subset of patients may deserve prospective trials for validation.

P021

INTRA-OPERATIVE RADIOTHERAPY (IORT) FOR TREATMENT OF LOCALLY ADVANCED ESOPHAGEAL CANCER: PRELIMINARY RESULTS IN A SERIES OF 17 PATIENTS

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Purpose: To describe our experience with intraoperative radiotherapy (IORT) as a boost after preoperative chemo-radiotherapy (RT) in patients with locally advanced esophageal cancer.

Materials and Methods: From 2007 to 2016, seventeen patients (pts), median age 61 years, with locally advanced esophageal cancer were enrolled in our institutional protocol and underwent pre-operative chemo-radiation therapy followed by surgery with IORT boost. Tumor locations were: 2 in upper, 11 in middle and 4 in lower esophageal third. Pathology was squamous cell carcinoma in 15 cases and adenocarcinoma in 2 cases. Clinical stages were: 2 pts stage II, 13 pts stage III and 2 pts stage IV. Pre-operative radiotherapy was prescribed with conformal technique by using 6-15 MeV X-rays to a total dose of 44 Gy in 22 fractions (2 Gy/fr) and one patient to total dose of 41,4 Gy in 23 fractions (1,8 Gy/ fr). Chemotherapy was given concomitantly to radiotherapy with cisplatin and 5-FU and in one case with carboplatin and taxol. IORT was performed after surgical resection to the tumor bed and/or regional lymph nodal areas by a dedicated linear accelerator (Mobetron, Intraop, Sunnyvale, CA). A single dose of high-energy electrons (6, 9 or 12 MeV) of 10-15 Gy was delivered by collimator (3-5,5 cm) with bevel 0°-30°. Procedure timing was 20-25 minutes.

Results: One of 17 pts received only preoperative RT for severe renal failure and one patient required in urgency surgery for mediastinitis. Four pts developed chemo-related toxicity. Surgery consisted of total or sub-total esophagectomy with lymphadenectomy. One patient died during surgery for massive bleeding; two pts died just after the surgery for pulmonary embolism and gastric necrosis. Postoperative complications occurred in 7/14 cases and consisted of pulmonary embolism, gastro-tracheal fistula, mediastinitis, respiratory distress. Median follow up was 24 months (range 1-92). Survival at 1, 2, 4 years was 71%, 50%, 40% respectively. Causes of death were: 1 pulmonary embolism, 1 pulmonary distress,1 cardiac failure and 10 progression desease with distant relapse, only 2 cases of these (20%) showed regional recurrences after 11 and 21 months from surgery.

Conclusions: IORT during surgery for esophageal carcinoma seems to be a feasible procedure combined with preoperative chemo-radiotherapy, although toxicity is not negligible. Larger number of patient and longer follow-up are needed to assess long-term outcome.

P022

ROLE OF MRI TEXTURE ANALYSIS AS PROGNOSTIC FACTOR IN PATIENTS WITH GLIOBLASTOMA DIAGNOSIS UNDERGOING ADJUVANT CHEMO-RADIATION

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Aims: The present study was designed to evaluate MRI texture analysis (TA) as a prognostic factor in patients with glioblastoma diagnosed with undergoing adjuvant chemo-radiation.

Methods: We performed a retrospective analysis on forty patients with glioblastoma undergone partial surgery and adjuvant chemo-radiotherapy (C-RT) between January 2010 and December 2015. The gross tumor volume (GTV) was evaluated at baseline by MRI and contoured on T1, DWI, and FLAIR sequences, and multiple derivative parameters evaluated by means of a LifeX Software. By performing univariate analysis and a multivariate analysis (logistic regression), these TA parameters were then correlated, together with clinical parameters and blood tests with patients' clinical outcome (in terms of overall survival, progression free survival).

Results: A total of 40 patients were included in the analysis (mean age 61 years, mean 60 years, range 35-80 years, 22 males and 18 females). Twenty-eight (70%) developed recurrence, whereas 24 patients (60%) died. Parameters significantly correlated with recurrence included lymphocyte counts (p:0.036), platelet counts (p:0.043), TA parameters (see Table for description of textural parameters) Mdc-Energy (p:0.046), Mdc-LGRE (p:0.041), Mdc-SRLGE (p:0.031), whereas parameters significantly correlated with OS included MGMT status (p:0.012), Age (p:0.030), Mdc-Compacity (p:0.018), Mdc Sze (p:0.037), Flair-GLCM-Homogeneity (p:0.021). AUC for recurrence (within 12 months) was 0.817 (95% CI 0.543-0.944), whereas AUC for overall survival (>12 months) was 0.885 (95% CI 0.733-0.941).

Conclusions: Our results suggest that TA, toghether with blood tests and clinical parameters have a significant predictive and prognostic value in the management of glioblastoma patients.

P023

CONFORMITY INDEX (CI) IN THE OPTIMIZATION OF DOSE DISTRIBUTION IN CASE OF IRREGULAR-SHAPED RELAPSE OF ACOUSTIC NERVE NEURINOMA.

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Aims: neurinoma of acoustic nerve, a benign tumor originating from Schwann cells of vestibolococlear nerve (VIII C.N.) involves hearing reduction, it is diagnosed by MR with contrast medium, slim slices of 1-3 mm and it is treated by surgery and/or radiotherapy. Verify the conformity index in case of significant irregularity in the target's shape in the optimization of the dose with tomotherapy. In literature the CI for those kinds of volume is 1,1.

Methods: On November 2016, a postoperative relapse of neurinoma of right acoustic nerve was treated at San Giovanni Addolorata Hospital. Dosimetric planning was prepared by CTV contouring after fusion of MR images with contrast medium and slim slices of 1 mm (T2 weighed), by following AIRO guidelines. PTV was contoured considering an isotropic wedge of 2 mm from CTV. Brain stem, cochleas, acoustic channels, crystalline lens, optic nerve and chiasm were contoured as OARs. The prescribed dose at PTV was 25 Gy in 5 fractions, corresponding at a biological equivalent dose of 67 Gy ($\alpha/\beta = 3$). Conformity Index (CI) was evaluated as ratio between normal tissue volume and PTV volume that received 100% of the prescription dose (1+V100_Norm/V100_PTV). Hi-Art Planning Station 5.1.0.4 was the TPS used.

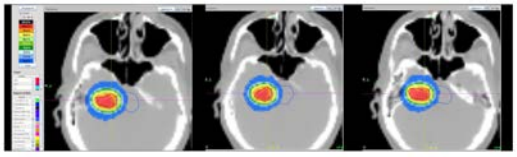

Figure 1

Results: PTV volume was estimated to be 4.55 cc with an extremely irregular shape, and it partially overlapped with brain stem. The resulting CI was 1.06. Dose constraints of the OARs were respectful of the guidelines raccomandations in order to avoid serious side effects. Regardless of the overlapping with PTV, the maximum dose of brain stem was lower than the prescription dose (Figure 1). The treatment time of every fraction was estimated to be around 5 minutes, after all acceptable even though compared to a VMAT timing.

Conclusions: Tomotherapy is highly effective to perform radiotherapy treatments on irregular-shaped relapse of acoustic nerve neurinomas.

P024

TOXICITY IN STEREOTACTIC RADIOTHERAPY IN BRAIN METASTASES WITH OR WITHOUT CONCOMITANT IMMUNOTHERAPY OR TARGETED THERAPY

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Aims: Stereotactic radiosurgery (SRS) and immune or targeted therapy play an increasingly important role in personalized treatment of metastatic disease and the concurrent application is rapidly expanding in daily clinical practice. The purpose of our mono-institutional study is to evaluate if radiation-induced brain toxicity increases with concomitant application of new drugs.

Methods: Between February 2012 and May 2017 sixteen patients (pts) with 27 cranial metastatic disease from several tumor types (lung, melanoma, breast and kidney) were treated, 8 pts (50%) with SRS and concurrent target or immune therapy (Group 1) and 8 pts (50%) with exclusive SRS (Group 2). Median age was 70 years (range 43-87 years), female/male ratio was 11/5. All pts were treated using Helical Tomotherapy (HT). For treatment setup the patients were immobilized with InterFix RS Kit and underwent to CT scan with 2.5 mm of slice thickness and images were fused with the 3D MPRAGE images of Magnetic Resonance Imaging (MRI) with 1mm of slice thickness that was performed the day before on a GE SIGNA 3T scanner. Contouring of Target and Organs at Risk (OARs) was performed, the Gross Tumor Volume (GTV) was increased with isotropic margins of 3 mm obtaining Planning Target Volume (PTV). SRS was defined by single fraction of 21 Gy each lesion; 10/16 pts (62,5%) occurred two and more lesions and 6/16 pts (37,5 %) only one. Target therapy had to be given concurrently to SRS, or initiated within 30 days before or after radiation. SRS was combinated with BRAF-inhibitors (Vemurafenib, Dabrafenib) in 2 pts (12,5%), with ALK-inhibitors (Crizotinib, Ceritinib) in 2 pts (12,5%), with Tyrosine kinase inhibitors (Sorafenib, Pazopanib) in 2 pts (12,5%), with EGFR-inhibitors (Erlotinib, Gefitinib) in 2 pts (12,5%).

Results: Each patient was sent to clinical evaluation with MRI scans initially 1 month after SRS and then every 3 months after SRS. Median follow-up was 25 months (range 1-64). Toxicity had to be either graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE). No

grade 4 and 5 toxicity were reported in both groups. In Group 1 grade 3 toxicity within the irradiated volume consisted of radionecrosis (n =2, 25%), and edema (n=1, 12,5%). Conversely, in Group 2 toxicity was: radionecrosis in 1 pts (12,5%) and edema in 3 pts (37,5%).

Conclusions: Our analysis, although based on very limited data, comparing SRS alone to SRS with targeted therapy found that toxicity rate did not differ significantly and even not appeared to be increased.

P025

WHOLE BRAIN RADIOTHERAPY WITH SIB (SIMULTANEOUS INTEGRATED BOOST) IN PATIENTS WITH BRAIN METASTASES: PRELIMINARY RESULTS

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Aims: To evaluate feasibility and safety of the Whole brain radiotherapy (WBRT) with simultaneous integrated boost (SIB) in patients with brain metastases.

Patients and Methods: From February 2016 to April 2017, patients with brain metastases of various primary tumors were treated with WBRT and SIB. In some patients was performed an hippocampal sparing tecnique.

Results: Ninteen patients were treated at our centre, in twelve of them we have performed a radiation treatment with the sparing of the bilateral hippocampi. The median age was 58 (range 48-74). The median Performance status (ECOG) was 2 (range 0.5–3). The median GPA score was 1.5 (range 0.5-3.5). The doses delivered to the whole brain were 17.5 Gy, 20 Gy, 27 and 30 Gy. SIB was performed with doses varying from 25 Gy to 50 Gy on one to multiple (2-6) lesions. The range of Dmean to the bilateral hippocampi was 12-23 Gy. The total of mestastases treated were 38. The radiotherapy techniques employed were IMRT (9 non coplanar fields) and VMAT (4 non coplanar arcs). The median follow up was 5 months. In 5/19 patients a complete to partial response was observed. 13/19 patients had a stable disease. A patient had local progressive disease. 8/19 patients died for systemic progressive disease. The median overall survival was five months. No evident acute and/or late toxicities grade >1 were observed.

Conclusions: Our preliminary results of WBRT with SIB for whole brain metastases confirm the feasibility of the technique and an acceptable toxicity.

P026

OPPORTUNISTIC INFECTIONS AMONG PATIENTS AFFECTED BY GRADE III-IV GLIOMAS TREATED WITH HIGH DOSE CORTICOSTEROIDS DURING CONCOMITANT CHEMO-RADIOTHERAPY

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Aims: the treatment of high grade gliomas (HGG) often involves surgery followed by adjuvant chemo(CT)-radiotherapy(RT), with concurrent high dose corticosteroids(CS) to reduce intracranial swelling and alleviate symptoms. CS are generally administered for 8-12 weeks putting patients(pts) at risk of opportunistic infections potentially causing CT-RT interruption. Hughes A. et al. demonstrated among this pts cohort a significant decrease of CD4 associated to higher infections and hospitalization rates. According to these data we decided to estimate among our records the incidence of opportunistic infections ascribable to CS correlated immunosoppression.

Methods: from January 2015 to December 2016, 27 newly diagnosed HGG pts underwent surgery followed by CT-RT within 45 days. Radical excision was performed in 13 pts, subtotal in 12, exclusive biopsy in 2. Histology was grade IV Glioblastoma in 18pt, grade III Anaplastic Astrocytoma in 8 and Anaplastic Oligodendroglyoma in 1. RT was planned at the total dose of 60 Gy/30 fractions(f) in 24pts. In 3 cases hypofractioned RT (50Gy/25f or 40Gy/15f) was chosen for comorbidity. During RT Temozolomide was administered daily at the dose of 75 mg/mq monitoring weekly blood count. With the aim of avoiding intracranial swelling, CS (Dexamethasone or Methylprednisolone) has been given for a median duration of 8.2 weeks. Substance ad dosage have been adapted to the clinical course and are reported in Table1.

Table 1.

SUBSTANCE	N°	DOSAGE	N°	CHANGE
IM Dexa	10	4 mg	8	1 increased to 8 mg and 1 decreased to 2 mg
	8 mg			
OS Dexa	8	4 mg	5	
		2 mg	3	
OS Met	9	8 mg	3	1 increased to 16mg and 2 shift to Dexa 8 mg IM
		16 mg	6	1 shift to Dexa 8 mg IM

Dexa= Dexamethasone; Met=Methylprednisolone; IM=intramuscular; OS=oral

Results: CT scheduling was respected in 25pts. In 2 cases CT was early interrupted for non hematologic toxicity. 25pts completed the planned RT. In 1pt it was interrupted after 54Gy for clinical worsening. One pt (3.7%), after 20Gy, developed pneumonia in absence of

blood count decrease. Hospitalization and antibiotic therapy have been mandatory. RT was interrupted for 12 days and then started again and completed. Neutropenia and thrombocytopenia were highlight only in 1 pt who hasn't developed infections. In all of cases CS well controlled neurologic symptoms.

Conclusions: In our experience profilactic CS use during CH-RT for primary brain tumors isn't correlatet with a significant increased risk of opportunistic infections and provides adequate intracranial swelling control.

P027

IRRADIATION BY INTRACRANIAL STEREOTACTIC TREATMENT IN PATIENTS WITH CEREBRAL METASTASES

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Aims: Evaluate the maximum tolerated dose and the volume reduction of secondary lesions in metastatic patients after intracranial stereotactic treatment with VMAT (Volumetric Modulated Arc Therapy) technique

Materials and Methods: Between October 2012 and September 2016, 35 patients were treated with stereotactic radiotherapy ; Of these 8 patients had previously been subjected to whole brain radiotherapy as a primary treatment with a dose of 30 Gy administered in 10 fractions of 3 Gy/die , 5 days a week. The average age of patients in the analyzed sample is 51 years (40-78 y range), 40% of them were affected by primitive lung cancer, 20% melanoma, 18% breast cancer, 22% respectively rectal colon cancer, stomach cancer and ovarian cancer. Average dimensional value of the lesions is 14 mm. For 27 patients the stereotactic treatment dose was 20 Gy in a single fraction, for other 8 patients the dose was 24 Gy delivered in 3 fraction of 8 Gy. Average dose was 22Gy (20-24 Gy). 41% of treated patients had a single lesion, 48% two lesions, 11% three lesions. The stereotactic radiation therapy was delivered with a TRILOGY VARIAN linear accelerator with VMAT technique, with day-to-day CBCT (cone beam computer tomography).

Results: Of the 35 patients treated, 16 are deceased, 5 interrupted the follow-up at 3 months, 14 are living. The average survival value of the sample analyzed after an average 14-month follow-up period (3-34 months) was 12 months. Six months after the treatment, in 12% of patients lesions disappeared, in 41% had a volumetric reduction with a mean size of 1.1 cm (6-34 mm range).

Conclusions: At six months from the treatment, the study showed a volume reduction of lesions in 41% of patients, with the disappearance in 12%. Moreover, 40% of patients showed good tolerance to treatment with a 12-month survival of 58%.

P028

FOLLOWING THE SWALLOWING: PRELIMINARY RESULTS OF LARYNGEAL MOTION EVALUATION FOR MAGNETIC RESONANCE (MR) GUIDED RADIATION THERAPY

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Aims: One of the major concerns in the treatment of head and neck cancer (HNC) is intrafraction motion, which is typically attributed to organ and tumor motion induced by deglutition. Intra-fraction motion may assume greater clinical significance whenever intensity modulated techniques with smaller margins are used. The goal of this study was to quantify the intra-fraction displacement of the glottis in order to optimize the irradiation of early glottic cancers.

Methods: HNC patients treated with VMAT at Gemelli ART underwent simulation with on-board 0.35-T MRI with MRIdian radiation therapy system (ViewRay™, Cleveland, Ohio). Sagittal cine MR images were acquired along the medial axis by a true fast imaging with steady-state free precession sequence. A tracking point was set at the level of the thyroid cartilage isthmus. Two consecutive sets of cine MR images taking 180 seconds were acquired: the first one in normal condition ("free-swallowing", FS) and the second one after having instructed the patient not to swallow (NS). For both situations, the displacement of the tracking point along the cranio-caudal (CC) and anterior-posterior (AP) directions was recorded for a period of three minutes to simulate the typical duration of a VMAT session delivery. In particular: movements exceeding 3 mm were considered (representing the CTV-PTV margin commonly accepted for IMRT treatments with ordinary IGRT); shifts lasting less than 1% of the monitoring time were considered negligible.

Results: Laryngeal motion was assessed in six patients tumor site: 1 nasopharyngeal, 2 laryngeal, 2 oropharyngeal, 1 oral cavity cancer). Maximum laryngeal displacement in the FS and NS image sets (mean value) was 7.5 and 6.7 mm in the CC and 4.8 and 4.0 in the AP direction respectively. Laryngeal motion exceeded 3 mm for more than 1% of the monitoring time in three and one patients in the FS and NS image sets respectively. Particularly in one/6 patients, laryngeal motion exceeded 3 mm for 5% of the monitoring time in the NS condition.

Conclusions: These preliminary results support the hypothesis that intra-fraction laryngeal motion could have an impact on the dose distribution for early glottic cancer, particularly if tight CTV-PTV margins are used. Asking the patient not to swallow during the treatment might help to reduce such intra-fraction motion but may not be sufficient in some patients. These patients might therefore benefit from MR-guided irradiation.

P029

KEY ROLE OF MEK/ERK PATHWAY IN SUSTAINING TUMORIGENICITY AND IN VITRO RADIORESISTANCE OF EMBRYONAL RHABDOMYOSARCOMA STEM-LIKE CELL POPULATION

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Aims: Radiation therapy significantly contributes to childhood soft-tissue Rhabdomyosarcoma (RMS) treatment: however, resistance still occurs and one underlying reason might be attributable to cancer stem cells (CSC) population. Thus, the identification of signaling pathways that affect the cancer stem-like phenotype may provide insights into therapeutic targets for combating RMS. The aim of this study was to investigate the role of the MEK/ERK pathway in controlling the cancer stem-like phenotype using a model of rhabdospheres derived from the embryonal rhabdomyosarcoma cell line (RD).

Methods: Rhabdospheres enriched in cancer stem like cells were obtained growing RD cells in non adherent condition in stem cell medium. Stem cell markers were evaluated by FACS analysis and immunoblotting. ERK1/2, myogenic markers, proteins of DNA repair and bone marrow X-linked kinase (BMX) expression were evaluated by immunoblotting analysis. Radiation was delivered using an x-6 MV photon linear accelerator. Xenografts were obtained in NOD/SCID mice by subcutaneously injection of rhabdosphere cells or cells pretreated with U0126 in stem cell medium.

Results: MEK/ERK inhibitor U0126 prevented rhabdosphere formation and down-regulated stem cell markers CD133, CXCR4 and Nanog expression, but enhanced ALDH, MAPK phospho-active p38 and differentiative myogenic markers. By contrast, MAPK p38 inhibition accelerated rhabdosphere formation and enhanced phospho-active ERK1/2 and Nanog expression. RD cells, chronically treated with U0126 and then xeno-transplanted in NOD/SCID mice, delayed tumor development and reduced tumor mass when compared with tumor induced by rhabdosphere cells. U0126 intraperitoneal administration to mice bearing rhabdosphere-derived tumors inhibited tumor growth. The MEK/ERK pathway role in rhabdosphere radiosensitivity was investigated in vitro. Disassembly of rhabdospheres was induced by both radiation or U0126, and further enhanced by combined treatment. In U0126-treated rhabdospheres, the expression of the stem cell markers CD133 and CXCR4 decreased and dropped even more markedly following combined treatment. The expression of BMX, a negative regulator of apoptosis, also decreased following combined treatment, which suggests an increase in radiosensitivity of rhabdosphere cells.

Conclusions: MEK/ERK inhibition combined with traditional radiotherapy may provides a promising therapy for embryonal rhabdomyosarcoma.

P030

SET-UP DISPLACEMENTS IN HEAD AND NECK CANCER PATIENTS UNDERGOING IMAGE-GUIDED RADIATION TREATMENT. RELATIONSHIP TO BMI AND WEIGHT LOSS

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Aims: To assess translational and rotational set-up errors in head and neck cancer patients treated with IMRT and VMAT using daily pretreatment CBCT guidance and to correlate set-up errors to patient-specific factors, weight, height, BMI and weight loss.

Methods: A total of 274 CBCTs referred to 30 patients were investigated. A customized immobilization system was employed during both planning CT and treatment phase. CBCTs were obtained according to an internal protocol consisting of 4 consecutive CBCTs during the 1st week of treatment and weekly afterward. Mean translation of first 4 CBCTs was calculated; this value was considered as systematic set-up error; displacements >3 mm were corrected, according to literature data and action limit defined in our protocol. Action limit for rotation acceptance was ≤3°. Mean translations for CBCTs weekly performed during the remaining treatment course were calculated, too. For each patient, height, weight and BMI (pre, mid, end of treatment) were recorded. Percentage of weight loss (mid- and at end treatment) was calculated. Statistical analysis was performed to evaluate correlation between translational displacements and body changes.

Results: Mean translational and rotational set-up errors during the first 4 CBCTs were 0.15 mm (LR), 0.1 mm (AP), 0 mm (CC) and 0.7°(LR-axis), 1°(AP-axis), and 0.6°(CC-axis). Mean translations and rotations of subsequent CBCTs were 0.02 mm (LR), 0.03 mm (AP), 0 mm (CC) and 0.6°(LR-axis), 1°(AP-axis), and 0.7°(CC-axis). Median pre-treatment height, weight and BMI were 170.2 cm (148-186), 77.97 kg (42-114) and 26.72 (18.58-34.58), respectively. All patients presented weight loss. Median weight variation at the 15th treatment session was 4.3% (1.28-11.1) and at the end

of treatment was 7% (2.56-17.46). Statistical analysis showed no statistically significant correlation between mean displacements of first four CBCTs and mean of following CBCTs and no statistically significant correlation was observed between set-up errors and weight, height, BMI or weight change during treatment sessions.

Conclusions: Translations and rotations recorded in this study were in agreement with literature data. Weight loss occurred in all treated patients but was not found any correlation between patient weight, height, BMI or weight loss. Therefore, we cannot support the hypothesis that set-up errors during radiotherapy are correlated to patient weight, height, BMI or weight loss.

P031

THE EPHRIN RECEPTOR KINASE INHIBITOR GLPG1790 REVERTS ONCOPHENOTYPE, INDUCES MYOGENIC DIFFERENTIATION AND RADIOSENSITIZES EMBRYONAL RHABDOMYOSARCOMA CELL LINES

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Aims: Rhabdomyosarcomas (RMS), the most common soft-tissue sarcoma in childhood, derive from skeletal muscle cell precursors and localizes in the head and neck region in 40% of cases. Treatment of embryonal RMS (ERMS), the most frequent histotype of RMS, is based on surgery combined to radio-chemo-therapy. Despite the multimodality approach, often treatments fail providing only a transient tumor control. In this scenario, radiosensitizing cancer cells represents a strategic goal in ERMS treatment. Eph receptors are the largest receptor tyrosine kinase family of transmembrane proteins with an extracellular domain capable to recognize signals from the cells' environment and influence cell-cell interaction and cell migration. Whether Eph abnormal expression has been shown in several cancer types and related to tumor onset, progression and metastasis, the biological function of Eph signaling and its role in ERMS radioresistance are still largely unknown.

Methods: This report describes the effects of GLPG1790, a new potent pan-EPH inhibitor, in human RD and TE671 human ERMS cell lines in in vitro and in vivo experiments.

Results: GLPG1790: i) induced G1-growth arrest affecting the G1-related cell cycle molecular machinery responsible for G1/S phase transition; ii) reduced the migratory capacity and the clonogenic potential of ERMS cells; iii) prevented the rhabdosphere formation and down-regulated CD133, CXCR4 and Nanog stem cell markers expression; iv) committed ERMS cells towards skeletal muscle terminal differentiation by inducing a myogenic-like phenotype and increasing MYOD1, Myogenin and MyHC levels; v) significantly radiosensitized ERMS cells in *in vitro* and *in vivo* experiments by affecting the DNA double-strand break repair pathways and so increasing RT-induced DNA damages. Finally, we showed, for the first time, a significant up-regulation of the most oncogenic EPH-receptor and ephrin ligand: the EPH-A2 and related Ephrin-A1, found up-regulated in 14 ERMS tumour samples in comparison to normal skeletal muscle.

Conclusions: Data support the development of GLPG1790 in ERMS and show a novel mechanism-of-action that is under investigation in other cancer types overexpressing EPHs. Efforts are now underway to identify biomarkers of tumor cell radiosensitivity and target expression in patient derived material.

P032

C-MYC SUSTAINS TRANSFORMED PHENOTYPE AND PROMOTES RADIORESISTANCE OF EMBRYONAL RHABDOMYOSARCOMA CELL LINES

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Aims: Rhabdomyosarcomas (RMS), the most common soft-tissue sarcoma in childhood, derive from skeletal muscle cell precursors. Treatment of embryonal RMS (ERMS), the predominant subtype that particularly in children, prefers the head and neck region, is based on surgery combined to radio-chemo-therapy. Despite the multimodality approach, often treatments fail providing only a transient tumor control. In this scenario RT is a major tool in the treatment of RMS. Expression of certain oncogenes has been shown to alter cellular radiation responses; however, it is still not clear what marker or combination of markers would best indicate a radioresistant tumor and how these markers govern the cancer cells radioresistance at molecular level. We have previously reported that the RAS/MEK/ERK signal transduction pathway promotes c-Myc oncoprotein accumulation and sustains in vitro and in vivo transformed phenotype and radioresistance of ERMS cell lines. Whether c-Myc protein abnormal accumulation can be

responsible for RMS radioresistance is still understood and this relationship has been here investigated and characterized.

Methods: RD and TE671 cell lines conditionally expressing the c-Myc-dominant negative MadMyc chimera protein or shRNA directed to c-Myc, were used.

Results: Targeting c-Myc counteracted *in vitro* ERMS adherence and in suspension, growth motility and the expression of pro-angiogenic factors. c-Myc depletion decreased MMP-9, MMP-2, u-PA gelatinolytic activity, neural cell adhesion molecule sialylation status, HIF-1α, VEGF and increased TSP-1 protein expression levels. Rapid but not sustained targeting c-Myc radiosensitized ERMS cells by radiation-induced apoptosis, DNA damage and impairing the expression of DNA repair proteins RAD51 and DNA-PKcs, thereby silencing affected ERMS radioresistance. c-Myc sustains ERMS transformed phenotype and radioresistance by protecting cancer cells from radiation-induced apoptosis and DNA damage, while promoting radiation-induced DNA repair.

Conclusions: This data strongly indicate a role for c-Myc in ERMS radioresistance and confirm again the strategic role of targeting by specific inhibitors, the RAS/MEK/ERK-c-Myc axys.

P033

ROLE OF PERFUSION CT IN THE EVALUATION OF FUNCTIONAL PRIMARY TUMOR RESPONSE AFTER RADIOCHEMOTHERAPY (RCT) IN HEAD AND NECK CANCERS (HNCS): PRELIMINARY FINDINGS

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Aims: To report the initial results of a prospective study aimed at evaluating the CT perfusion parameter changes (ΔPCTp) of the primary tumour after radiochemotherapy (RCT) in head and neck cancer (HNC) and to correlate with positron emission tomography (PET)/CT response.

Methods: Eligibility criteria included HNC (Stage III–IV) candidates for RCT. Patients underwent perfusion CT (PCT) at baseline and at 3 weeks and 3 months after treatment. Blood volume, blood flow, mean transit time (MTT) and permeability surface (PS) product were computed. Moreover, PET/CT was performed at baseline and 3 months after treatment. The ΔPCTp were evaluated between baseline and 3-week/3-month evaluations, whereas PET/CT response was based on the maximum standardized uptake value changes according to the European Organization for Research and Treatment of Cancer criteria.

Results: Between July 2012 and July 2015, 25 patients were enrolled. A significant reduction of all CT tumour perfusion parameters (PCTp) was observed from the baseline to after RCT (p,0.001). Specifically, a significant reduction was shown at 3 weeks for all PCTp except MTT (from 6.18 to 5.14s; p=0.722). Differently, a significant reduction of all PCTp (p,0.001) including MTT (from 6.18 to 2.24s; p=0.001) was shown at 3 months (Table 1). Moreover, the reduction of PS resulted in a significant prediction of PET/CT response at 3 months (p=0.037) with the trend also at 3 weeks (p=0.099) at the multivariate analysis.

Conclusions: Our preliminary findings seem to show that almost all PCTp are significantly reduced after RCT, whereas PS seems to come out as the strongest factor in predicting the PET/CT response.

Table 1. Tumor perfusion parameters variations scores from baseline to post treatment

	BV(ml/100g/min)	BF(ml/100g)	MTT(s)	PS(ml/100g/min)
Baseline				
Mean	32,53	396,76	6,18	47,63
Range	5,48-84,66	76.67-880.62	2,16-11,21	4,41-98,80
3 weeks				
Mean	13,42	192,12	5,14	24,07
Range	0-52,61	0-679,61	0-11,96	0-74,75
3 months				
Mean	5,67	74,26	2,24	11,58
Range	0-48,97	0-536,77	0-18,94	0-92,81

Abbreviations: BV: Blood Volume; BF: Blood Flow; MTT: Mean Transit Time; PS: Permeability Surface

P034

ANDROGEN RECEPTOR SIGNALING SUSTAINS EMBRYONAL RHABDOMYOSARCOMA ONCOPHENOTYPE AND RADIORESISTANCE

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Aims: Rhabdomyosarcoma (RMS) is a pediatric sarcoma that develops from skeletal muscle cells failing in differentiation. RMS rarely occurs in adults, prefering male subjects and the head and neck region and for unknown reasons, adults with RMS have worse outcomes. Treatment of RMS is complex, including multi-drug chemotherapy, radiotherapy (RT) and surgery. Androgens play a key role in skeletal muscle homeosta-

sis promoting myogenic differentiation and increasing both the size and strength of skeletal muscle via diverse mechanisms. It has been recently shown that androgen stimulation promotes human RMS cell lines proliferation, chemotaxis, cell adhesion and activation of RAS/MEK/ERK signaling, that we previously showed to sustain rhabdomyosarcoma onset, progression and radioresistance.

Methods: This report describes the effects of testosterone (T) and bicalutamide (BCLT), the most widely used androgen receptor (AR) antagonist, in human RD and TE671 human embryonal rhabdomyosarcoma ERMS cell lines in in vitro and in vivo experiments.

Results: Our study show, for the first time, a significant up-regulation and nuclear distribution of AR in ERMS tumour samples and cell lines respectively, in comparison to normal skeletal muscle (NSM). Physiological concentration of T i) promoted AR nuclear accumulation and binding with c-Myc and Cyclin-D1, two of the most important oncogenic transcription factor; ii) drastically reduced ERMS proliferation doubling time; iii) up-regulated Cyclin D1, Cyclin E2 and c-Myc and down-regulated p21 and p27 protein expression; iv) enhanced ERMS oncogenic phenotype; v) promoted non-genomic effects by potentiating the activation of several oncogenic signal transduction pathways. Interestingly, T increased ERMS radioresistance which grade paralleled the levels of AR nuclear translocation. T-related effects as well as radiosensitization occurred when ERMS were pre-treated with BCLT.

Conclusions: Collectively, our data indicate a strategic role for androgens in sustaining ERMS onset, progression and radioresistance and suggest a rational approach for using anti-androgens therapy in combination with radiotherapy.

P035

WEIGHT LOSS IN HEAD AND NECK CANCER PATIENTS TREATED WITH CURATIVE RADIOTHERAPY: PROPOSAL FOR A STEPPED-WEDGE NUTRITIONAL PROTOCOL BY THE EUROPEAN INSTITUTE OF ONCOLOGY

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Aims: Despite the crucial role of nutritional support in head and neck cancer (HNC) patients (pts) treated with curative radiotherapy (RT), no consensus exists on the optimal nutritional protocol to apply in daily clinical practice. The aim of our study was to evaluate the impact on weight loss of a standardized nutritional stepped-wedge protocol on consecutive HNC pts treated with curative a RT course.

Methods: We prospectively collected data of pts followed by a trained dietitian according to a pre-defined stepped-wedge protocol (Figure 1). Inclusion criteria were: 1) histologically-confirmed HNC, 2) no previous radical surgery (excluded excisional biopsy and ipsilateral neck dissection), 3) indication to curative-intent RT. Exclusion criteria were: 1) swallowing defect at the baseline, 5) weight loss (WL)>10% in the three months prior to the beginning of RT. WL percentage was assessed both as a continuous and a categorical variable, according to Common Terminology Criteria for Adverse Events (CTCAE v4.03). Nutritional status was assessed at the baseline and weekly during the whole course of RT by an expert dietitian. Fluid intake and caloric intake were assessed through a 24-hour recall. Estimated caloric requirement was determined by the Harris Benedict equation. Symptom valuation was performed through a reduced version of the validated Patient-Generated Subjective Global Assessment.

Results: Between May 2010 and March 2011, 42 pts (30 male, 12 female, median age 63 years, range 34-76 years) were considered eligible. Median total RT dose was 70 Gy (mean: 69.7 Gy, range: 64-70 Gy). Nine (21%) pts underwent induction chemotherapy and 36 (86%) pts were treated concurrent systemic treatment (25 pts with platinum-based chemotherapy, 11 pts with Cetuximab). WL according to CTCAE 4.03 was: G0 in 23 (55%) pts, G1 in 14 (33%) pts, G2 in 5 (12%) pts. All pts received ONS. Thirty-five (83%) pts did not require enteral nutrition. Among the seven pts with indication to enteral nutrition, three pts refused insertion of a nasogastric tube thus, globally, 90% of pts completed RT without interruption of oral feeding.

Conclusions: Despite the high toxicity profile of curative-intent RT on HNC pts, here we propose a standardized stepped-wedge protocol that allowed prevention of severe WL in most (83%) of the analyzed pts. Further larger prospective studies are warranted to validate this approach and to achieve consensus on nutritional intervention in this subset of pts.

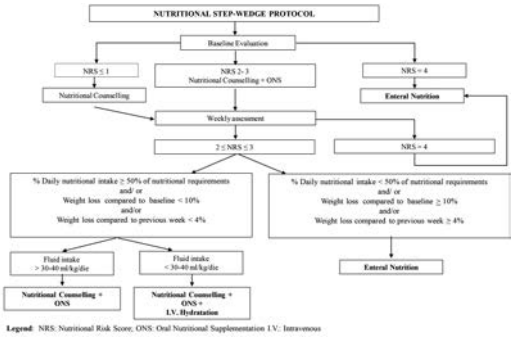

Figure 1.

P036

INTRAVOXEL INCOHERENT MOTION MRI AND DYNAMIC CONTRAST-ENHANCED MRI TO EVALUATE THE EARLY RADIATION-INDUCED CHANGES OF PAROTID GLANDS

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Aims: To evaluate the potential of Intravoxel Incoherent Motion (IVIM) imaging and Dynamic contrast-enhanced (DCE) MRI for early radiation-induced changes of parotids.

Materials and Methods: Twenty-eight patients with oropharyngeal squamous cell carcinoma were included in a prospective study. All the patients underwent both IVIM diffusion weighted imaging (DWI) and DCE-MRI examinations at baseline; IVIM-DWI was repeated at the 10th fraction of treatment. IVIM-DWI was performed using nine b values in the range 0-800 s/mm^2. The apparent diffusion coefficient (ADC), ADClow derived using data in the b value range (0-150 s/mm^2), perfusion fraction f and tissue diffusion coefficient Dt were estimated both at baseline and during RT. Both quantitative and semi-quantitative parameters, including the transfer constant Ktrans and the initial area under gadolinium concentration curve (IAUGC) were calculated from DCE-MRI

The volumes of the single parotids were outlined before, at the 10th fraction and 8 weeks after RT. The parotid shrinkage during RT and at the end of RT was correlated with pre-treatment values of diffusion and perfusion parameters and the changes of the diffusion parameters. Parotid mean dose (Dmean) and percentage volume receiving more than 30 Gy (V30) were evaluated. Univariate and multivariate analyses were conducted.

Results: The study population included 20 men and 8 women, with an average age of 63.3 years (range, 45, 81 years). The final patient weight variation was -7.6 Kg (range, -18, +1 Kg). A total of fifty six parotids were analyzed. Dmean and V30 were 33.6±8.0 Gy and 49.5%±18.1%, respectively (mean value and standard deviation). At the 10th fraction, the parotid volume decreased from 33.4±10 cm3 to 27.7 ±9.2 cm3, with a mean shrinkage of 17.3±10.4%. Eight weeks after RT, it decreased to 22.7±7.7 cm3, with a mean shrinkage of 29.3±13.7%. The age, ADC and Ktrans values at baseline were the best predictors for the parotid shrinkage during RT. The baseline IAUGC and the changes in Dt were the best predictors for the parotid shrinkage after treatment. Moderate correlations were found between changes in ADC and Dmean ($r = 0.287$, $p = 0.037$).

Conclusions: IVIM-DWI and DCE-MRI, in conjunction with clinical parameters, may be clinically useful to early predict the change in parotid volume, which was found to be significantly related to both vascular and cellular tissue properties.

P037

PREDICTIVE AND PROGNOSTIC VALUE OF PRE-TREATMENT [18F] FDG-PET PARAMETERS IN HEAD-AND-NECK CANCER TREATED BY CT-RT

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Aims: To evaluate the predictive and prognostic value of [F18] FDG-PET parameters performed prior to radiotherapy in head-and-neck cancer patients.

Methods: Thirty-eight patients with newly diagnosed head-and-neck cancer treated with concomitant chemoradiotherapy underwent [F18] FDG-PET before the treatment course. The maximum and the mean standardized uptake value (SUVmax, SUVmean), the metabolic tumor volume (MTV), and total lesion glycolysis (TLG) were analysed. Multiple threshold levels were tested in order to define the most suitable threshold value for the metabolic activity of each patient's tumour: the fixed threshold of the 41% and 50% of the maximum uptake value (SUV41%, SUV50%) and an adaptive threshold algorithm (ATA) implemented on the iTaRT workstation (Tecnologie Avanzate, Italy). We evaluated the relationship of mean values of SUVmax, SUVmean, MTV, and TLG with tumour characteristics, treatment response, local recurrence, distant metastasis and disease-related death. Receiver-operating characteristic (ROC) curve analysis was done to obtain optimal predictive cut-off values for PET parameters. Disease-free (DFS) and overall survival (OS) disease-related were examined according to these cut-offs.

Results: The mean value and range of each parameters were calculated Table1. Higher SUVmeanATA was associated to higher primary tumour staging ($p= 0.04$).

Thirty-two/38 patients (84.2%) had a complete response, 4/38 (10.5%) a partial response, and 2/38 (5.2%) a no response 8 weeks after the completion of treatment. SUV parameters resulted not predictive of tumour response. After a median follow-up of 22 months, 6/38 (15.8%) patients developed local recurrence and 6/38 (15.8%) distant relapse. Eight patients (21.1%) died of tumour progression. The TLGATA was predictive of local recurrence ($p=0.04$). ROC curves analysis revealed a cut-off value of 19.6 for SUVmax, and 13.7 for SUVmeanATA (AUC 0.72, $p=0.03$ and AUC 0.72 $p=0.03$, respectively). The 2-year DFS rate was significantly lower in patients with a SUVmax

>19.6 (p= 0.001) and with a SUVmeanATA >13.7 (p= 0.02). ROC curves analysis revealed a cut-off value of 19.6 for SUVmax, 8.6 for SUVmeanATA and 49.1 for TLGATA (AUC 0.8, p=0.03; AUC 0.9 p=0.007, and AUC 0.8 p= 0.01 respectively). The 2-year OS rate was significantly lower in patients with a SUVmax >19.6 (p= 0.004), with a SUVmeanATA >8.6 (p= 0.03) and TLGATA >49.1 (p=0.004).

Conclusions: Adaptive threshold-based SUVmean, MTV, and TLG and SUVmax could have a role in predicting local control and survival in head and neck cancer patients treated with chemoradiotherapy.

Table 1. [18F] FDG-PET paramenters based on multiple threshold levels.

	Parameters			
	SUVmax	SUVmean	MTV (cc)	TLG
Adaptive threshold algorithm (ATA)	16.37 (4.41 – 34.53)	9.15 (2.8 – 19.71)	17.21 (1.5 – 61.53)	149.89 (5.3 – 877.85)
SUV41%	16.37 (4.41 – 34.53)	10.50 (2.94 – 21.78)	10.30 (1.02 – 58)	130.90 (3 – 850.86)
SUV50%	16.37 (4.41 – 34.53)	11.45 (3.33 – 23.73)	7.79 (0.45 – 47.11)	107.77 (2.10 – 736.33)

P038

A [18F] FDG-PET ADAPTIVE THRESHOLDING ALGORITHM FOR THE DELINEATION OF RADIOTHERAPY TUMOUR VOLUMES OF HEAD AND NECK CANCER

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Aims: A standardized way of converting PET signals into target volume is not yet available. The aim of this study was to evaluate a [18F] FDG-PET adaptive thresholding algorithm for the delineation of the biological tumour volume for the radiotherapy (RT) treatment planning of head and neck cancer patients.

Methods: Thirty-two patients, who underwent exclusive intensity modulated RT with simultaneous integrated boost (IMRT-SIB) for head-and-neck squamous cell carcinoma (3 oral cavity, 7 nasopharynx, 15 oropharynx, 6 hypopharynx, and 1 larynx cancer) were included in the present study. Thirty/32 patients presented a locally advanced disease (93.8%). For all patients, [18F] FDG-PET/CT was performed in treatment position with the customized thermoplastic mask. Two radiation oncologists defined the primary biologic tumour volumes (BTV) using the adaptive thresholding algorithm implemented on the iTaRT workstation (Tecnologie Avanzate, Italy). The algorithm used specific calibration curves that depended on the lesion-to-background ratio (LB ratio) and on the amplitude of reconstruction smoothing filter (FWH). The evaluation of reproducibility of adaptive thresholding algorithm for volume estimation was determined by the volume overlap of multiple segmentation of the same lesion by two radiation oncologists. Each primary tumour volume was segmented by the adaptive thresholding algorithm (BTVATA). The target volumes for the primary tumours previously delineated on the planning computed tomography (CT) scan using anatomic imaging (CT and MRI) (gross tumour volume standard GTVST) and a fixed image intensity threshold method (41% of maximum intensity) of [18F] FDG-PET standardized uptake value (GTV41%SUV) were used to perform a volumetric comparison.

Results: The algorithm generated a tumour volume in all but two patients. The mean values with standard deviation (SD) of volumes based on the three different methods were reported in Table 1. The BTVATA was significantly smaller than the GTVST (17 vs. 21 cc, p= 0.04); the conformity index (CI) was 0.46, and the similarity coefficient (DICE) was 0.7 (Sensibility 66%, specificity 85%). BTVATA is a part of the GTVST. The BTVATA was bigger than the GTV41%SUV (17 vs. 15 cc) but the difference was not statistically different (p> 0.05), the CI was 0.8 and the DICE was 0.2.

Conclusions: The proposed adaptive thresholding algorithm resulted robust and reproducible in the clinical context of head and neck tumours. The tumour volumes obtained by the algorithm were a part of the GTVST and were similar to GTV41%SUV. This tumour volume could allow the delineation of a BTV for dose escalation in head and neck cancer treated with IMRT-SIB.

Table 2. Tumour Volumes defined by the three different methods.

GTV	Mean Volume (cc)	Ranges	Standard Deviation
GTV_{ST}	21.4	4.5 – 66.3	±16.0
$GTV_{41\%SUV}$	14.7	1.3 – 58.5	±13.7
$GTV\ T_{ATA}$	17.2	1.5 – 61.5	± 12.8

P039

CARDIAC IMPLANTABLE DEVICES AND RADIATION THERAPY: OUR MONO-INSTITUTIONAL EXPERIENCE

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Aims: The number of cardiopathic patients (pts) receiving radiotherapy (RT) has increased. The rapid diffusion of implantable cardiovascular devices (CIEDs), such as pacemakers (PMs) and implantable cardiac defibrillators (ICDs), requires particular attention to the management of pts undergoing RT. The absorption of ionizing radiation by these devices is cumulative, so the risk of dysfunction increases with doses and the dose to the CIED should be limited as much as possible. The most critical defects comprise altered sensing or stimulation, loss of telemetry, complete loss of function.

Therefore, close collaboration among radiation oncologists, cardiologists and physicists is needed. We describe the management of pts with CIEDs, dosimetric characteristics, effects of radiation on devices and multidisciplinary approach at our University Hospital.

Methods: From October 2006 to April 2017, 13 pts with PMs (8) or ICDs (5) and affected by head and neck or thoracic tumors underwent RT. The average age of the devices was 4,1 years. 9 pts were treated by Three-Dimensional Conformal RT, 4 pts by Volumetric Modulated Arc Therapy. All pts were informed about the risk of CIED dysfunctions. Dependent CIED pts and pts receiving >2Gy were monitored during each therapy session by the electrophysiologist. The audiovisual observation of the pts during radiation was mandatory. Treating staff was informed about the management of pts in case of complications during treatment. An equipment for cardiopulmonary resuscitation was available. All pts were monitored at 1, 3, 6 months after RT and twice a year later.

Results: Median follow-up was 37 months (range: 1-81). TPS used was Oncentra EB with 6MV photons to decrease scattering and to completely avoid neutron activation. Doses to CIEDs were evaluated on DVH (median: 1.6; range: 0.8-9Gy). CIEDs receiving ≥10Gy were displaced controlaterally. No CIED dysfunction was observed in any of the reported pts, except for premature battery depletion in 3 pts.

Conclusions: Many guidelines stratify CIED pts according to their class of risk and it is usually recommended to keep total doses lower than 2Gy for PMs and 1Gy for ICDs. In our experience doses <10Gy did not cause adverse effects. The use of more modern techniques has led to a reduction of dose to organs at risk and CIEDs. Our study confirms the safety of RT for pts implanted with CIED. A standardized protocol is advisable in order to improve pts management during RT and follow-up.

P040

THE IMPACT OF FLUORO-DEOXY-GLUCOSE PET CT(FDG-PET) IN THE TUMOR VOLUME DELINEATION FOR HEAD AND NECK CANCER (HNC) DEFINITIVE RADIO-CHEMOTHERAPY: A RETROSPECTIVE ANALYSIS

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Aims: Target volume delineation for radiation treatment to the head and neck area traditionally is based on physical examination, computed tomography (CT) and magnetic resonance imaging (MRI). Additional molecular imaging with FDG- PET may improve definition of gross tumor volume (GTV). Aim of this study is to analyze the impact of PET/CT in the radiotherapy planning for HNC.

Materials and Methods: 32 patients with stage II-IV squamous cell HNC were treated between January 2012 and March 2017 with definitive image-guided intensity modulated radiotherapy and simultaneous integrated boost. All patients were simulated with the same immobilization for CT and PET/CT and the two imaging modalities underwent coregistrered. Tumor GTV (T-GTV) and nodal GTV (N-GTV) were countured first on CT,using MRI-delineation guide, and then on PET/CT. Absoluted GTV volumes were compared and overlap analysis was performed.

Results: T-GTV was significantly larger as delineated on CT than PET/CT in 28/32(88%) patients Nevertheless, PET/CT detected tumor extension outside the GTV delineated on CT in 4/32(13%) patients. The analysis of N-GTV has shown a substantial volume overlap between CT/MRI and PET/CT countouring for nodal disease > 1.5 cm. However, in 5/32 (16%) cases small malignant lymph nodes PET/CT positive, not detected using CT or MRI criteria alone, were included in the high risk volume.

Conclusions: This retrospective analysis shows the considerable role of PET/CT for the delineation T-GTV and N-GTV in order to individualize the treatment planning in HNC patients. Further studies are need to evaluate the impact of this multimodality imaging strategy on long-term outcomes.

P041

CLINICAL IMPACT OF INTEGRATED PET-MR HEAD-NECK CANCER IMAGING IN OUR PRELIMINARY EXPERIENCE

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Aims: Both CT and MR with contrast enhancement are accepted clinical imaging tools for the staging of head and neck cancer. Hybrid PET-MR imaging offers high sensivity and specificity, enabled by the functional imaging of PET and soft tissue discrimination by MR imaging. It is useful for staging T status, in particular for the valuation of tumors arising in locations difficult to assess, such as those near or in skull base, floor of the mouth and base of tongue. Furthermore whole-body imaging allows to evaluate N and M status and the tumor recurrence or any second primary malignancies. PET-MR allows also investigating fundamental points that need to be addressed, such as depth of invasion, crossing of midline, infiltration of bone, great vessels and the presence of perineural spread. The purpose of our study was to evaluate the clinical impact and the feasibility of PET-MR with FDG for staging of head

and neck cancer.

Methods: 22 consecutive patients aged between 40 and 79 years (mean age 61± 21, 15 males and 7 females), with histologically confirmed head and neck malignancy, underwent PET-MR examination on a integrated whole body scanner (mMR Biograph- Siemens) between July 2016 and May 2017. PET-MR for assessing H&N cancer include two steps: a low-resolution AC MR scan of the whole body and a diagnostic MR scan of H&N region using contrast enhancement. The whole body PET-MR protocol includes: Dixon, T2 HASTE axial, T1 VIBE axial, T1 coronal. The neck PET-MR protocol includes T2 BLADE, T1 VIBE pre & post contrast medium, DWI. Exclusion criteria of the procedure consisted of >150 mg/dL fasting blood glucose, pregnancy and standard controindication for MRI.

Results: The primary tumour was detected by PET-MR in 6 out of 7 patients in whom this imaging was performed at diagnosis. In only 1 patient lymph nodes suspicious for metastatic disease were seen but the malignancy remained of unknown origin. In another patient no lymph nodes were detected at diagnosis. One patient had bones metastasis and another one lung lesions at onset. In the patients in whom PET-MR was performed for follow-up, 3 disease recurrence, 4 lung metastasis and 1 brain metastasis were detected.

Conclusions: PET-MR allows a more complete characterization of malignancies; our study demonstrates the feasibility of PET-MR imaging for primary tumors and recurrent tumors evaluations of head-neck malignant lesions, allowing simultaneous collection of multiparametric metabolic and functional data.

P042

HYPOFRACTIONATED RE-IRRADIATION IN RECURRENT HEAD AND NECK CANCER

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Aims: To evaluate toxicity, progression free survival and overall survival, in head and neck cancer patients submitted to reirradiation for local regional recurrence during the last year.

Materials and Methods: We retrospectively (from January 2012 to December 2016) evaluated patients treated with radiation therapy for locoregional recurrence after a previous full course of irradiation. For the evaluation of toxicity we used RTOG/EORTC morbidity score.

Results: 21 patients (13 males and 8 females) were reviewed. The primary tumor site was oropharynx (10 cases), nasopharynx (6), larynx (3) and hypopharynx (2). The sites of recurrence were rhinopharynx 4 cases, oropharynx in 5 cases, skull base (5), lymph nodes (7) case respectively. Re-irradiation was delivered using robotic arm stereotactic radiotherapy (14 patients); IMRT/VMAT (7). With stereotactic technique a median dose of 24 Gy (range 10-36 Gy) was delivered in a median of 3 fractions (range 3-5). With IMRT/VMAT a median dose of 20 Gy (range 8-26) was delivered in a median of 3 fractions (range 1-12). 2/21 patients received also a third re-irradiation. The median follow-up, including who died, was 25 months (4-60). The median time to progression of disease between the first complete treatment and re-irradiation was 25 months. Acute toxicities were: dysphagia G1 (4 cases), G2 (3); cutaneous G1 (1), G2 (3). Late G4 toxicities were observed in two patients (one skin and one vascular). The actuarial one year survival from the time of the retreatment was 12 months. At the time of the last follow up 9 patients died.

Conclusions: Our experience seems to confirm literature data on this issue. In particular, our study shows how the re-treatment of head and neck cancer is feasible with acceptable toxicities with discrete survival profile.

P043

CAN NEW TECHNOLOGIES HELP MODERN DENTAL IMPLANTS IN CHEMO-RADIOTHERAPY TREATED HEAD AND NECK CANCER PATIENTS?

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Aims: Modern radiotherapy (RT) improved overall survival (OS) of head and neck cancer patients and life quality is something we cannot overlook. Functional restoration is also significantly improved, thanks to the innovation in prosthetic rehabilitation after RT. Our aim is to illustrate the idea of overlap both radiation planning CT scan and cone beam CT (CBCT) to create a fusion imaging that allows planning of the most suitable areas for implant placement, substantially reducing the risk of osteoradionecrosis after the surgical procedure.

Methods: Four patients, aged between 48 and 73 years, underwent radiation therapy for head and neck squamous cell carcinomas (HNSCC). After RT treatment, every patient needed a prosthetic rehabilitation. Depending on patient's need, total or partial removable prosthesis with metallic hook were made and with such devices in place, a radiological template using CBCT was obtained. Co-registration of planning CT merged with isodose values and CBCT template was obtained. Areas which received more than 45 Gy were regarded not suitable for implants, remaining areas were used to complete implant placement program schedule.

Results: Safe areas were identified in 3 of 4 patients and therefore implant procedures were completed. One patient did not undergo surgery because of the 50 Gy or higher dose in the allegedly appropriate implant area. The images obtained from this procedure are currently used to plan irradiated patients' rehabilitation and implant placement. Those files allow the clinician to plan the implant placement in the most precise and safe

way, significantly reducing the risk of implant failure and osteoradionecrosis. After a 3-year follow-up lapse, no case of implant rejection or osteonecrosis were observed.

Conclusions: This study displays a novel method to program implants placement and it showed to be safe, fast and easy to obtain. It is authors' opinion that it could easily become a new routine procedure in rehabilitation for patients who undergo radiation therapy treatment of the head and neck neoplasms. This work is in a preliminary phase of realization and needs further and more detailed evidences to verify its effectiveness.

P044

RADIATION-INDUCED ACUTE DYSPHAGIA: A PROSPECTIVE OBSERVATIONAL STUDY ON 42 HEAD AND NECK CANCER PATIENTS

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**at the time of the study*

Aims: Acute toxicity in head and neck (H&N) cancer patients treated with definitive radiotherapy (RT) has a crucial role in compliance to treatments. The aim of this study was to correlate doses to swallowing-associated structures and acute dysphagia. Methods We prospectively analyzed 42 H&N cancer patients treated with RT. Inclusion criteria were (i) curative RT (using 3-dimensional conformal RT or IMRT) for head and neck cancer associated or not with concurrent and/or induction chemotherapy, (ii) written informed consent. Exclusion criteria were (i) prior surgery in head and neck region, (ii) baseline mechanical dysphagia, (iii) clinically relevant weight loss in the 3 months prior to RT, (iv) requirement of enteral nutrition (nasogastric tube or PEG insertion) before RT.Dysphagia (grade ≥3) according to CTCAE V.4.03 and indication to percutaneous endoscopic gastrostomy (PEG) insertion (according to a predefined stepped-wedge protocol) were classified as acute toxicity. Ten swallowing-related structures were considered for the dosimetric analysis: pharyngeal mucosa, base of tongue, constrictor muscles of the pharynx axis (superior, middle and inferior), cricopharyngeal muscle (CPM), soft palate, cervical esophagus (CE), oral cavity, supraglottic larynx. The correlation between clinical information and the dose absorbed by the contoured structures was analyzed. Multivariate logistic regression method using resampling methods (bootstrapping) was applied to select model order and parameters for normal tissue complication probability (NTCP) modelling. Results Nine (21.4%) patients developed acute toxicity: 2 patients required PEG insertion, 3 patients developed dysphagia with grade >3 and 4 patients had both indication for PEG insertion and dysphagia with grade >3. Among the analyzed swallowing-related organs, several dosimetric variables for the inferior constrictor muscle (ICM), CPM and CE were highly correlated with severe acute dysphagia. A two-variable model was suggested as the optimal order by bootstrap method. The optimal model (Rs=0.452, p<0.001) includes V45 of the cervical esophagus (OR=1.016) and Dmean of the cricopharyngeal muscle (OR=1.057) [Figure 1]. The model AUC was 0.82 (95% CI 0.69-0.95). Conclusion Our results suggested that the absorbed dose to the cricopharyngeal muscle and cervical esophagus might play a relevant role in the development of acute RT-related dysphagia.

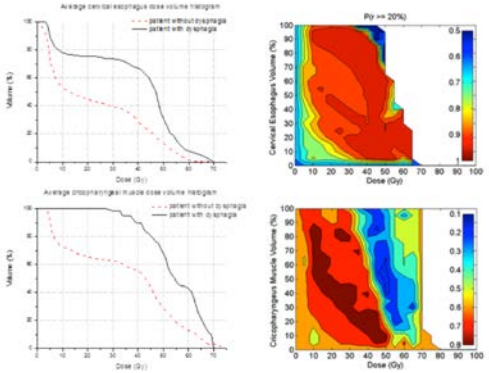

Figure 1. Average cumulative dose volume histograms (DVHs) of cervical esophagus and cricopharyngeal muscle for patients who developed or not toxicity (left panel). Probability maps of toxicity incidence obtained using cervical esophagus and cricopharyngeal muscle DVHs (right panel). Iso-probability lines are calculated for a tolerance rate of 20%. The top-right most line marks the edge of the area of no DVHs data.

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CLINICAL IMPACT OF ADOPTING MONTE CARLO TREATMENT PLANNING FOR VOLUMETRIC MODULATED ARC THERAPY IN NASOPHARYNGEAL TUMORS

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Aims: To assess the clinical implications of the Monte Carlo dose calculation algorithm implemented in the Elekta Monaco treatment planning system for VMAT treatments of nasopharyngeal tumors (NPC), after a transition from Pencil Beam algorithm (PBC) and Collapsed Cone Convolution (CCC).

Methods: Ten plans initially produced for patients with NPC with PBC algorithm were recalculated using the CCC algorithm and the MC algorithm. Doses of 70.5, 60.0 and 55.5 Gy were prescribed in 30 fractions to the primary tumour (PTV70.5), high-risk (PTV60.0) and low-risk nodal area (PTV55.5) in a simultaneous integrated boost strategy. The PTV70.5 was also separated into components in tissue (PTVtiss) and air (PTVair) to better understand the impact of air cavities on dose distributions. Differences in dose distribution for PTVs and OARs were assessed using different metrics as mean doses, near-minimum dose (D98%), target coverage (D95% and V95%), doses to 1cc of serial OARs.

Results: PBC algorithm overestimated dose to PTVs for all considered metrics. For PTV70.5, Dmean and D95% calculated by MC decreased by 3.1% (range:2.1%-4.7%) and 4.7% (range:2.6%-7.6%), respectively. In particular, D95% decreased by 4.5% for PTVtiss and 7.5% for PTVair. D98% decreased by 5.0% (range:2.5%-8.8%), with average values of 4.8% in tissue and 8.8% in air. Percentage differences in V95% was 22.5% (21.8% in PTVtiss and 28.1% in PTVair). The magnitude of dose differences was strongly correlated with the amount of air cavities in PTV70.5. Differences between MC and CCC were found within 0.5% for all metrics in PTVs and PTVtiss. However, CCC showed a significant underestimation of the Dmean, D95% and D98% doses in the air cavities by 3.0% with respect to MC. With regard to OARs irradiation, doses to 1cc for PRV spine and PRV brainstem were found to be approximately 3.0 Gy lower with MC; mean dose for parotids was lower by 2.7%.

Conclusions: MC is recommended instead of PBC for avoiding serious overestimation in target doses. A key question remains open: should the prescription dose be adjusted to the actually delivered dose, more accurately predicted by MC algorithm? If radiation oncologists wanted to keep the PBC original dose prescription and the same accepting criteria for target coverage when switching from PBC to MC, up to 8% more radiation doses would be given.

P046

FDG-PET-BASED RADIOTHERAPY TREATMENT PLANNING IN HEAD&NECK DISEASE: DOSIMETRIC IMPLICATIONS

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Aims: To evaluate dosimetric differences in PET/CT-based radiotherapy treatment planning and conventional CT-based treatment planning in head and neck disease.

Methods and Materials. For the evaluation of the dosimetric differences in PET/CT-based and conventional CT-based radiotherapy treatment planning of head and neck disease, we have performed a retrospective analysis of 31 treatment planning concerning patients with head and neck cancer who underwent conformal-3D Radiotherapy. The anatomical area of this disease was divided into: oropharyngeal, laryngeal and oral cavity cancer. Gross tumour volumes were delineated on CT images (CT_GTVs) by an expert radiation oncologist blinded to PET data. Successively another set of target volumes was defined taking into account the combined PET/CT information and the Biological Target Volumes of the primary tumour and lynph nodes (BTVT/N) identified with PET were added on CT images. 3D-Radiotherapy planning was performed on CT_GTVs. Dosimetric assessment of primary tumour and lynph node BTVs coverage were calculated from dose-volume histrograms.

Results: 3D-Radiotherapy planning implemented on conventional CT_GTVs showed that, whitout PET data included in target volume definition, severe underdosages of BTVT/N (up to -95%) occur in oropharyngeal, oral and hypo-naso pharyngeal cancer treatments while in laryngeal cancer treatments the dose differences are not significant (within ± 5%). 20% of the analysed patient population have important underdosages on the BTVT in the range of (-96.5% ÷ -27.4%) while the BTVN was underdosaged in the range of (-99.1% ÷ -48.3%) for 24% of the patients. The average dose to BTV(T/N) was < -10% in 31% of the patient population.

Conclusions: In radiotherapy treatment planning of head and neck disease PET/CT provide a more precise target definition and prevent exclusion of pathologic areas. In our population addition of PET information to CT avoids significant underdosages of gross tumour volumes and biological tumour volumes in 31% of the patients. The most serious underdosages are observed in oropharyngeal and oral cavity cancer groups. In the laryngeal cancer group conventional CT_GTVs overlaps entirely the PET_GTVs in almost the analysed patients and therefore for these cases the PET involvement allows a target volume reduction with a consequent better critical organ preservation and lower toxicity.

P047

TOXICITY OF CONCOMITANT CHEMOTHERAPY AND IMRT IN LOCALLY ADVANCED OPSCC: SEQUENTIAL VS SIB TECHNIQUE

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Aims: A comparison between sequential IMRT (S-IMRT) and simoultaneous integrated boost-IMRT (SIB-IMRT) was planned.The aim was to evaluate the tolerability and safety of SIB regimen in HPV negative patients with locally advanced oropharingeal squamous cell carcinoma.

Methods: Patients with histologically proven HPV negative OPSCC, staged T3-4 with or without involved lymphonodes at diagnosis, who received primary CRT, were included. S-IMRT was defined as radiotherapy equivalent to 70 Gy (2Gy/fraction). SIB-IMRT was administered to a total dose of 67.5Gy (2.25Gy/fraction) to high dose volume and 60 (2Gy/fraction) and 54 Gy (1.8Gy/fraction) to high risk and low risk volumes respectively. Fusion CT–MR imaging with a deformable registration software was performed to accurately localize target volumes and organs at risk. Concomitant cisplatin (100 mg/m^2 on day 1 and day 22 day of treatment) was used.

Results: A total of 46 patients (31 males, 15 females) with a median age of 64 years (range 41-75) were examined between February 2009 and March 2016. 20 patients received sequential IMRT and 26 patients received SIB-IMRT. All patients completed the programmed CRT treatment. No patients suspended planned chemotherapy and all patients received the IMRT prescribed total dose. No severe life risking complications occurred and no significant differences between S-IMRT and SIB-IMRT were observed in term of major acute toxicities.

Conclusions: Our data shows that IMRT-SIB with 2.25 Gy/fraction with concurrent platinum-100- based chemotherapy is a safe treatment approach without increasing toxicities. This regimen is therefore acceptable for the therapy of locally advanced oropharyngeal cancer and patients with poor prognosis as HPV negative OPSCC could benefit from it. A longer follow up is needed to fully evaluate late toxicity and survival.

P048

COMBINED RT & EPIDERMAL GROWTH FACTOR RECEPTOR INHIBITOR MONOCLONAL ANTIBODY (MOABEGFR) TREATMENT OF HEAD & NECK CANCER (HNC): RADIOBIOLOGICAL MODEL FOR FAMOSO PROTOCOL

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Aims: administration of MoAbEGFr inhibitor during RT of HNC has shown radiosensitizing effect as compared to RT alone. MoAb-EGFr concentration and radiosensitizing effect varies day by day after every week administration. A radiobiological (RB) model accounting for this variation was adopted in the clinical protocol FAMOSO "Frazionamento Accelerato MOdulato in SIB-IMRT dei tumori testa-collO", in order to optimize daily RT dose with unchanged biological effect on tumor and potentially reduced toxicity vs. standard RT (7 weeks, tumor: 70Gy; margin: 63Gy; lymph nodes: 58Gy). Our aim was to assess the feasibility, toxicity, and response rate of the accelerated modulated fractioning.

Methods: The literature shows that higher MoAb-EGFr concentrations correspond to steeper tumor cell survival curves. RB parameters were derived from it and included in the model to obtain the daily dose to be delivered to each target volume. To date, 2 of the 10 expected pts (pt1 oropharyngeal; pt2 supraglottic squamous cell carcinoma) have been recruited in the FAMOSO protocol for curative intent.

Results: The RB model suggested 6 weeks with daily increasing dose/fractions: tumor 1.70, 1.95, 2.15, 2.30, 2.35Gy; margins 1.50, 1.75, 1.95, 2.05, 2.10Gy; lymph nodes 1.40, 1.60, 1.80, 1.90, 1.95Gy. Both pts concluded the RT treatment (pt1 planned schedule; pt2 with interruption of MoAbEGFr, last 10 days with standard RT fractions), with total dose to tumor 62.7 and 61.8 Gy, respectively. Maximum acute toxicity (skin,

mucosa) was G3. Follow up is 6 and 2 months (pt1: partial response; pt2 still under evaluation).

Conclusions: New treatment strategies combining RT with radiosensitizing drugs, even accelerated, are feasible. The RB model is adequate provided RB parameters are available from clinical data. Preliminary data from FAMOSO are encouraging, suggesting feasibility with acceptable toxicity. Longer follow up and more patients studied are needed to confirm toxicity findings and assess response rate.

P049

DECODING OROPHARYNGEAL CARCINOMA (OPCC) PHENOTYPE BY NONINVASIVE IMAGING USING A QUANTITATIVE RADIOMICS MAGNETIC RESONANCE IMAGES (MRI)-BASED APPROACH

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Aims: Oropharyngeal cancer (OPC) is characterized by phenotypic, histological, biological and clinical heterogeneity. Radiomics focuses on extracting a large number of quantitative imaging features, that could be correlated with tumor histology, grades, stage, metabolism, underlying patterns of gene expression and various other clinical outcomes in a non-invasive manner. We propose a radiomic approach using Magnetic Resonance Images (MRI) to decode tumor phenotype characteristic and treatment response by mean of quantitative features.

Methods: We retrospectively reviewed all pts with OPC treated at our Institute. Inclusion criteria were: diagnosis of squamous cell carcinoma of the oropharynx, availability of a baseline MRI, availability of a pathologic specimen (biopsy or surgical specimen) and a follow-up of at least 2 years. To build a prognostic radiomic signature, the whole analysis will be divided in sequential a training (current analysis) and a validation (prospective study) phase.

Results: Forty-eight pts met inclusion criteria and are currently under investigation. All pts underwent staging MRI at 1.5T with a 3D T1 weighted VIBE sequence (isotropic voxel) after gadolinium contrast injection. Fifteen pts were excluded from the analysis, because of the significantly different voxel size (6 pts) and the extremely small lesion volume (9 pts), which could both affect the texture analysis. IBEX software was used to extract more than 1000 tumor radiomic features from the MR images, after ROI tumor contouring by two radiologists (FDP-EA) and image preprocessing, including normalization. Clustering was performed to reduce the number of features and identify the most representative ones, after classifying pts in different groups according to the performed treatment. Considering the sample size, for the correlation analysis between the resulting features and the clinical parameters, no more than 2 features were tested at a time. Association between radiological and clinical features (in terms of overall survival, locoregional recurrence and HPV status) will be investigated by statistical analysis.

Conclusions: The main goal of this proposal it to decode tumor phenotype in OPC pts by noninvasive imaging using a quantitative radiomics approach. The extracted radiomic features will be correlated with clinical outcome of 33 selected OPC patients.

P050

DEFORMABLE REGISTRATION ON KV-CBCT IN HEAD AND NECK CANCER: PRELIMINARY GEOMETRIC AND DOSIMETRIC ANALYSIS.

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Aims: Intensity Modulated Radiotherapy has represented the milestone in the attempt to realize high conformal dose distribution, realizing high dose gradients among tumor and OARs. Anyway it needs very precise positionig of patients and accurate administration of variability due to motion and change of different organs, that may affect LC or lead to serious toxicity. Technological progress in verification systems has lead to “Image Guided RT” and “Adaptive RT” (ART), which consists of following every day anatomical and dosimetric variations of tumor and OARs and “adapting” the treatment to modifications by replanning. ART is a very complex process, consisting of many steps, such as on-line imaging, image deformable registration (DR) and cumulative dose calculation. The aim of this study is to evaluate if dose-tracking performed on Cone Beam Computed Tomography (CBCT) could replace new CTs acquired during treatment to evaluate the need of replanning.

Methods: The analysis was performed on 2 patients affected by head and neck cancers starting definitive RT. They were treated with VMAT and IGRT. They received daily CBCT and weekly CT. All the images were rigidly registrated with planning CT, contours were propagated by DR and corrected by Radiotherapist. Replanning was performed in case of high dosimetric variation. CT and CBCT were compared by geometric and dosimetric analysis. In the first Volume and Dice Similarity Coefficient (DSC) of structures on CT and CBCT images were compared; the

second one examined dose tracking made on weekly CT, daily and weekly CBCT. We considered CT the gold standard.

Results: In patient 1 volumetric reduction of GTV appeared higher on CBCT than on CT. DSC was high (0.94-0.99). Dose tracking with daily CBCT, daily and weekly TC was similar. In patient 2 volumetric reduction of GTV seemed higher on CT than on CBCT, whereas parotid glands analysis reported similar results (medium variation 0%, st.dev. 8%). DSC ranged 0.86-0.98 and was inversely proportional to volume reduction. Variation in dose-tracking was high, up to 33%.

Conclusions. DR in contour propagation on CBCT resulted to be reliable in volumetric analysis; however dosimetric results showed variation in dose-tracking on CBCT comparing to CT up to 33%. Therefore this procedure could only be used to intensify dose tracking performed on scheduled CTs; however, nowdays, it seems quite unsafe, especially in patients whose RT plans had DVH values closed to constraints.

P051

ROLE OF CONE BEAM-CT IN MONITORING WEIGHT LOSS OF HEAD AND NECK CANCER PATIENTS DURING RADIOTHERAPY TREATMENT

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Aims: We report our preliminary analysis of the relationship between weight loss (WL) and head and neck volume variations (VV) in the first patients treated in our department for head and neck cancer with Volumetric Modulated Arc Therapy (VMAT) and Image Guided Radiation Therapy (IGRT).

Methods: Patients treated with VMAT for locally advanced head and neck cancers in Radiation Oncology Division, Cà Foncello Treviso Hospital, were evaluated weekly by attending Radiation Oncologist and Nutritionist. The volume of a significant portion of the neck (using the caudal margin of lateral process of C1, encompassing the cranial limit of the II nodal level,as cranial margin, and the upper limit of hyoid bone, encompassing the cranial limit of the III nodal level,as caudal margin) was contoured and measured retrospectively using on-board cone beam computed tomography images at the same time intervals of medical examinations (1th, 6th, 11th,16th, 21th, 26th and last fraction).

Results: Twenty five patients were selected from institution's database.Thirteen were oropharynx cancer, 4 oral cavity, 3 hypopharynx, 2 nasopharynx and 3 nodal metastases from unknown primary. Median dose was 66 Gy in 30 fractions. No G3 mucositis or more was recorded, G1 and G2 mucositis were 56% and 36% respectively, no G3 erythema or more was recorded, G1 and G2 erythema were 64% and 28% respectively. One hundred seventy-five contoured volumes and the same number of weight assessments were collected. On the last fraction mean WL was 6% (range 17%, +1%), and mean VV 5,56% (range -12,85%, +4,33%), the mean WL at 6th, 11 th, 16th, 21th, 26th, were 1%,1%, 2%, 4%, 5%, 6% respectively, the corresponding VV were -1%, -1,84%, -3,11%, -4,41%, -4,72% respectively. The largest weight reduction is between the 16th and 21th fraction and it corresponds to the greater volume variation.

Conclusions: In our experience, thanks to appropriate nutritive support in patients treated with VMAT for locally advanced head and neck tumor, toxicity and weight loss were limited and all patients received their treatment as planned, without interruptions. However, neck volume shrinkage is significant and volumetric IGRT with Cone-beam CT can be a useful tool in order to recognize clinically and dosimetrically relevant changes in patients shape and volume and can be a guide to select patients who can benefit from an Adaptive RT approach.

P052

PROSPECTIVE ASSESSMENT OF ORAL MUCOSITIS AND ITS IMPACT ON QUALITY OF LIFE AND PATIENT REPORTED OUTCOMES DURING RADIOTHERAPY FOR HEAD AND NECK CANCER

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Aims: Oral mucositis (OM) is a common acute side effect during RT for head and neck cancer (HNC), with a potential impact on patient's compliance, quality of life (QoL) and clinical outcomes. Several quantitative scoring scales are available to properly assess OM and its influence on patient reported outcomes (PROs) and QoL

Methods: We prospectively assessed OM in a cohort of HNC patients undergoing RT using the Oral Mucositis Assessment Scale (OMAS), while its impact on PROs and QoL was evaluated with The Oral Mucositis Weekly Questionnaire-Head and Neck Cancer (OMWQ-HN) and the Functional Assessment of Cancer Therapy Head and Neck Cancer (FACT-HN). Evaluation of OMAS scores highlighted a progressive increase in OM during RT and a partial recovery thereafter. These trends were correlated to PROs and QoL as evaluated with OMWQ-HN and FACT-HN questionnaires. In the present study, we provided a quantitative assessment of OM, PROs and QoL.

Results: Mean mucositis score was 0.03 at baseline. It increased during RT at week 6 to 0.62 and decreased after to 0.40. Weighted mean mucositis score was 0.04 at baseline, increased to 0.69 at week 6 and decreased at 0.41 at week 2 after RT. The extent of mucositis score was 0 at baseline, increased to 0.81 at week 6 and decreased to 0.19 at week 2 after RT. For worst site mucosits score: 0.19 at baseline, 2.48 at week 6 and

1.67 after 2 week from RT. The 12-item OMWQ-HN score was 11.00 at baseline, increased to 24.52 at week 6 of treatment and to 24.67 at week 1 after RT to decrease to 19.81 at week 2. The FACT-HN total score is the summation of PWB, SWB, EWB, FWB and HNCS scores. It was 110.56 at baseline, decreased to 89.80 at week 6 of RT and increased to 96.05 2 weeks after RT. The FACT general (FACT-G) score is the summation of PWB, SWB, EWB, FWB scores. It was 81.70 at baseline, decreased to 70.50 at week 6 of RT and increased to 73.91 2 weeks after RT. The FACT Trial Outcome Index (FACT-TOI) score is the summation of PWB, FWB and HNCS scores. It was 67.62 at baseline, decreased to 52.39 at week 6 of RT and increased to 58.01 2 weeks after RT.

Conclusions: We observed a progressive increased of OM extension and intensity during the course of treatment as evaluated with the OMAS score. This was correlated to pain experienced during RT and impacted on global health status, general QoL and head and neck specific PROs. We provided a quantitative assessment of clinical endpoints potentially useful for future comparisons.

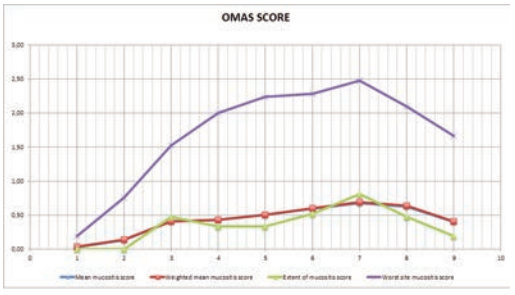

Figure 1.

P053

CISPLATIN AND RADIOTHERAPY – INDUCED NAUSEA AND VOMITING: IMPACT OF FOSAPREPITANT IN LOCALLY ADVANCED SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK – A PROSPECTIVE COHORT STUDY

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Aims: Cisplatin based chemotherapy has a well-known emetogenic potential. Preliminary evidence suggests that IMRT may worsen chemotherapy-induced nausea and vomiting (CINV) in head and neck cancer. The aim of our study is to report on the role of fosaprepitant in the prevention of CINV.

Methods: We performed a prospective cohort study in patients affected by locally advanced squamous cell carcinoma of the head and neck (HNSCC) undergoing standard concurrent radio-chemotherapy (RTCT). A total dose of 66 – 69.9 Gy was administered with an IMRT-SIB technique (highest dose per fraction: 2-2.12 Gy) over 33 fractions. Concurrently, cisplatin was given according to one of the following schedules: 1. 100 mg/m^2 q21; 2. 40 mg/m^2 q7; 3. 30 mg/m^2 q7. Fosaprepitant was administered at a dose of 150 mg over a 30-minutes ev infusion as part of standard antiemetic prophylaxis. Acute toxicity was evaluated according to CTCAE v.4. In addition, incidence of CINV was estimated with the FLIE questionnaire. Quality of life was also assessed with the EORTC HN43 questionnaire. The timing of CINV assessment was as follows: twice during RTCT (week 2 and 5) and one week after the end of treatment.

Tabele 1.

Total n. of patients: 22		
Average Age (range 47-73)	64	
Sex	M 77.3%	
	F 22.7%	
Primary Tumor	Nasopharynx 9.1%	
	Oropharynx 59.1%	
	Oral cavity 13.6%	
	Larynx 9.1%	
	CUP 9.1%	
Stage	II 9.1%	
	III 31.8%	
	IVa 50%	
	IVb 9.1%	
Charlson Comorbidity Index (Range 2-7)	2 4.5%	
	3 22.7%	
	4 27.%	
	5 22.7%	
	6 9.1%	
	7 13.6%	
PS	0 68.2%	
	1 31.8%	
	>1 0%	
CDDP regimen	30 mg/mq 14%	Mean n. of cycles 6.3
	40 mg/mq 45%	Mean n. of cycles 5.2
	100 mg/mq 41%	Mean n. of cycles 2.3
Dose intensity CDDP (range 100% - 66.6%)	100% 18.2%	
	85.7% 27.3%	
	71.4% 22.7%	
	66.6% 31.8%	
RT delivery dose	100%	

Results: Between July 2016 and May 2017, 22 patients were enrolled. Treatment and patients' characteristics are summarized in table 1. Mean dose intensity of cisplatin was 79.5% (range 66.6% - 100%). According to CTCAE v.4, the highest rate of nausea was 36% (8/22), 36% (8/22), 28% (6/22) and 0% for G0, G1, G2 and G3, respectively. Regarding vomiting, only one case of G2 toxicity was observed (4.5%; 1/22), whereas the majority of patients (G0: 73%, 16/22; G1: 22.5%, 5/22) had no or mild side effects. According to FLIE, the mean scores of patient-reported nausea and vomiting were 30.5 (range 21-49), 30 (range 15-52) and 29.8 (range 15-52) and 29.2 (range 26-45), 27.4 (range 23-41) and 27.7 (range 23-41) at designated timepoints, respectively. Further analyses evaluating the rate of concordance between CTCAE and FLIE and the presence of predictive factors for worse CINV are planned. Experimentally, in order to quantify the potential contribution of dose distribution to CINV, dosimetric

analysis of vomiting center structures (dorsal nucleus of vagus and area postrema) is ongoing.

Conclusions: The use of Fosaprepitant in the prevention of CINV yielded a very low rate of moderate-severe nausea and vomiting with good compliance to treatment, resulting in optimal delivery of cisplatin dose intensity.

P054

INTENSITY-MODULATED RADIOTHERAPY VERSUS 3D CONFORMAL RADIOTHERAPY IN PATIENTS WITH ORAL CAVITY TUMOR: HOW ACUTE AND CHRONIC TOXICITY CHANGES?

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Aims: Intensity-Modulated Radiotherapy (IMRT) is a technique that allows delivery of lower doses of radiation to normal tissues, while maintaining or increasing the tumour dose, compared with three-Dimensional Conformal Radiotherapy (3DCRT).The aim of this study was to compare the impact of the IMRT technique on acute and late toxicity and to analyze the differences with 3DCRT technique in oral cavity tumor. Methods:Between June 2005 and June 2016, 88 patients were treated with Radiotherapy (RT) at our Department. Definitive RT was performed in 25 patients, while 63 patients underwent previous surgery. Associated chemotherapy was administered in 32%. RT median dose was 66 Gy (range 50-70 Gy). 41% of patients were treated with IMRT, the others with 3DCRT technique. We retrospectively analized acute toxicity (dysphagia, mucositis, xerostomia) and late toxicity (dysphagia, mucositis, xerostomia, fibrosis) and their correlation between radiotherapy technique in all patients .We also analyzed Overall Survival, Disease Free Survival and Cancer Specific Survival. Results:The median follow-up time for surviving patients was 60 months, and the median time to progression for all patients was 7,1 months. Locoregional and distant metastasis rates were 57%. Patients who underwent associated chemotherapy experienced a higher acute and late toxicity rate (p=0.056 and p=0.06 respectively), Acute dysphagia was significantly lower with the IMRT technique (p=0,037), while a trend for worse fibrosis was observed with IMRT technique (p=0,052), respect to 3DCRT. Dose > 66 Gy was associated with a higher rate of late dysphagia while not achieving statistical significance (p=0,08). In our analysis acute dysphagia was related to late toxicity (xerostomia). Conclusion: Our study showed that IMRT technique greatly improved acute dysphagia in oral cavity tumor treated with RT. Our data are preliminary and need to be confirmed in more extensive population but it provided an important starting point for future studies.

P055

CAN IMRT TECHNIQUE INFLUENCE SURVIVAL IN ORAL CANCER?

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Aims: To report outcome in patients with oral cavity cancer treated with radiotherapy (RT).

Methods: From june 2005 to june 2016, 88 patients were treated with 3DCRT and IMRT technique (IMRT was used in 41% of cases), at the Radiotherapy Unit of San Donato Hospital -Arezzo. Definitive RT was performed in 25 patients, while 63 patients underwent previous surgery. Associated chemotherapy, mainly weekly cisplatin, was administered in 32% of patients

Results: 88 patients were retrospectively review, 61% were male and 39% were female. After a median follow up of 60 months(12-120), 50 patients relapsed (local recurrence and distant metastases) with five-year disease free survival rate of 42,6%. Presence of lymphovascular invasion and 3DCRT technique were significantly associated with worse DFS (p= 0.01 and p=0.05 respectively). Five year cancer specific survival (CSS) was 42,8 %. Five year overall survival (OS) was 39,8%. IMRT technique and absence of lymphovascular invasion were associated with better Overall Survival (p=0.01 and p=0.02 respectively).

Conclusions: RT technique and the presence of lymphovascular invasion can influence the results in term the outcome in oral cancer patients.

P056

EVALUATION OF THE ACCURACY OF A HYBRID PRIMARY TUMOR GTV (MR+PET) CONTOURING METHOD IN RADICAL DOSE-PAINTED IMRT (DP-IMRT) FOR PRIMARY LOCALLY ADVANCED OROPHARYNGEAL CANCERS: A RETROSPECTIVE ANALYSIS

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Aims: To evaluate the accuracy of a hybrid GTV (MR+PET) contouring method of primary locally advanced oropharyngeal cancers in a retrospective series of 12 patients (pts) treated with radical dose-painted (DP) IMRT.

Methods: From January 2012 and May 2014, 12 pts, 10 males and 2 females, age 48-77 yrs, affected

with locally advanced squamous cell oropharyngeal carcinomas, stage IVA-IVB, received radical DP-IMRT with 2 dose levels of 54/66 Gy (8 pts) and 3 dose levels of 54/60/66 Gy (4 pts) in 30 fractions. All pts received also concomitant chemotherapy with CDDP. Primary GTV was delineated on CT-simulation scans: 16 detector lines spiral CT, 3 mm slices thickness, 0 mm gap, patient in supine position with headrest and a 5-point customized head-shoulders thermoplastic immobilization mask. Three superficial markers were positioned on the mask at the intersection of sagittal and medial laser, images acquired from vertex to toracic inlet. Pre/post-contrast MR (1.5 T) was performed with head and neck coil, headrest without mask, patient alignment with MR lasers on skin markers coincident with those positioned on the mask before CT simulation. CT and "phased array" coil MR sequences were then fused by an automated rigid mutual information system, according to a specific protocol, previously verified both in Lucite cylinder phantom and in patient CT/MR images identifying 5 anatomical bone markers. FDG PET-CT was acquired in treatment position, reconstructed at 2 mm slice and a voxel size of 2^3 mm. The definition of tumor VOI on PET-CT was based on SUV image segmentation by an isocontour automatic segmentation algorithm with SUV threshold=2.5. An hybrid MR/PET-CT GTV was finally reconstructed on CT-simulation scans by Boolean operators; CTV was delineated with margins of 1-1.5 cm around GTV, CTV-PTV margins: 6 mm.

Results: With a median follow-up of 48.5 months (29-57), 9 pts were alive without evidence of disease, 1 pt interrupted follow-up 5 months after the end of RT and 2 pts died of disease. Overall, 2/12 pts showed disease persistence at primary site: 1 pt died of disease and 1 pt was rescued by salvage surgery. In both pts, patterns of local persistence were at the primary hybrid GTV and well inside the high dose PTV.

Conclusions: Our analysis, although in a small series of 12 pts treated with radical DP-IMRT, indicates a good accuracy of the method used for hybrid GTV delineation and encourages its introduction in routine clinical practice at our Center.

P057

OPTIMUM CYLINDRICAL PHANTOM GRID SIZE CALCULATION TO EVALUATE THE ACCURACY OF GAMMA INDEX FOR TIMES OPTIMIZING IN THE PRE-TREATMENT QUALITY ASSURANCE PROCEDURE OF VMAT AND IMRT TECNIQUES

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Aims Intensity modulated radiation therapy (IMRT) and volumetric modulated arc therapy (VMAT) are state-of-the-art irradiation techniques for the delivery of highly conformal radiation fields to the target volume. The use of quality assurance tools for the verification of the planned dose distribution prior to the treatment of the patient has become a standard procedure in clinical routine. Aim of this study is to evaluate the optimal grid size on cylindrical phantoms to determine the gamma index (γ) levels for the routinely pre-treatment dosimetric Quality Assurance

Methods The measurements were made on a Elekta Precise linear accelerator and compared with the created plans by the Philips Pinnacle Treatment Planning System (TPS). The pre-treatment evaluations were made with the PTW OCTAVIUS 4D phantom with the 729 cubical ion chambers arranged in a 2D matrix of 27cm x 27cm. In the course of the measurements the complete phantom volume is covered by measuring points. The beam incidence is always perpendicular to the surface of the detector panel and the data were collected and evaluated by means of the VeriSoft software package. On 72 patients who underwent to radiotherapy with VMAT or IMRT of the head neck region, were evaluated the γ between the dose deliveries and the dose calculations on the cylindrical phantom with cubic step size of 4mm, 3mm and 2mm. For each phantom grid size the γ value with [3mm;3%], [2mm;2%] and [1mm;1%] as distance and dose difference criteria respectively were determined

Results The mean percentage ratios were found equal to γ[2mm;2%]/γ[3mm;3%]=92% and γ[1mm;1%]/γ[2mm;2%]=69%. For each fixed γ[d(mm);D(%)] criteria the γ differences respect to the 3mm voxel phantom calculation, followed a Gaussian distribution. That mean that there isn't a correlation between the used phantom grid size and γ accordance. The agreement in γ was found within 2% (2SD) and 3% (2SD) and 5% (2SD) respectively for γ[3mm;3%], γ[2mm;2%] and γ[1mm;1%]

Conclusions Due to the computer limits and the large amount of calculation, the TPS algorithms are

often time consuming and may require up to 1 hour and more, strongly depending on the set grid size calculation. Many TPS manuals suggest to use a 2mm o smaller grid size on phantom to evaluate the agreements of the γ. These results show that for busy Center a voxel grid size of 3mm is enough appropriate and suggest to refine calculations only in cases where gamma index is near the established level in the Center.

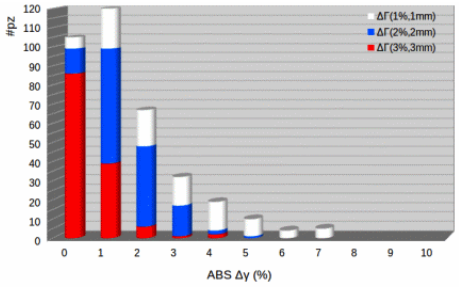

Fig *Absolute differences between the gamma index [3%,3mm] and [1%,1mm] respect to gamma index [2%,2mm]*

P058

LOCAL TUMOR CONTROL OF LOCALLY ADVANCED (CT3-T4, N0-N3, M0) NASOPHARYNGEAL CANCER PATIENTS TREATED WITH MIXED BEAM (PHOTONS-PROTONS) RADIOTHERAPY: PRELIMINARY RESULTS IN 17 PATIENTS

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Aims: Management of locally advanced nasopharyngeal cancer (LANPC) is challenging due to poor local and distant control. Our aim was to evaluate clinical outcome and radiation-related acute and late toxicity (tox) in patients (pts) with LANPC treated with a mixed beam protocol (sequential Intensity Modulated Radiotherapy -IMRT- followed by Intensity Modulated Protontherapy –IMPT-boost) Methods: We reviewed all pts with LANPC (cT3- 4) enrolled in a mixed beam protocol CNAO06/2011 ("Phase II study of protontherapy (hadrontherapy) boost in locally advanced head and neck cancer") at Centro Nazionale di Adroterapia Oncologica (CNAO, Pavia). Acute and late toxicities were evaluated according to Common Terminology Criteria for Adverse Events (CTCAE V4.03) scale. Local control and overall survival were assessed.

Results: Seventeen pts (13 pts from the European Institute of Oncology, Milan, 3 pts from the University of Turin, 1 patient the from University of Piemonte Orientale, Novara) were analyzed. All pts received IMRT to a total dose of 54-60 Gy (2 Gy/die, 5 fractions a week) and sequential boost with IMPT up to a total dose of 70-74 Gy(RBE) (2 Gy(RBE)/die, 5 fraction a week) administered at CNAO. Median total dose was 72 Gy(RBE) (mean 71, range 64-74). All pts received platinum-based concurrent chemotherapy and 11 pts received also induction chemotherapy. Eight pts developed grade 3 tox: mucositis 1 patient mucositis, dysphagia 4 pts and hematologic tox 3 pts. No patient had grade 4 acute tox. Fifteen pts had a minimum follow-up of 6 months and therefore were evaluated for late tox and oncologic outcome. After a median follow-up of 29 months (mean 30 months, range 10–52) local tumor control was achieved in 14/15 (93.3%) pts. Only 1 patient experienced 'in field' tumor progression and died 11 months after the end of treatment. At last follow-up, 12/15 (80%) pts were alive: 11 (73%) pts without disease and one (7%) patient with distant metastases. Two pts died for distant metastases after 50 and 27 months, respectively. No grade 3 and 4 late tox was found. Grade 2 tox was recorded in 8 pts: xerostomia 5 pts, hearing impairment 2 pts, endocrine disorders 1 patient.

Conclusions: Sequential mixed beam (photons-protons) treatment for LANPC is feasible, safe and offers high local control (>90% at 30 months) also combined with chemotherapy regimens. Distant metastases remain a criticism in long-term survivors. Larger pts' accrual is required to confirm these preliminary data.

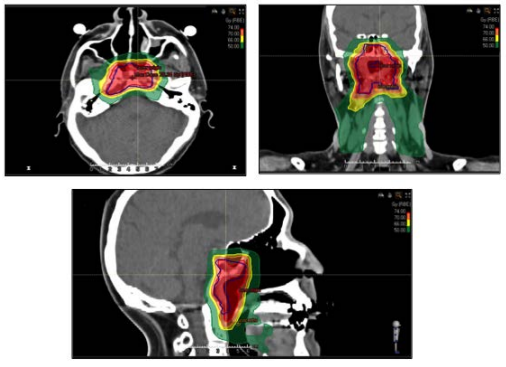

Figure 1. Example of a radiotherapy plan sum: 60 Gy [RBE] Intensity Modulated Radiotherapy followed by 14 Gy [RBE] Intensity Modulated Protontherapy boost. The blu line represents the clinical target volume. The red, orange, yellow and green lines represent 74, 70, 66 and 50 Gy [RBE] isodose levels, respectively

P059

18F-FDG-PET IN GUIDING DOSE-PAINTING WITH VMAT IN LOCALLY ADVANCED HEAD AND NECK CANCER TREATED BY CHEMO-RADIOTHERAPY-OUR EXPERIENCE

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Aims: Our study aimed to test the feasibility and safety of 18F-FDG-PET dose-painting with VMAT in locally advanced H&N cancer. The primary outcome is to evaluate the acute toxicity and clinical outcome in terms of local control.

Methods: From February 2016 to February 2017, seven patients, average age 60.5 (47-79), with Stage II-IV HNSCC were included. Five of these were Oropharyngeal Tumours and two were Nasopharynx Tumours. Before treatment each patient underwent head and neck endoscopy, contrast enhanced TC or MRI and 18F-FDG-PET scan. All patients were concomitantly treated with chemotherapy. The PET avid gross tumour volume [GTV(T- N) 18F-FDG-PET] is defined in planning PET/CT into the radiotherapy planning system in which we also define the PTV1-PTV2 and OARs. Treatment is delivered over 6 weeks in 30 daily fractions, at 3 dose levels (Simultaneous Integrated Boost): PTV1- moderate risk neck lymph nodes- 54 Gy; PTV2 primary tumours and involved/high risk neck lymph nodes- 60 Gy; GTV T and N 18 F-FDG-PET -68.1 Gy. Toxicity were recorded according to RTOG/EORTC criteria at six weeks and three months after radiotherapy for acute toxicity.

Results: Target volume objectives were met in all patients, whilst respecting normal tissue tolerances and PTV hotspot constraints (Table 1). At 6 weeks after treatment G1 of mucositis was observed in 4/7 patients (57%), G2 in 2/7 patients (29%) and G0 in 1/7 patients (14%). Regarding xerostomia we detected G0 in 1/7 patients (14%) and G1 in 6/7 patients (86%). 4/7 patients developed G2 dysphagia (57%) , and pain G1 was reported by 4/7 patients (57%) while G2 was reported by 3/7 patients (43%). In 5/7 patients we observed G2 dermatitis (71%) and in 2/7 patients G1 dermatitis (29%). At 3 months only one patient showed G1 of mucositis, 3 patients showed G1 of xerostomia and 3 patients G2. Only one patient showed G1 of dysphagia and no patients showed dermatitis and pain. No grade 3 or 4 toxicities were recorded.

Conclusion: 18F-FDG-PET guided selective dose escalation is feasible. Acute toxicity rates are acceptable and appear similar to those observed with standard treatment. There are no cases of Grade ≥ 3 acute toxicity at 6 weeks and at 3 month after treatment. At 3 months all patients have had a complete metabolic response but one patient had a systemic disease. To date, 5 patients are disease free, one had local recurrence and one had systemic disease. Late toxicity assessment and overall survival are ongoing.

Table 1.

PET-GTV (T+N)	
Volume (cc)	Mean 62.20 cc (Range 40.75-86.9 cc)
Median D95 (%)	97.84% (Range 95%-102.6%)
Median D5 (%)	102.79% (Range 99.6%- 104.4%)
PTV2	
Median D95 (%)	98.11% (Range 95.7%-103.4%)
PRV Spinal Cord max	Mean 43.9 Gy (Range 34.3 Gy- 47.6Gy)
PRV Brainstem max	Mean 39.8 Gy (Range 29.9Gy-58.2Gy)
Ipsilateral Parotid (mean dose)	Mean 23.2 Gy (Range 16.2Gy-24.8Gy)
Contralateral Parotid (mean dose)	Mean 23.5 Gy(Range 19.5Gy- 26.0Gy)

P060

WHAT IS THE RATIONAL FOR PRIMARY DEFINITIVE RADIATION TREATMENT OF UNRESECTABLE JUGULOTYMPANIC PARAGANGLIOMA? BENEFIT/COST RATIO IN A REPRESENTATIVE CASE

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Aims: Jugulotympanic paraganglioma (JP) is a rare tumor, often locally aggressive, of the 5th or 6th decades of life. Surgical excision is the primary definitive treatment, but it is affected by high morbidity rates, not acceptable considering the benign nature of JP; in addition, JPs can be often unresectable because of the intracranial extension and Fisher stage. In these cases conventional or stereotactic radiotherapy can be a valid option. Radiotherapy goal is disease control or growth inhibition rather than tumor elimination and its use is often associated with significant radiation-induced sequels. We present the case of unresectable JP treated with primary IMRT.

Methods: a 68-year-old woman presented with tinnitus and paresis of the right hemi-tongue, hyperaemia of lower quadrants of tympanic membrane and peripheral paralysis of XII cranial nerve. Head CT and MRI revealed findings consistent with a large right-sided JP of 4 cm. Head & Neck team concluded for unresectable JP (C3 class according to FISH); an evaluation for proton-therapy was performed but patient refused treatment, therefore she underwent IMRT, with a prescription dose of 50.4 Gy/1.8 Gy fraction. Planning CT was acquired using thermoplastic mask for head immobilization in neutral position; a 2 mm slice thickness was employed. Planning CT was co-registered with both diagnostic TC and MRI. GTV was defined as macroscopic disease visible on diagnostic imaging, a 1.5 cm isotropic margin around GTV was added to obtain CTV, a geometric 3 mm expansion was applied to obtain PTV. Brain, eyes, lens, optic nerves, cochlea, parotid glands, brainstem, spinal cord were considered as organs at risk. Acute and late toxicities were

recorded according to CTCAE v. 4.0 scale; clinical and radiologic follow-up was performed every 3 months during the first year.

Results: Radiation treatment was completed without interruption. Acute G1 radiodermatitis, oral mucositis, dysphagia and oral candidiasis occurred. After 6 months of follow-up neither clinic nor radiologic response was obtained; MRI showed unmodified dimensions of JP. Actually, tinnitus and tongue paresis persist, in addition radiological and clinical findings of mastoiditis occurred.

Conclusions: growth control of JP was obtained, without a clinical benefit and at price of increased toxicity. IMRT can potentially reduce side effects, long-term follow-up studies are still in progress but strong evidence are lacking.

P061

USE OF 18F-FDG-PET IN TARGET VOLUME DELINEATION FOR MALIGNANT PLEURAL MESOTHELIOMA IMRT: OUR EXPERIENCE

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Aims: Radiotherapy of malignant pleural mesothelioma (MMP) requires a precise identification of the extent of the disease in order to spare normal tissues and escale the dose. As a result, there is considerable interest in investigating functional imaging, like 18F-FDG-PET, that provides improved delineation of the target volume. However, due to a lack of anatomical information, a careful correlation must be made between FDG-PET and structural images in order to precisely localize the tumor. A range of image registration strategies allows FDG-PET images to be directly incorporated into computed tomography (CT) images. So we have a single image set. The aim of our study was to evaluate the role of 18F-FDG PET/CT integrated imaging in planning the radiotherapy treatment of patients with malignant pleural mesothelioma.

Methods: The inclusion criteria for the studies were: histologically confirmed MPM, clinical stage of I-III disease, ECOG 0-1. We enrolled eleven patients with these features. An 18F-fluorodeoxyglucose positron emission tomography (FDG-PET) scan was done to evaluate macroscopic disease and baseline residual lesions. All patients underwent PET/CT simulation in the supine position, while immobilized with a customized vacuum. The clinical staging was analyzed by comparing the PET/CT with the CT observations alone. For clinical purposes, the PET image was always considered as additional information to the CT image for tumor staging or target contouring for treatment planning. Clinical target volume (CTV), using fully fused PET/CT imaging with simulation CT, was defined as a ring encompassing the whole lung composed of the pleura and the chest wall of the entire hemithorax. PTV was created by adding 1 cm isotropic margin to CTV, to account for respiratory movements and received a dose of 5040 cGy in 28 fractions using IMRT static step and shot technique.

Results: After fusion PET-CT the CTV was modified in 33% of cases, in three patients it decreased by 24%, while it increased by 16% for two patients. In the remaining patients the fusion allowed the most accurate target volume delineation.

Conclusions: Based on the results from the present study, the future scenario of the imaging for RT of malignant pleural mesothelioma may include the use of functional imaging, such as FDG-PET/CT, with the aim of characterizing the biological features of the tumor and optimizing the use of highly conformal and biologically effective RT.

P062

SAFETY AND EFFICACY OF RADICAL HYPOFRACTIONATED RADIATION THERAPY IN LOCALLY ADVANCED NSCLC: A SYSTEMATIC REVIEW ON BEHALF OF LUNG CANCER AIRO STUDY GROUP

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Aims: To assess the benefit in terms of effectiveness and feasibility of hypofractionated radiation therapy (HypoRT), with or without chemotherapy (CT), in the treatment of locally advanced non small cell lung cancer (NSCLC).

Methods: A systematic PubMed search was performed to identify all studies, published from 2007 onwards, on patients with locally advanced NSCLC treated with hypoRT with radical intent, with a minimal dose per fraction of 2.4 Gy, with or without concurrent chemotherapy.

Results: Twenty-two studies that met the inclusion criteria were identified, for a total of 2266 patients. Patients were divided in the concurrent chemo-radiation

therapy group (CT-RT) and non concurrent chemotherapy group (radiotherapy alone, RT). In CT-RT group the delivered dose ranged from 52.5 to 75 Gy, with a dose per fraction ranging from 2.4 to 3.5 Gy. Actuarial 2-year progression free survival (PFS) and overall survival (OS) ranged from 19% to 58%, and from 28% to 68.7%, respectively. The overall incidence of grade 3 acute and late lung toxicity was 0-11.7% and 0-23.5%, respectively. Acute grade 2 and 3 esophagitis occurred in 3% to 51%, while late esophageal toxicity occurred in 0% to 11%. In RT group the delivered dose ranged from 45 to 85.5 Gy, with a dose per fraction from 2.4 to 4 Gy. Actuarial 2-years PFS and OS ranged from 28% to 50%, and from 20% to 36%, respectively. Acute Grade ≥ 3 pneumonitis occurred in 0% to 14.3%, whereas late G ≥3 pneumonitis occurred in 0% to 23%. Acute Grade ≥ 3 esophagitis occurred in 0% to 10.7%, while late esophageal toxicity was 0% - 19%.

Conclusions: HypoRT with or without concurrent chemotherapy seems to be safe in patients with locally advanced NSCLC. The encouraging survival results of several studies analyzed in the present review suggest that hypofractionated radiation schemes should be further investigated in the future.

P063

EPID-BASED *IN VIVO* DOSIMETRY FOR ACCURATE DELIVERY OF LUNG STEREOTACTIC RADIOTHERAPY USING MULTIPLE BREATH-HOLD SEGMENTED VOLUMETRIC MODULATED ARC THERAPY

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Aims: In vivo dosimetry (IVD), a direct method of measuring radiation doses to cancer patients during treatment, has shown unique features to trace deviations between planned and actually delivered dose distributions. Lung stereotactic ablative radiotherapy (SBRT) involves the delivery of high doses in a few fractions for ablative purposes. Then SBRT treatments strongly benefit from IVD procedures, as any uncertainties in dose delivery is more detrimental for treatment goals. We assessed the feasibility of EPID-based IVD for clinical lung SBRT treatments using VMAT technique.

Methods: 8 patients with lung metastases treated with Elekta VMAT were enrolled. Dose prescription was 50Gy in 5 fractions. Patients were simulated and treated using the Active Breath Coordinator (Elekta), a spirometer enabling a temporary controlled interruption of patient breathing at the end of inspiration phase. VMAT plans were generated with Ergo++ TPS with a single 360° arc; the VMAT delivery sequence was divided into multiple subarcs according to the patient predefined breath-hold periods. IVD was performed using SOFTDISO software (Best Medical Italy). IVD tests were evaluate by means of (i) R ratio between isocenter daily in-vivo dose and planned dose and (ii) g-analysis between EPID integral images in terms of percentage of points with g-value smaller than one (g%) and mean g-values (gmean), using a global 3%-3 mm criteria. Alert criteria of ±5% for R ratio, g% <90% and gmean > 0.67 were chosen., the last two in order to accept only 10% of the values to exceed 3%/3mm and an average discrepancy of the order of 2%/2mm, respectively.

Results: A total of 40 transit EPID images were acquired. Two images (5%) were removed from analysis for image deterioration and/or electronic acquisition failures. The overall mean R ratio was equal to 0.999 ± 0.021 (1 SD) for all patients, with 100% of tests within 5% alert criteria. The 2D portal images g-analysis show an overall gmean of 0.29±0.11 with 100% of tests within alert criteria, and a mean g% equal to 97.9±3.2% with 100.0% of tests within alert criteria. The results are supplied in quasi real-time, with IVD tests performed and displayed after only 1 minute from the end of arc delivery.

Conclusions: Our results showed that the integration of ABC multi-segmented breath-hold control into the VMAT-SBRT delivery strategy translated in high reproducibility treatments.

P064

FIRST STUDY UNDER HIGH ENERGY PHOTON BEAMS ABOUT JARVIK2000 VENTRICULAR ASSIST DEVICES

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Aims: In the last year, the number of treatments in

patients with Ventricular Assist Devices (VADs) is increasing. However, data reported in literature are scarce. JARVIK2000 (J) (Jarvik Heart Inc. New York, NY) is a new VAD system that only recently has been introduced on the market and implanted in patients. Aim of this work is to test, in vitro, the correct functionality of the device electronic components under high energy photon beams.

Methods: The J has been designed to provide circulatory support to patients with severe heart failure. It consists of a turbine pump (2.5x5.5cm, 85g) with a neodymium-iron-boron magnet impeller housed inside a welded titanium shell. It's supported by ceramic bearings and spins blood with a flow rate of 5-7 L/min and a rotation speed of 8-12Krpm. It's connected to an external FlowMaker Controller via tunneled driveline that delivers power. Controller allows adjustments of the pump speed. Measurements were made at the Radiotherapy Dept. of SS. Annunziata Hospital in Chieti. The pump was deep in water inside a plexiglass siliconized box and connected both to a controller and a fully charged lithium ion battery. The pump was irradiated using 6 and 10MV photon beams produced by a Synergy Agility linear accelerator (Elekta, Crawley), firstly considering a10x10cm^2 field size and then a VMAT plan. The J-isocenter distance was set to 10cm. The doses to pump were measured placing Ionization Chambers (Farmer and Semiflex ICs, PTW) in the same pump position. Battery discharge time was recorded after sessions. Electronic components were controlled before, during and after the irradiations with measure of voltage, current (Fluke 87 True Rms Multimeter) and frequency(Fluke PM6669UFC) of three phases of J's alternating power supply. The sound frequency spectrum during the operation, was also monitored using microphone plugged in FujitsuA512 with MSWindows7 and Audacity(R) Software. Data were collected and analyzed in five weeks.

Results: The functionality of the VAD system did not seem to have been compromised by the irradiation in every step of measurement and session .Independent sounds measurements confirmed these findings.

Conclusions: These preliminar results seem to indicate that the irradiation under high photon beams does not compromise the pump functionality. However, direct irradiation with higher doses are needed to confirm these data.

P065

LONG TERM OUTCOME IN PATIENTS TREATED WITH ERLOTINIB AND CONCURRENT CHEMORADIATION FOR LOCALLY ADVANCED DISEASE

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Aims: To report the long term outcome of the combination of Erlotinib and concurrent chemoradiation in pretreated patients with locally advanced or metastatic NSCLC.

Materials and Methods: An updated analysis of a published retrospective trial on 60 consecutive patients with NSCLC treated with erlotinib and concurrent chemoradiation to primary tumor was conducted. Long term toxicity and updated survival have been explored. Moreover, local and distant progression site have been investigated. CTC vers 3.0 has been applied.

Results: A median follow up for alive patients of 8.9 years, late pulmonary fibrosis has been reported in 14 of 60 enrolled patients. The rate of G2 toxicity (defined as: "patchy or bi-basilar changes with estimated radiographic proportion of total lung volume that is fibrotic of 25 – <50%") has been reported in two patients. In twelve cases only a fibrotic proportion less than 25% has been documented. No late esophageal toxicities have been reported. The median OS was 23.3 months as reported in the previous work, and 6 patients are actually alive (10%). Four patients are alive without evidence of disease. Two patients are alive with disease and chemotherapy and target agents have been started. In the previous work the EGFR mutational status was recorded in 32% of cases and it was always wild type. Actually one patient is in treatment with gefitinib because a new biopsy revealed the EGFR mutational status. The other alive patients are wild type. The mean PFS was 4.7 months, 1 year PFS was 21%, 2 years 11%. Local disease control at 1 year was 73%.The median MFS was 7.5 months. The 1-year MFS was 21%, at 2 years 23%

Conclusions: No unexpected long term toxicities have been documented with long term follow up in patients treated with erlotinib and chemoradiation in inoperable NSCLCs. A 10% of survivors at long term follow up is an interesting finding, considering that just one patient had EGFR mutation.

P066

STEREOTACTIC BODY RADIOTHERAPY (SBRT) IN PATIENTS WITH LUNG OLIGOMETASTASES: A MONO-INSTITUTIONAL EXPERIENCE

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Aims: Stereotactic body radiotherapy (SBRT) for metastatic lung lesion is today a new standard of care for patients with oligometastastic desease who presented inoperable small lung metastases or refuse to undergo surgery for lung recurrence. The aim of this study is to evaluate outcomes and safety of SBRT in a cohort of patients treated with SBRT delivered in all active lung metastases.

Methods: Between May 2011 and April 2016, 218 lung metastases in 62 patients (pts) affected by oligometastatic desease were treated with SBRT to all active

sites of disease. The primary tumors were colorectal cancer in16 pts (25.8%),lung in 32 pts (51.62%), head and neck cancer in 3 pts (4.84%), breast in 4 pts (6.45%) and other sites (kidney, prostate, endometrial and urothelial cancer) in 7 pts (11.29%). All lesion was contured on CT scan data sets acquired in supine position using wing boards and dual legs. CT was acquired in breath old using Active Breathing Coordinator (ABC) device in 39 pts, for 23 pts was used a 4-dimensional (4D) CT. Treatment were planned using MONACO TPS and Montecarlo optimization SBRT was delivered with a Elekta 6-MV Linear Accelerator and Beam modulator. The prescribed dose was 26-30 Gy to 70% isodose line in single fraction for peripheral or small tumors (< 3cm) or 30-36 Gy to 70% isodose line in 3 fractions for centrally located or large tumors. Patient set-up and isocentre position was controlled before each fraction by Cone-Beam CT. The results were assessed by contrast enhanced CT and FDG/PET-CT scan 2 months after SBRT and every 4 months successively. The Response Evaluation Criteria in Solid Tumors (RECIST modified adding PET scan) was used to assess the response to SBRT. Treatment related-toxicity was graded according to CTCAE v 4.0.

Results: Median follow up was 19 months (range 3-53). The median OS was 19 months; 6-months, 12-months and 24-months OS were 100 %, 100%, 98%, respectively. Median PFS was 9,5 months (range 4-34) The treatment was well tolerated: grade 1 pneumonitis occurred only in 2 patients; no grade 2 or higher acute or late toxicity was observed.

Conclusions: In our experience, SBRT appears a safe and effective treatment of lung metastases and ours results are favorably comparable with surgery.

P067

CLINICAL-DOSIMETRIC ASSESSMENT OF PATIENTS TREATED RADICALLY FOR NSCLC WITH THE PRODVH SOFTWARE: A RETROSPECTIVE ANALYSIS

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Aims: To retrospectively analyze overall survival (OS), acute and late lung toxicity in a cohort of patients undergoing radiotherapy, with (RTCT) or without (RT) chemotherapy at our Institution. To investigate possible correlations between dosimetric data and clinical outcomes, and assess the role of 3 dimensional conformal RT (3DCRT) and intensity modulated RT (IMRT) in terms of coverage of target volumes and preservation of the major organs at risk (esophagus, lungs, heart).

Methods: Data of all patients (pts) treated with radical RT or RTCT for lung cancer were reviewed. Overall survival (OS), acute and late lung toxicity (ALT and LLT) according to CTCAE V3.0 scale, were analysed. Kaplan-Meyer curve and log-rank test were used for survival analysis, while chi-square test was calculated to compare the different variables. P< 0.05 was considered significant. Furthermore, the data of all patients were evaluated with PRODVH, a homemade software developed to compare biologically equivalent DVHs and calculate mean DVH within clinically relevant groups (type of treatment, technique used, OAR and PTV)

Results: From 2004 to 2014 87 patients were treated with radical intent with RT or RCTC for primary lung cancer. Clinical and therapeutic data of the series have been reported in Table 1. The 1, 2 years overall survival rates resulted to be 58.8%, 39.5% and 75.5% respectively. Analysis of PRODVH showed that increasing treatment volume worsened the DVHs of OARs and preservation of healthy contralateral lung reduced the risk of lung fibrosis. Moreover, a considerable increase in the low doses to OARs resulted from using non-3D techniques, counterbalanced by a benefit in terms of target coverage.

Conclusions: Locally advanced lung cancer remains a poor prognosis tumour related to a relevant risk of toxicities. Single plan DVH does not represent by itself the best approach to estimate treatment-related toxicity. PRODVH produces an average DVH giving more accurate information on the dosimetric features related with an increased risk of toxicity.

Table 1. Clinical and therapeutic variables.

Characteristics	Number (%)
Total patients	87 (100)
Age	
average (range)	65 [41-85]
Median age	
≤ 65 years	44 (50.6)
> 65 years	43 (49.4)
Gender	
male	70 (80.5)
female	17 (19.5)
Karnosky	
≤ 80	78 (89.7)
> 80	9 (10.3)
Staging PET	
no	17 (19.5)
yes	70 (80.5)
Stage	
Stage I-II	17 (19.5)
Stage IIIA	44 (50.6)
Stage IIIB	26 (29.9)
Histology	
adenocarcinoma	32 (36.8)
squamous carcinoma	45 (51.7)
others NSCLS	10 (11.5)
Radiation setting	
exclusive RT	24 (27.6)
concomitant RCT	20 (23.0)
sequential RCT	30 (34.5)
CT neoadjuvant treatment + concomitant RCT	13 (14.9)
Dose	
60 Gy	27 (31.0)
>60 Gy	60 (69.0)
Technique	
3DCRT	49 (56.3)
IMRT/VMAT/TOMO	38 (43.7)
IGRT	
no	46 (52.9)
yes	41 (47.1)

P068

NIVOLUMAB AND RADIOTHERAPY IN ADVANCED NSCLC: RESULTS OF LUNG CANCER MULTIDISCIPLINARY TEAM OF FERRARA

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Aims: In the last decade the discovery of immune checkpoint inhibitors such as PD-1 inhibitor Nivolumab had revolutionized the treatment of advanced NSCLC. The combination with radiotherapy is of particular interest, due to some preliminary observations reporting additive o synergist effect in some tumors. The purpose of this study was to retrospectively evaluate the role of radiotherapy on the effect of an immune checkpoint inhibitor (Nivolumab) in terms of activity and toxicity in pretreated locally advanced or metastatic lung cancer patients.

Methods: From March 2015 to December 2016, 35 consecutive patients (15 men and 5 women) received Nivolumab for a advanced NSCLC. Fifteen received an hypofractionated radiotherapy as palliative measure, and in these patients Nivolumab was administered at least one week from radiotherapy end. The median age was 69 years, 23 patients (65.7%) had an ECOG score 0-1. All patients had received, previously at least one systemic regimen, for only 3 (8.6%), nivolumab was a third treatment line. The two groups of treatment (radiotherapy-nivolumab and nivolumab alone) were well matched for baseline characteristics.

Results: At a median follow-up of 7.4 months, the 1-year overall survival rates were 57.8% for patients treated with radiotherapy-Nivolumab and 27.4% for patients treated with Nivolumab alone (p=0.043). The 1 year progression free survival was 57.8% in the radiotherapy-nivolumab group and 20.6% in the Nivolumab alone group (p=0.040). No difference in adverse event was detected.

Conclusions: Radiotherapy and Nivolumab can be combined in advanced, pretreated NSCLC patients, with potential benefit in overall survival and progression free survival, without significant increase in acute toxicities. Prospective studies are needed to confirm these results.

P069

A RANDOMISED PHASE II STUDY OF A COMBINATION OF IMMUNOTHERAPY AND STEREOTACTIC ABLATIVE RADIOTHERAPY IN LIMITED METASTATIC LUNG CANCER: IMMUNOSABR-PROJECT

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Aims: Despite decades of research, the overall survival (OS) in lung cancer remains poor. IMMUNOSABR is a multicentric randomised phase II study in which the main objective is to test if the combination of stereotactic ablative radiotherapy (SABR) and the immunocytokine L19-IL2 has clinical meaningful activity in patients (pts) with limited metastatic non-small cell lung cancer: (≤10 sites, WHO 0-1: "oligo+"). The secondary endpoints are OS, Quality of Life and out of field radio-immune effect response.

Methods: The trial provides two patient cohorts: a group with maximal 3 metastatic lesions eligible for ablative treatment of all tumour sites using SABR (ablative cohort-AC) and a second group with up to 10 metastasis, not eligible for ablative treatment (non-ablative cohort-NAC). After randomization only pts ending up in the experimental arm (ARM B) will receive up to 6 cycles of the immunocytokine. The pts in the control arm (Arm A) will receive follow up (FUP) until disease relapse. Pts in the NAC can be included into the trial following first line treatment with a platinum doublet. They will be randomized between standard of care (SOC) (ARM C) or SABR followed by L19-IL2 and SOC (ARM D) (see Figure 1). Radiotherapy in AC will be performed as SBRT with a total dose of 15 to 60 Gy in 1 to 12 fraction with a minimal dose/fraction of 7Gy while NAC will receive 3x8Gy in 3D-CRT. L19-IL2 will be administered on day 1, 3 and 5 q21-day cycle starting within 72 hours following the SABR. Toxicity will be scored at every administration and on day 7, 14 and 21 of the cycle, according to the CTCAE4.03. Hematology, liver and kidney function will be assessed prior to L19-IL2. The minimum follow-up will be 1.5 years.

Results: The protocol was submitted for the H2020, SC1-PM-09-2016 topic, and was accepted for funding by the European Commission. The consortium involved 17 European centres from Netherlands (coordinator), Denmark, Belgium, Italy, France, Germany and United Kingdome. The work packages (WP) are 6 and we has to conduct the WP3: "to conduct a Phase II trial to assess the clinical efficacy of our bi-modal treatment strategy, i.e. progression free survival (PFS)".

Conclusions: The protocol is closing the grant agreement preparation, before starting to enroll pts.

IMMUNOSABR is complemented by two biomarker works. This work plan will spur further development of L19-IL2 as a commercial drug and translate the treatment strategy towards clinical implementation.

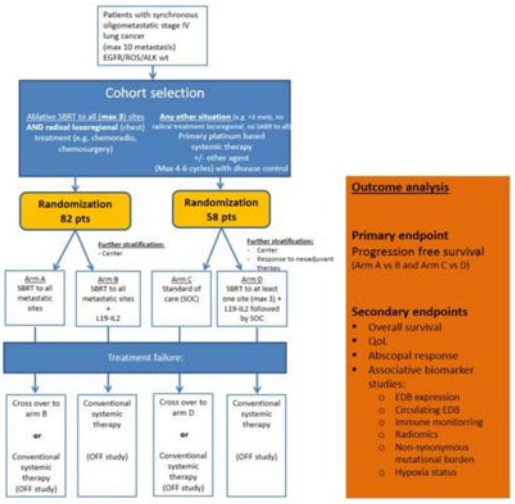

Figure 1. Overview of the IMMUNOSABR trial.

P070

MANAGEMENT OF RADIATION ONCOLOGY PATIENTS WITH A PACEMAKER OR ICD PRELIMINARY EXPERIENCE

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Background: Radiation therapy in elderly patients is more frequent in clinical practice. The number of patients with chronic cardiovascular disease has also increased. Pacemaker and Implantable Cardioverter Defibrillator (ICDs) are called Cardiac Implantable Electronic Devices (CIEDs). Patients with ICDs have a relative contra-indication for radiotherapy because may sustain damage during a course of radiation therapy. The proper functioning of CIEDs devices can be influenced to ionizing radiation or electromagnetic interference produced by modern linear accelerators. Depending on the intrinsic patient's rhythm and pacemaker setting, pacemaker or ICD stimulation may occur occasionally or continuously. ICDs are devices that incorporate pace-maker functionality as well as the ability of producing a high voltage shock to terminate potentially lethal cardiac arrhythmias. For this reason, the need for accurate monitoring and accurate clinical evaluation before and during radiation treatment.

Materials: From January 2016 to May 2017 were treated at Radiotherapy Department of University Hospital of Ferrara, five patients (one female four male age 71-85 mean 78.6) with CIEDs : one patient bilateral breast cancer; one patient with oral cancer; two patients with prostate cancer ; one patients a lung cancer. Two patients were CIED-dependent, the other three non dependent. All patients received cardiological evaluation for the correct functioning of CIEDs before and after the radiation treatment with LINAC and energy photons 6-15 MV.

Results: During radiant treatment the monitoring was performed continuously with a portable electrocardiograph. Two patients pace maker dependent were deactivated with magnet above the CIEDs, to eliminate the risk of interference during radiation delivery. According with guidelines, in all patients device was contouring to evaluate the absorbed daily dose and, so, to assess the category risk : low <2 Gy; Medium 2-10 Gy ; high >10 Gy. Only one patient received more than 2 Gy.

Conclusions: All patients have completed radiation treatment without malfunction of CIEDs. No arrhythmias during the treatment was registered. In our experience the preliminary assessment of the absorbed dose, continuous monitoring during treatment and multidisciplinary collaboration with cardiologists, make it safe radiation treatmente in the setting of patients

P071

PRELIMINARY RESULTS OF STEREOTACTIC BODY RADIOTHERAPY (SBRT) WITH HELICAL TOMOTHERAPY (HT) FOR EARLY STAGE NON SMALL CELL LUNG CANCER (NSCLC) AND LUNG METASTASES

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Aims: To investigate the effectiveness of stereotactic body radiotherapy with Helical TomoTherapy (HT-SBRT) in early stage primary NSCLC or secondary lung cancer.

Methods: Between March 2014 and January 2017, 48 patients (pts), median age 72 years (range 26-91) underwent ablative SBRT performed with HT: 28 pts (58.3%) for primary NSCLC and 20 pts (41.7%) for lung metastasis. In 6 pts, without pathological diagnosis, treatment decision was based on PET/ CT findings. Staging was performed with contrast-enhanced chest CT and positron emission tomography (PET)-CT scans. Pts were immobilized with breast board and an abdominal pressure mould mask. The planning target volume (PTV) included a margin of 10 mm in craniocaudal direction and 5 mm in all other directions around the internal target volume (ITV) defined by the volumetric sum of the clinical target volumes of a free breathing planning CT and pretreatment MVCT scan in treatment

position. Basing on the tumor site, different fractionation schedules were used: 40 Gy, 50 Gy and 60 Gy in 10 fractions for central lesions and 60-70 Gy in 8-10 fractions for peripheral lesions. For 20 pts (41.7%), radiotherapy was delivered on alternate days. Toxicity was weekly evaluated during treatment and at each follow-up visit, according to CTCAE v4.0 criteria. Chest CT and/or PET were used to evaluate response every 3 months for the first year and thereafter every 6 months.

Results: Mean RT treatment time was 15 days (range 10-21), median BED10 was 96 Gy (range 56-119) and median PTV was 20.85 cc (range 5.15-131.03). With a median follow-up of 12 months (range 3-37) only 1 patient showed G2 radiation pneumonitis; 1 patient showed G2 chest pain, 4 pts (8.3%) G1 esophagitis and no ≥G2 esophagitis was registered. During follow-up, 4 pts died: one for renal failure and three for distant recurrence, reporting 1- and 2-yrs Overall Survival rates of 93.3% and 78.1% (94.4% and 75.6% for early NSCLC and 92.3% and 83.9% for metastases). To date, local failure occurred in patients treated with BED < 100 Gy, resulting in 1- and 2-yrs Local Control Rates of 94.5% (96.4% for early NSCLC and 92.9% for lung metastases). Distant progression occurred in 10 pts (20.8%), resulting in cumulative 1- and 2-yrs Progression Free Survival respectively of 79.5% and 62.4%.

Conclusions: Use of HT-SBRT for early NSCLC and lung metastases results in high local control and overall survival rates with minimal toxicities.

P072

STEREOTACTIC BODY RADIOTHERAPY (SBRT) WITH HELICAL TOMOTHERAPY (HT) FOR EARLY STAGE NON SMALL CELL LUNG CANCER (NSCLC): A SINGLE CENTER EXPERIENCE

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Aims: To report midterm clinical outcomes of Stereotactic body radiotherapy (SBRT) with Helical TomoTherapy (HT) for early stage NSCLC.

Methods: Between October 2014 and January 2017, 28 early stage NSCLC patients (pts), median age 72 years (range 58-91 years), underwent 8-10 fractions HT based SBRT. Staging was performed with contrast-enhanced chest CT and positron emission tomography (PET)-CT scans. A confirmed histological diagnosis was obtained for 22 (78.6%) patients: 14 pts (50%) with adenocarcinoma and 8 pts (28.6%) with squamous cell carcinoma. Pts were immobilized with breast board and an abdominal pressure mould mask. Planning target volume (PTV) was generated adding a margin of 10 mm in cranio-caudal direction and 5 mm in all other directions around gross tumor volume (GTV). According to tumor site different dose fractionation schedules were choosen: 50-60 Gy in 10 fractions and 60-70 Gy in 8-10 fractions for central and peripheral lesions respectively. Treatment related toxicity was weekly evaluated during treatment and at each follow-up visit, using CTCAE v4.0 scale. Serial follow up with physical examination and CT or FDG-PET/CT was performed every 3 months for the first year after treatment and thereafter every six months. LC (Local Control) and OS (Overall Survival) at 12 and 24 months from the end of SBRT were calculated using Kaplan Meier analysis.

Results: All pts completed treatment without any interruption. Mean duration of RT was 16 days (range 10-21); median BED10 was 105 Gy (range 75-119) and median PTV was 41.86 cc (range 10.16-131.03). With a median follow up of 12 months (range 4-31), no patient experienced ≥G3 toxicities; only one case (3.6%) of G2 radiation pneumonitis was registered successfully treated with steroids. At 12 and 24 months, actuarial LC rate was 96.4% and OS rates were 96.4% and 75.6%.

Conclusions: 8-10 fractions schedule- HT based SBRT for early NSCLC results in high local control and overall survival without severe toxicities.

P073

LUNG OPTIMIZATION TREATMENT (LOT) IN PATIENTS WITH LUNG LESIONS TREATED WITH SBRT: OUR EXPERIENCE.

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Aims: To evaluate technical features in 13 patients treated with SBRT using LOT tracking system, in our department.

Materials and Methods: In January 2017 a LOT tracking was installed in our Cyberknife system. We reviewed the technical data in a series of 13 patients treated from January 2017 to April 2017.

Results: We reviewed technical data of 9 males and 4 females patients. The median age was 70 (range 48-85 years). Seven patients had lung metastases (colon cancer, breast cancer, and testicular seminoma,kidney cancer). Six patients were affected by primitive lung cancer (3 cases of adenocarcinoma, and 3 cases of squamous carcinoma). The site of tumors was: RSL in four cases, LSL in 5 cases, LIL in 3 cases, right pulmonary ilus in one case. The mean CTV volume was 20.86 cc(2 cc-68.5 cc) Our patients received a mean dose of 34 Gy (range 15 Gy-60 Gy) delivered in 1-5 fractions. We used three options of lung treatment: 0-view in 5 cases, 1-view in 3 cases and 2 view in 5 cases. No evident acute toxicities grade >1 were observed in this group of patients.

Conclusions: Using LOT system it is possible to treat lung lesions without the insertion of gold fiducials.

In this small preliminary series, LOT system confirms the fluency to treat lung lesions.

P074

STEREOTACTIC BODY RADIOTHERAPY APPROACH FOR PRIMARY NSCLC IN MEDICALLY INOPERABLE PATIENTS

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Aims: To evaluate early local tumor control and side effects in medically inoperable patients (mainly due to cardiovascular or respiratory co-morbidity) with Stage I non small lung cancer treated with Stereotactic Body Radio Therapy (SBRT).

Matherials and Methods: 38 patients(pts) with Clinical stages of T1N0M0 or T2(<5 cm) N0M0, not amenable to surgery for comorbidity. 21 pts presented at the beginning of treatment COPD, emphysema, cough and different grade of cardiopathy ; mainly central lesions were positioned near the mediastinum or the bronchus. The median age was 72 years (range:65- 80 years). Treatment plans has been defined using PET-TC aid. Stereotactic three-dimentional treatment was performed using Volumetric modulated arc therapy (Rapidarc) , with one or two non-coplanar partial dynamic arcs. SBRT was delivered with a Trilogy Varian linear accelerator. Prescribed total dose and fractionation, based on tumor size and proximity to organs at risk, was 8Gy in 5 fractions 40 Gy. The calculated biological effective dose (BED) was 88 Gy (alfa/beta=10).

Results: From February 2013 to February 2017, 38 pts (21 ADK, 6 Epidermoid Carcinoma and 11 other histologies) were treated with SBRT. At the time of analysis, 6 months local control was reported in 60.5% (23/38pts).In particular in 10pts(25.6%) occurred regression of disease , in 13pts (33.3%) occurred stability of disease and only in 5pts (12.8%) progression of disease. Ten pts (25.6%) died due to the aggravation of general conditions. During follow-up (median 8.5months; range 3-45 months) pulmonary complications, according to CTCAEV4.0.3, Grade >2 (dyspnoea and pneumonia symptoms) were observed in 9 pts(23.6%). The median Overall Survival(O.S.) was 11.5months; the O.S. at 2 years was 7.9% (3/38pts) and the 6 months Overall Survival was 36%.

Conclusions: These preliminary results highlighted the feasibility and safety of linac-base SBRT for primary inoperable NSCLC in not Performans Status patients. Necessary to confirm the efficacy of this treatment modality is a more accurate selection of patients.

P075

STEREOTACTIC RADIOTHERAPY WITH HELICAL TOMOTHERAPY FOR PULMONARY OLIGOMETASTASES: OUR PRELIMINARY EXPERIENCE

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Aims: To report toxicity and clinical outcomes of Stereotactic Body Radiotherapy (SBRT) with Helical Tomotherapy (HT) for pulmonary metastases (mts)

Methods: Between March 2014 and January 2017, 20 patients (pts) with pulmonary mts were treated with HT-SBRT; primitive tumors were as follows: Non Small Cell Lung Cancer in 9 pts, colorectal cancer in 4 pts, bladder cancer in 3 pts, seminoma, hepatocellular carcinoma, parotid gland cancer and melanoma in remaining 4 pts. Immobilization was performed with the aid of a breast board and an abdominal pressure mould mask. The Gross Tumor Volume (GTV) was defined merging the treatment planning CT with a MegaVoltage CT scan. The planning target volume (PTV) was obtained by adding a 10 mm margin in cranio-caudal direction and a 5 mm margin in all other directions. Treatment schedules differed according to the lesion site: 40-50 Gy in 10 fractions for centrally located disease and 50-60 Gy in 8-10 fractions for peripheral mts. Radiotherapy was daily delivered in 13 pts (65%), and on alternate days for 7 pts (35%). Median BED10 was 75 Gy (range 56-105); median PTV was 17.68 cc (range 6.19-59.85). Toxicity was weekly evaluated during treatment and at each follow-up visit, using CTCAE v4.0 scale. For the first year after treatment, physical examination and chest CT were conducted every 3 months and thereafter every 6 months.

Results: All patients completed RT with no interruptions, with a mean treatment time of 15 days (range 10-20). After a median follow-up of 15 months (range 3–37), we observed no ≥G2 radiation pneumonitis, detecting only G1 in 6 pts (30%). One patient experienced G2 non-cardiac chest pain and one G1 esophagitis. We reported 1- and 2-yrs Local Control Rates of 92.9%. Distant progression occurred in 5 pts (25%), resulting in 1- and 2-yrs Progression Free Survival respectively of 77.9% and 69.3%. During the follow-up period, 2 pts died, one as a consequence of distant progressive disease and one from renal failure, resulting in 1- and 2-yrs Overall Survival Rates respectively of 92.3% and 83.9%.

Conclusions: Our preliminary data support safety and efficacy of 8-10 fractions SBRT with HT for lung metastases, reporting high local control rates with acceptable toxicity, detecting only one G2 adverse event.

P076

USE OF PET-FUSION FOR PLANNING TREATMENT IN NSCLC: EVALUATION OF TARGET VOLUMES AND OAR'S DOSE CONSTRAINTS

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Aims: Target volumes and OAR's dose evaluation by the use of PET-Fusion in treatment planning for NSCLC.

Methods: In our department we usually employ PET-Fusion as gold standard for treatment planning of NSCLC since 2010 (66 patients from January 2010 to April 2017). We have selected randomly 1 patient affected by NSCLC with atelectasis in the adjacent pulmonary parenchyma. For this patient, two 3D conformal treatment plans were made: one with a CT based PTV and one with a PET-CT based PTV, both to deliver 60 Gy in 30 fractions. First of all we analysed GTV and PTV volumes. The prescribed radiation dose for CT vs PET-CT PTV was calculated based on constraints for the lung, the oesophagus, the heart and the spinal cord. We analysed the following constraints: for the lung V20<32% and MLD (Mean Lung Dose) <20 Gy; for the oesophagus V55<28% and Dmean <32 Gy; for the spinal cord Dmax<50 Gy; for the heart V30<46% and Dmean<26 Gy. For the calculation of the Vlung20, we used the volume of both lungs reduced by the PTV, whereas for the mean lung dose (MLD), the volume of both lungs minus the GTV was considered. Plan evaluation was made by TPS Oncentra Exernal Beam v4.5.2.

Results: These are our results for the patient we selected. CT based GTV volume was 78.46 cc vs PET-TC based GTV volume 19.78 cc; CT based PTV volume was 685.14 cc vs PET-TC based PTV volume 108.09 cc. Lung: V20 24.10% vs 12.05% for CT plan and PET-CT plan respectively; MLD 19.4 Gy vs 11.71 Gy for CT plan and PET-CT plan respectively. Oesophagus: V55 0% for both CT plan and PET-CT plan; mean oesophageal dose 12.86 Gy vs 7.55 Gy for CT plan and PET-CT plan respectively.

Spinal cord: Dmax 44.49 Gy vs 32.32 Gy for CT plan and PET-CT plan respectively. Heart: V30 11.48% vs 0.45% for CT plan and PET-CT plan respectively and Dmean 15.13 Gy vs 9.07 Gy for CT plan and PET-CT plan respectively.

Conclusions: We conclude that the use of PET-fusion for planning CT reduces OAR's radiation exposure and, in our selected patient, can decrease the GTV and PTV volumes. The use of this technique could improve the quality of radiotherapy planning, minimize the risk of geographic misses and spare unnecessary toxicity to normal tissues by taking into account the metabolic and biologic features of cancer.

P077

POTENTIAL ROLE OF NIVOLUMAB AS CONSOLIDATION AFTER RADIOTHERAPY IN ADVANCED NON-SMALL CELL–LUNG CANCER (NSCLC): A CASE REPORT

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Aims: Nivolumab is a fully humanized IgG4 mAb that targets PD-1 with an anticancer activity against NSCLC. In advanced metastatic patients the association of Nivolumab with hypofractionated radiotherapy (RT) has allowed promising results in light of the "Abscopal Effect". Sequential consolidation therapy with Nivolumab in poor responders irradiated local advanced NSCLC patients after curative radiotherapy has not yet been investigated. This case report may suggest a research-hypothesis to validate the role of Nivolumab in this set of patients.

Methods: On February 2014 a 80 years smoker old man complained of a Squamous Cell G3 cancer in the right lung PET/CT staged T3 N1 M1pul (2 nodules in the contralateral lung). After 2 cycles of chemotherapy (CDDP and NVB) discontinued for hematological toxicity and 4 cycles with NVB monotherapy the disease down staged to T3 N1 M0. On November 2015, he underwent 3D-Conformal RT (2 Gy/fr /66 Gy) on the residual disease. One month after RT completion he developed an acute radiation pneumonitis. The PET/CT 3 months later showed an active unmodified disease and Nivolumab monotherapy 3 mg/ kg iv every 3 weeks for 8 total cycles was started.

Results: After 4 cycles the disease disappeared on the PET/CT leaving a large empty space in the contest of a chronic lung fibrosis. Pruritus was the main adverse effect. Metabolically and radiological complete remission without symptoms was observed after 8 cycles.

Conclusions: Up to now Nivolumab has been delivered as second-line therapy; this case-report suggests the hypothesis of consolidation with Nivolumab in patients who are poor responders to RT. The mechanism of this association is probably due to a radiation recruitment and activation of inflamed cells as APC, dendrytic , T lymphocytes and endothelium in the irradiated site allowing a favorable microenvironment to inhibit PD-1of irradiated tumor cells.

P078

INTRAOPERATIVE PARTIAL BREAST RE-IRRADIATION IN 114 PATIENTS WITH LOCAL FAILURE AFTER CONSERVATIVE TREATMENT FOR BREAST CANCER: MULTICENTER STUDY OF THE AIRO IORT WORKING GROUP

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Aims: To analyze the clinical outcome after partial breast re-irradiation (re-PBI) with intraoperative radiotherapy with electrons (IORT) for ipsilateral breast tumor recurrence (IBTR).

Methods: Patients (pts) affected by IBTR and treated with salvage BCS and IORT between 1999 and 2015 in 8 Italian centers were entered in a dedicated database. All pts had previously received whole breast radiotherapy. Efficacy of re-PBI was evaluated by means of second IBTR and distant metastases (DM) rates. Tolerability was assessed based on postoperative complications.

Results: The study (promoted by the IORT Working Group of Italian Association of Radiation Oncology (AIRO)) included data of 114 pts. Median age at first BCS was 61.44 years. Median time to the first IBTR was 12.3 years. Site of the first IBTR was the same as the index tumor in 38.6% of pts, while in 52.6% of pts it occurred in other quadrants (missing data in 10 pts). Pts received lumpectomy alone in 57% of cases. Most patients had sentinel node biopsy (axillary dissection only in 1.8% of cases). Most tumors were endocrino-responsive, grade 3 in 23% and Ki-67 ≥ 20% in 50% of cases. All pts received IORT full dose as re-PBI. IORT dose was 18-21 Gy in 83% of cases, median collimator size was 4 cm, median electron energy was 7 MeV. Complications were evaluated in 77 patients: 84% of them had none. In particular, seroma and hematoma were observed in 5% and 4% of cases respectively. Lyponecrosis, edema and infection were experienced in 1% of cases. About 5% of pts complained pain after salvage surgery. With a median time from first IBTR to second oncological event of 55.1 months (range: 0.9-144.6 months), 27.2% pts (31/114) had a second IBTR and 3.5% pts (3/114) had DM. In particular, regarding second IBRT, 12.2% relapsed near the first IBTR site, 9.6% in other quadrants, 3.5% had skin involvement (1.7 pts went missing). Twenty-four pts underwent second salvage surgery (19 mastectomy and 5 quadrantectomy) while the remaining received palliative treatments. At median follow-up of 7.7 years, 5.2% pts died from disease progression, 78.2% pts are alive without disease, while 11.4% pts were alive with disease and 2.6% pts had other primary tumors (2.6 pts were missing).

Conclusions: Re-PBI was safe while local control obtained with IORT was not optimal, but comparable to other series of re-PBI reported in literature, which range between 7% and 32%. An multivariate analysis is ongoing to identify predictive factors.

P079

HALFMOON IMPLANT-SPARING HYPOFRACTIONATED HELICAL TOMOTHERAPY (HT) FOR INTERMEDIATE-RISK BREAST CANCER FEASIBILITY STUDY WITH DOSIMETRY AND TOXICITY DATA

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Aims: To investigate the potential of intensity modulated radiotherapy with helical modality in postmastectomy and breast reconstruction setting. To evaluate particular dose distribution (halfmoon shape) that spares the deepest part of the implant and the consequent cosmetic outcome of such planning.

Methods: Study population consists of breast cancer patients at intermediate-risk, for whom the risk of deep chest wall relapse was considered negligible. Patients that underwent mastectomy and implant breast reconstruction were irradiated from April 2016 to May 2017 using Tomotherapy Hi-Art System (Tomotherapy Inc., Madison, WI) with helical modality. Total dose was 40 Gy in 15 fractions (2.67 Gy each) over 3 weeks. Predefined constraints for implant sparing were set up: D30%< 28 Gy; D50%< 24 Gy; D70%<20 Gy; Dmean < 25 Gy.

Results: At the time of this analysis,12 patients were

enrolled to this feasibility HALFMOON study. Median age was 49 (range 35-68). None but one had concomitant disease (arterial hypertension). Pathological stage was IIA, IIB, IIIA and IV in 6, 3, 2 and 1 patients, respectively. Concerning planning target volume (PTV) coverage for the chest, median value of V95% (PTV receiving 95% of prescribed dose) was 89%, median value of V90% (PTV receiving 90% of prescribed dose) was 96.95 %, median maximum dose 108.1% of the prescribed dose, median mean dose was 99.3%. The median values for implant sparing constraint were as follows: D30% 33.75 Gy; D50% 31.45 Gy; D70% 26.15 Gy; Dmean 30.35 Gy. Acute toxicity, assessed at the end of radiotherapy, consisted of G1 erythema in 11/12 patients. No ≥ G2 toxicities occurred. After median follow-up of 3.5 months, a plastic surgery examination detected changes in breast reconstruction including capsular contracture (CC) according to Baker classification, in 10/12 patients: 5 had Baker 2 CC and 1 Baker 3 CC, 6 had retractions with asymmetry, light radiodystrophy was present in 2 and moderate in 1 case.

Conclusions: In order to ensure optimal chest wall PTV coverage implant sparing constraints were not satisfied. These empirically established constraints are too restrictive and need to be redefined. Acute toxicity was very low. Preliminary data on implant reconstruction changes were promising, but they need to be confirmed with a longer follow-up and larger population size.

P080

EVALUATION OF TARGET COVERAGE IN LUNG STEREOTACTIC RADIOTHERAPY WITH CYBERKNIFE SYSTEM

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Aims: Lung Optimized Treatment (LOT) is an innovative CyberKnife procedure that provides three fiducialless motion management approaches. In 2-view (2V) the tumor is visible in both orthogonal X-ray images and full motion tracking is performed. In 1-view (1V) the tumor is visible in a single X-ray image, therefore motion tracking is combined with an internal target volume (ITV)-based margin expansion. In 0-view (0V) the lesion is not visible, consequently the treatment relies entirely on an ITV-based approach. The aim of the study is the evaluation of target coverage in the above-mentioned modalities.

Methods: We analyzed data of 30 patients treated with LOT from November 2014 to February 2017 at Radiotherapy Division of European Institute of Oncology (Milan, Italy). Only 2V patients were selected since they provide comprehensive information on the three-dimensional tumor motion in correspondence to each X-ray image. Treatments in 1V and 0V modalities were simulated from these data by processing log files and planning volumes. In our Institution, planning target volume (PTV) margins are defined according to the tracking modality: end-exhale clinical target volume (CTV) +3mm in 2V and ITV + 5mm in 0V. In the 1V scenario, the ITV encompasses only tumor motion along the non-visible direction. Then, non-uniform ITV to PTV margins are applied: 3 mm and 5 mm in the visible and non-visible direction, respectively. CTV and PTV positions were derived from treatment log files according to the specific tracking modality. Then, a coverage measure was calculated as the intersection between CTV and PTV volumes in correspondence to each image acquired during irradiation. Similarly to dose-volume histogram, CTV coverage-volume histograms are derived for each patient and treatment modality.

Results: In Figure 1, the coverage-volume histogram curves report the Y% of the CTV that is within the PTV in at least X% of control images acquired during treatment. The coverage of the 95% of the CTV is defined as C95%. The median values of C95% among the patient population are comparable for the three tracking modalities and larger than 98.1%.

Conclusions: PTV margins are adequate to compensate tracking errors and tumor motion in all LOT treatment modalities. Since stereotactic body radiotherapy ensures high dose conformity to target volume, the reported converge measures could be indicative of the dose distribution that would be obtained through the different treatment modalities.

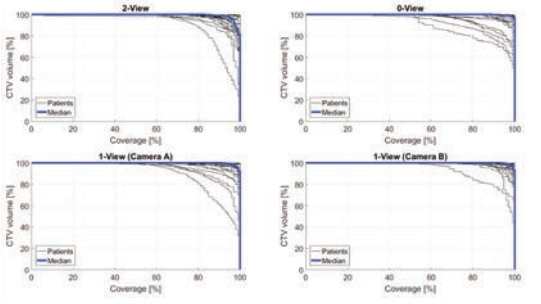

Figure 1: Coverage volume histograms for each LOT modalities. Individual patients are reported as black lines. Patient-wise median histogram are shown in blue. The 1-view tracking modality is evaluated considering the tumor visible in either camera A or B.

P081

WHOLE BREAST IRRADIATION WITH SIMULTANEOUS INTEGRATED BOOST USING AN HYBRID IMRT CLASS SOLUTION (MARA-3 TRIAL): PRELIMINARY TOXICITY RESULTS

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Aims: To evaluate the results in terms of acute (TAC) and late cutaneous (TTC) and subcutaneous (TTSC) toxicity of a clinical study (MARA-3) on whole breast irradiation with simultaneous integrated boost using an hybrid IMRT class solution.

Methods: Patients with low-moderate risk disease, post-menopausal status, no positive nodes nor close resection margins were enrolled in MARA-3 trial and treated with HMRT plans that were inversely optimized by combining two open fields with six-eight subfields in two tangential beams. Open fields were setup to include the whole breast with a 2 cm flash region and to carry the 80% of beams weight. Primary endpoints were TAC, TTC and TTSC scored by RTOG-EORTC scale. Secondary endpoints were local control and overall survival. All patients received 40 Gy (2.5 Gy/fraction) to the whole breast and an additional simultaneous 4 Gy (2.75 Gy/fraction) to the tumour bed over 16 fractions.

Results: 163 patients (median age: 65, range: 52-84; pT1N0: 81.6%, pT2N0: 18.4%) were enrolled and analyzed. 23% of patients underwent previous chemotherapy. The TAC rate was as follows: G1: 37.4%, G2: 12.3%, G3: 0.6%. Mild hematological (leucopoenia) or lung toxicity was registered in 3.7% of patients. 24 months grade 1 TTC and TTSC free survival were 52.7% and 67.3%, respectively, with no higher grade TTC and TTSC observed. Four patients (2.4%) had radiological findings of lung toxicity. With a median follow-up of 17-months (range: 4-116), no patient showed local or nodal recurrence.

Conclusions: An hybrid IMRT class solution produced negligible severe TAC as well as TTC and TTSC with an excellent local-regional control in patients with low-moderate risk invasive breast cancer.

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PRELIMINARY TOXICITY RESULTS OF MARA-4 TRIAL: A WHOLE BREAST IRRADIATION WITH SIMULTANEOUS INTEGRATED BOOST USING AN HYBRID IMRT CLASS SOLUTION

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Aims: To evaluate the results in terms of acute (TAC) and late cutaneous (TTC) and subcutaneous (TTSC) toxicity of a clinical study (MARA-4) on whole breast irradiation with simultaneous integrated boost using an hybrid IMRT class solution.

Methods: Pre- or peri-menopausal patients with negative lymph nodes and with or without close resection margins were enrolled in MARA-4 trial and treated with HMRT plans that were inversely optimized by combining two open fields with six-eights subfields in two tangential beam. Open fields were setup to include the whole breast with a 2 cm flash region and to carry the 80% of beams weight. Primary endpoints were TAC, TTC and TTSC scored by RTOG-EORTC scale. Secondary endpoints were local control and overall survival. All patients received 50 Gy (2 Gy/fraction) to the whole breast and an additional simultaneous 10 Gy (2.4 Gy/fraction) to the tumor bed over 25 fractions.

Results: 139 patients (median age: 50, range: 29-79; pT1N0: 82.1%, pT2 N0: 16.5%, pT3 N0: 0.7%, pT4 N0:0.7%) were enrolled and analyzed. 38% of patients underwent previous chemotherapy. The TAC rate was as follows: G1: 32.4%, G2: 33.1%, G3: 2.9%. Mild hematological toxicity was registered in 2.2% of patients. 24 months grade 1 TTC and TTSC free survival were 47.8% and 68.3%, respectively with no higher grade TTC and TTSC observed. Four patients (2.8%) had radiological findings of lung toxicity. With a median follow-up of 18-months (range: 5-83), no patient showed local or nodal recurrence.

Conclusions: An hybrid IMRT class solution produced negligible severe TAC as well as TTC and TTSC with an excellent local-regional control in patients with low-moderate risk of recurrence invasive breast cancer.

P083

ACUTE AND INTERMEDIATE TOXICITY IN 121 PATIENTS RECEIVING POSTMASTECTOMY LOCOREGIONAL IRRADIATION TO TEMPORARY TISSUE-EXPANDER OR PERMANENT BREAST IMPLANT

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Aims: The aim of the study is to evaluate acute and intermediate toxicity in postmastectomy patients (pts) with implant-based immediate breast reconstruction (IBR) receiving locoregional intensity-modulated radiotherapy (IMRT) with a hypofractionated scheme.

Methods: Consecutive postmastectomy pts with IBR who underwent locoregional Helical Tomotherapy (TomoTherapy® System, Accuray Incorporated, Sunnyvale, CA) between May 2012 and May 2015 with a hypofractionated scheme (2.67Gy/fr, 15 fractions) were evaluated. Acute toxicity was evaluated using RTOG/EORTC criteria, while late toxicity was recorded according to LENT/SOMA scale.

Results: The study included data of 121 patients. Breast reconstruction was performed with temporary tissue expander in 57% of pts (69/121, TE-pts) and with permanent implant in 43% of pts (52/121 PI-pts). All pts completed the treatment course without interruption for toxicity. In the TE group, one pt died for leukemia 20.3 months after radiotherapy and two had distant metastasis. Acute toxicity was assessed in 121 pts (mean follow up: 2.4 months, range: 0-8.1 months). No pts experienced grade >2 toxicities (edema, erythema or desquamation). No significant difference (p=0.06) in acute toxicities were observed between the type of allogenic reconstruction: 43.5% (30/69) of TE-pts and 26.9% (14/52) of PI-pts presented toxicities of grade 2. The most common toxicity was edema, which was of grade 2 in 33.3% (23/69) of the TE-pts and 21.2% (11/52) of PI-pts (p=0.141). Grade 2 acute erythema was observed in 14.5% (10/69) of TE-pts and 7.7% (4/52) of PI-pts (p=0.249). Statistically significant (p=0.04) higher incidence of grade 2 edema was found in patients with high BMI. This was found also in the PI-pts subgroup (p=0.05). Intermediate toxicity was evaluated at a median follow up of 14.2 months (range: 5.8-35.0) on 85 pts (54 expander-patients and 31 prosthesis-patients). No grade ≥2 skin dryness, telangiectasia, ulcer, hypo- and hyper-pigmentation were reported (Table 1).

Conclusions: Acute toxicity of Helical Tomotherapy-based IMRT after IBRT was satisfactory and intermediate toxicity was acceptable. Based on this preliminary analysis, hypofractionation might be considered also in the settings of locoregional treatments, providing advantages for patients' convenience and for fruitful use of resource.

Table 1. Intermediate toxicity evaluated at a median follow up of 14.2 months (range: 5.8-35.0) on 85 patient (54 belonging to the tissue expander subgroup and 31 belonging to the prosthesis subgroup).

	Entire patient cohort	Tissue-expander	Prosthesis	Pearson's chi-squared test
Pain				0.5922
G0	68 (80.0)	45 (83.3)	23 (74.2)	
GI	13 (15.3)	7 (13.0)	6 (19.4)	
GII	4 (4.7)	2 (3.7)	2 (6.5)	
Atrophy				0.6124
G0	68 (80)	44 (81.5)	24 (77.4)	
GI	16 (18.8)	9 (16.7)	7 (22.6)	
GII	1 (1.2)	1 (1.9)	0 (0.0)	
Skin dryness				0.8062
G0	75 (88.2)	48 (88.9)	27 (87.1)	
GI	10 (11.8)	6 (11.1)	4 (12.9)	
Hypopigmentation				0.2383
G0	78 (91.8)	51 (94.45)	27 (37.1)	
GI	7 (8.2)	3 (5.6)	4 (12.9)	
Hyperpigmentation				0.1598
G0	72 (84.7)	48 (88.9)	24 (77.4)	
GI	13 (15.3)	6 (11.1)	7 (22.6)	
Fibrosis*				0.1775
G0	66 (79.5)	45 (86.5)	21 (67.7)	
GI	11 (13.3)	5 (9.6)	6 (19.4)	
GII	4 (4.8)	2 (3.8)	2 (6.5)	
Edema**				0.6903
G0	70 (95.9)	46 (95.8)	24 (96.0)	
GI	1 (1.4)	1 (2.1)	0 (0.0)	
GII	2 (2.7)	1 (2.1)	0 (0.0)	
Arm lymphedema ***				0.7414
G0	65 (82.3)	41 (82.0)	24 (82.8)	
GI	13 (16.5)	8 (16.0)	5 (17.2)	
GII	-	-	-	
GIII	1 (1.3)	1 (2.0)	0	

** The evaluation of fibrosis was performed on 83 patients (52 expander-patients and 31 prosthesis patients). * *The evaluation of edema was performed on 73 patients (48 expander-patients and 25 prosthesis patients). *** The evaluation of the arm lymphedema was performed on 79 patients (50 expander-patients and 29 prosthesis patients).*

P084

FIRST-LINE BEVACIZUMAB IN COMBINATION WITH WEEKLY PACLITAXEL FOR METASTATIC BREAST CANCER: EFFICACY AND SAFETY RESULTS FROM A ROUTINE ONCOLOGY PRACTICE ANALYSIS

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Aims: First-line bevacizumab plus paclitaxel therapy for human epidermal growth receptor factor 2 negative (HER2-) metastatic breast cancer (MBC) demonstrated a median progression-free survival (PFS) of around 11 months in few pivotal randomized phase 3 trials (E2100, TURANDOT, and CALGB 40502). However median overall survival (OS) did not significantly differ

between treatment arms.

Methods: We analysed a series of MBC patients treated between 2008 and 2016 at our Department using bevacizumab plus paclitaxel regimen as first line (bevacizumab 10 mg/kg on days 1,15 q28 plus paclitaxel 90 mg/mq on days 1,8,15 q28). Primary endpoints were efficacy outcomes measured as PFS, overall response rate (ORR), clinical benefit rate (CBR), and OS on the whole series, and on selected subgroup of patients. CBR was defined as the percentage of patients who have achieved complete response, partial response or stable disease >=6 months. Toxicity profile of the treatment was recorded following the NCI CTCAE, version 4.

Results: We overall evaluated a series of 97 patients. The median PFS was 9 months (range 2-68); no significant differences were shown in patients previously treated with taxanes in (neo)adjuvant setting (p=0.42), and endocrine treatment for the MBC (p=0.53). The best ORR was 25% (24/96 cases), and the CBR was 72.9% (70/96 cases). No significant difference emerged in terms of presence of visceral disease (9 vs 19 months; HR 1.1 95%CI 0.67 to 1.9; p=0.63), triple negative (8 vs 13 months; HR 1.5 95%CI 0.74 to 4.67; p=0.19), age (<65 vs >=65 years; p=0.25), and time to failure from adjuvant treatment (<=18 vs >18 months; p=0.12). The median OS was 26 months (range 2-111). Patients showing a PFS longer than 18 months evidenced a significant OS improvement (21 vs 75 months; p<0.0001). Eleven grade 3 AE were reported: hypertension (5.1%), neutropenia (5.1%), and peripheral neuropathy (1%).

Conclusions: In our experience bevacizumab plus paclitaxel regimen as first line chemotherapy for HER2- MBC confirmed the efficacy results of pivotal trials. The regimen is highly effective and overall well-tolerated. Patients with prolonged PFS (>18 months) resulted in a significant better OS. Therefore, there is a strong need for studies aiming to identify predictive factors for response to treatment.

P085

A CRITICAL REVIEW OF THE QUANTEC CONSTRAINT ON HEART DOSE ABSORPTION DURING LEFT SIDED TANGENTIAL BREAST IRRADIATION: FALSE NEGATIVES ON THE LONG TERM CARDIAC EXCESS MORTALITY RISK

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Aims: Careful evaluation of the heart-absorbed dose has to be adopted in any Radiotherapy (RT) Center and although a risk of cardiac death <1% after breast RT is considered acceptable, V(25Gy)<10% is only necessary but not sufficient to limit the excess cardiac mortality risk. For each patient and for every RT schedule of tangential beams left sided breast RT. Aim of this work is to find a group of patient for which the dose constraint, above mentioned, is respected, but at a further investigation the excess cardiac mortality probability results greater than 1%. Than a correlation between these results and the dose volume histogram (DVH) has to be investigated

Methods: Analyzing the DVHs on TPS Philips Pinnacle of 240 women, who underwent to left sided breast tangential beams RT, came out that the constraint V25Gy<10% (percentage of heart volume that receives at least an absorbed dose of 25Gy) was respected. By inspecting the integral DVHs some patients were individuated as "probable false negatives". Were detected those cases where dose constraint was satisfied in a "weak" way: eg 9%≤V25Gy<10% or 8%≤V25Gy<9% and so down to 0%≤V25Gy<1%. The Relative Seriality model (α/β=3Gy, s=1, D50=52.4Gy and g=1.28) has been the method used to evaluate the probability of late cardiac mortality. However, the correction of the dose/fraction to the equivalent 2Gy fraction of the DVHs, which require physical DVH sampling every 0.5Gy and exporting the data to an electronic spreadsheet, has been considered

Results: For 19 patients the V25Gy was satisfied, but the probability of long-term cardiac mortality was found >1% and up to 6%. The dosimetric heart constraints V40Gy showed a good correlation (R=0.97) with the risk of cardiac death. The cut off level was V(40Gy)<1%, with equivalent 2Gy fraction for the dose level. Dose volume constraint V40Gy from the physical DVH is a practical constraint, because it is correlated to V40Gy(EQD) by obtaining similar values of volume within 2%

Conclusions: This probability was only a calculation and not an observation of mortality. Anyway modern TPSs should promote, even more, the use of either radiobiological DVHs or algorithm optimization, especially in the era of hypofractionation. Probably 25Gy is a too low dose level to be correlated with an end-point of a serial organ as the heart seems to be. Also due to the volume variability of heart size, may be more convenient to express the constraints in terms of cm^3 than the percentage of volume.

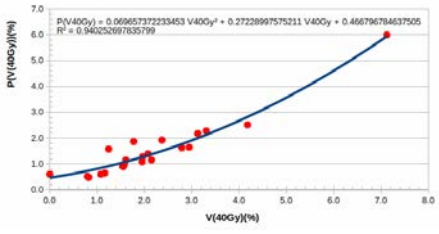

Figure 1.

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RECONSTRUCTION FAILURE RATE IN 100 PATIENTS AFTER POSTMASTECTOMY INTENSITY-MODULATED RADIOTHERAPY DELIVERED WITH A HYPOFRACTIONATED SCHEME TO TEMPORARY TISSUE-EXPANDER OR PERMANENT IMPLANT

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Aims: This study evaluates the reconstruction failures (RF) occurring in postmastectomy patients (pts) who underwent immediate breast reconstruction (IBR) with temporary tissue-expander (TE) or permanent implant (PI) and received locoregional hypofractionated intensity-modulated radiotherapy (IMRT)

Methods: Pts undergoing IBRT with TE (TE-pts) or PI (PI-pts) followed by locoregional irradiation with Helical Tomotherapy (Accuray Incorporated, Sunnyvale, CA) between May 2012 and May 2015 at the Radiotherapy Division of European Institute of Oncology (Milan, Italy) with a hypofractionated scheme (2.67Gy/fraction, 15 fractions) were selected. RF was defined as removal of PI, substitution of the PI with another PI or conversion to autologous tissue breast reconstruction. Follow-up started from the end of PMRT for PI-pts and from the end of two-stage reconstruction for TE-pts, when the TE was replaced with the PI (TE PI)

Results: The study included data of 115 pts: 69 TE-pts and 46 PI-pts. Median age was 46 years (25-73 years); median follow up from primary surgery with IBR was 36 months (10.8-60.1 months). RF was evaluated in 54 TE-pts with a median follow-up of 19.1 months (0.5-45.9 months) because 15 pts have never completed the conventional two-stage reconstruction (TE PI). In particular, 3 pts died before replacement of leukemia or disease progression, 4 pts kept the TE in place for personal reasons, 8 pts removed TE (1 disease progression and 7 pts had autologous reconstruction). Median time from reconstructive surgery to PMRT was 7.2 months (2.2-10.1 months), median time from the end of PMRT to the completion of two-stage reconstruction was 8.4 months (2.2-19.2 months). RF occurred in 11.1% (6/54) of TE-pts who substituted the PI after a median follow-up of 15.7 months (8.8-22.7 months). A further RF occurred in 1.9% (1/54) of TE-pts who substituted PI twice because of capsular contracture. RF occurred in 30.4% (14/46) PI-pts after 16.5 months (4.8-29.2 months). A further RF occurred in 6.5% (3/46) PI-pts (1 PI removal, 1 PI substitution and 1 final autologous breast reconstruction). RF characteristics between TE-pts and PI- pts are shown in Tab1. A statistically significant difference between RF rate in TE and PI groups was observed (chi squared test p=0.0334).

Conclusions: RF rate was significantly higher in the PI-group compared to TE-group. In the TE-group, PMRT with hypofractionation and IMRT seems to be feasible and at low risk of complications.

Tab.1 Reconstruction failure (RF) characteristics.
* One TE-patient substituted PI because of a trauma.

	Tissue expander (TE) reconstruction (pts=54)	Permanent implant (PI) reconstruction (pts=46)
Type of RF		
Loss of PI	0	1 (2.2%)
Substitution of PI	6 (11.1%)	11 (23.9%)
Change to autologous BR	0	2 (4.3%)
Cause of RF		
Capsular Contracture	1 (1.9%)	10 (21.7%)
Breast asymmetry	4 (7.4%)	3 (6.5%)
PI exposure	0	1 (2.2%)
Other*	1 (1.9%)	0
Time of RF		
<12 months	1 (1.9%)	4 (8.7%)
12-24 months	5 (9.6%)	7 (15.2%)
>24 months	0	3 (6.6%)
TOT	**6 (11.1%)**	**14 (30.4%)**

P087

HYPOFRACTIONATED INTENSITY MODULATED RADIOTHERAPY IN 121 PATIENTS WITH IMMEDIATE BREAST RECONSTRUCTION: DOSIMETRIC EVALUATION

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The aim of the study is to assess the dosimetric benefit of intensity-modulated radiotherapy (IMRT) in postmastectomy patients with implant–based immediate breast reconstruction (IBR), candidates to locoregional radiotherapy with hypofractionation.

Methods: Dosimetric data consecutive postmastectomy locoregional patients treated with Helical Tomotherapy (TomoTherapy® System, Accuray

Incorporated, Sunnyvale, CA) between May 2012 and May 2015 with a hypofractionated scheme (2.67Gy/fr, 15 fractions) have been prospectively collected. At the time of surgery, all patients underwent IBR using either temporary tissue expander or permanent prosthesis. The impact of immediate breast reconstruction on the planning was analyzed. Treatment plans were scored in terms of coverage of the planning target volumes (PTVs) (chest wall and supraclavicular region) and sparing of organs at risk (OAR) (heart, lungs and contralateral breast). The coverage of chest wall and supraclavicular region was evaluated according to the amount of volume receiving the 90% of the prescribed dose (V90%) while the sparing of each OAR was evaluated according to the number of satisfied constrains (Tab.1). A plan with optimal coverage of both PTVs had 2 PTV points, while a plan with optimal sparing of all OARs had 4 OARs points. An overall score was assigned to each plan.

Results: The study included data of 121 patients. 71.1% (86/121) of radiotherapy plans had high total scores (total score=6 points) as a result of an optimal coverage of both chest wall and supraclavicular region and optimal sparing of all OARs. The remaining 28.9% (35/121) of plans had a compromised distribution of dose (total score<6 points). In particular, 13.2% (16/121) of plans fully satisfied all the OAR constraint but at a cost of moderate coverage of chest wall (7/121 plans) or supraclavicular region (9/121 plans) target volumes. On the other hand, 13.2% (16/121) of plans fully satisfied coverage of both PTVs compromising the sparing of OARs (heart, ipsilateral lung, or contralateral breast). The residual 2.5% of plans (3/121) had both coverage of PTVs and sparing of OARs compromised.

Conclusion: In patients having implant-based IBR, IMRT allows optimal treatment plans in more than 2/3 of cases. Superior dosimetric results are even more important when hypofractionation is used and they are expected to translate into lower late toxicity and improved aesthetic outcome.

Table 1. Scoring tool was used to assess the quality of planned dose distribution considering both the coverage of PTVs and the sparing of OARs.

			Optimal 1 point	Compromised 0.5 point	Compromised 0 point
PTVs	Chest wall		$V_{90\%} \geq 95\%$	$90\% \leq V_{90\%} < 95\%$	$V_{90\%} < 90\%$
	Supraclavicular region		$V_{90\%} \geq 90\%$	$85\% \leq V_{90\%} < 90\%$	$V_{90\%} < 85\%$
OARs	Ipsilateral Lung	$D_{15\%} \leq 31$ Gy $D_{20\%} \leq 26.4$ Gy $D_{35\%} \leq 17.6$ Gy $D_{50\%} \leq 13$ Gy	All constraints are satisfied	3 out 4 constraints are satisfied	Less than 3 constraints are satisfied
	Contralateral Lung	$D_{20\%} \leq 13$ Gy $D_{35\%} \leq 10.6$ Gy $D_{50\%} \leq 9$ Gy	All constraints are satisfied	2 out 3 constraints are satisfied	Less than 2 constraints are satisfied
	Contralateral Breast	$D_{15\%} \leq 17.6$ Gy $D_{20\%} \leq 9$ Gy $D_{35\%} \leq 6$ Gy $D_{50\%} \leq 4.4$ Gy	All constraints are satisfied	3 out 4 constraints are satisfied	Less than 3 constraints are satisfied
	Heart*	$D_{15\%} \leq 17.6$ Gy $D_{20\%} \leq 13$ Gy	All constraints are satisfied	---	Not all constraints are satisfied
	Heart **	$D_{15\%} \leq 8$ Gy $D_{20\%} \leq 6$ Gy $D_{mean} \leq 5$ Gy	All constraints are satisfied	2 out 3 constraints are satisfied	Less than 2 constraints are satisfied

** Heart constraints refer to the first 22 patients treated between May 2012 and April 2013.*

*** Heart constraints refer to the remaining 99 patients treated from May 2013 to May 2015.*

P088

HYPOFRACTIONATED RADIOTHERAPY FOR DUCTAL CARCINOMA IN SITU (DCIS) USING VMAT: ACUTE SKIN TOXICITY AND COSMESIS

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Aims: Large randomized trials confirmed hypofractionation as a safe and effective adjuvant treatment for patients with early stage breast cancer. Nevertheless, the shorter schedule is not still the standard radiation treatment for ductal carcinoma in situ (DCIS) given the absence of strong prospective data for this specific subset of patients. The aim of this study is the evaluation of acute skin toxicity and cosmesis in DCIS patients enrolled in a phase II trial of hypofractionated breast irradiation.

Methods: Patients treated for DCIS with breast-conserving surgery were eligible for a phase II trial of hypofractionated breast irradiation. All DCIS patients underwent VMAT technique to irradiate the whole breast with a total dose of 40.5 Gy delivered in 15 fractions over 3 weeks, without tumor bed boost. Acute skin toxicities were recorded according to RTOG scoring criteria, and late skin toxicities according to CTCAE v4.0. Cosmetic outcomes were assessed as excellent/good or fair/poor according to the Harvard scale.

Results: From May 2013 to March 2016, 137 DCIS patients were accrued. Median age was 58 year (range 30-86 years). The median follow up was 22 months (range 6-45). Most of the tumors were moderately differentiated (49.6 %) with a no comedo subtype with necrosis DCIS histology (63.5%). Concomitant hormonal therapy was administered in 10.9%. At the end of RT treatment skin toxicity profile was G1 in 56% of the patients, G2 in 15%, no patients presented G3 toxicity. At one year of follow up skin toxicity was G1 in 12% of patients; no G2-G3 toxicity was recorded; cosmetic outcome was good/excellent in 96% of patients. After an early evaluation of clinical outcomes we found 5 (3.6%) cases of in-breast-recurrence.

Conclusions: These results evidence that hypofractionated radiotherapy using VMAT is a safe option for DCIS. A longer follow up is needed to assess clinical outcomes and late toxicity.

P089

INCORPORATING KI-67 INTO A PREDICTIVE MODEL FOR LOCO-REGIONAL CONTROL AND SURVIVAL IN LUMINAL BREAST CANCER PATIENTS SUBMITTED TO CONSERVATIVE SURGERY AND CONVENTIONALLY FRACTIONATED OR HYPO- FRACTIONATED RADIOTHERAPY

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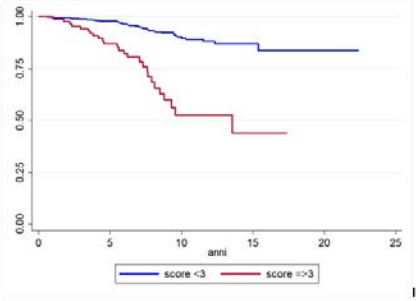
Ki67 index is one of the most important prognostic markers used by oncologists to select the treatment of estrogen receptor (ER) positive breast cancer patients. In this study, we aim to integrate the Ki67 index for stratifying patient prognosis and to create a comprehensive prognostic index for clinical applications. A mono-institutional cohort of 711 human epidermal growth factor receptor 2 negative/ER+ breast cancer patients treated with breast-conserving surgery and adjuvant radiotherapy, having complete clinical, histological, and follow-up data was collected. The 20 % Ki67 cut-off was correlated to disease-free interval (DFI) and disease-specific survival (DSS). To create a comprehensive prognostic index, we used independent variables selected by uni/multivariate analyses. In terms of DFI and DSS, patients with tumor with Ki67 > 20 % showed the poorest prognosis. Moreover, to tumor size, the number of metastatic lymph nodes and Ki67 > 20 % was given a score value, varying depending on definite cut-offs and used to create a prognostic index, which was applied to the population. Patients with a prognostic index ≥3 were characterized by significant risk of relapse [DFI: Hazard Ratio (HR) = 2.53, p < 0.001] and death (DSS: HR = 2.40, p < 0.001). We confirm that the 20 % Ki67 cut-off may be useful to stratify high-risk patients in luminal breast cancers, and we suggest to integrate it with other prognostic factors, to better stratify patients at risk of adverse outcome.



DFI	Score <3	Score ≥3	P Log-rank
5 anni	97.9 %	86.9 %	<0.001
10 anni	89.7 %	52.8%	

Figure 1.

P090

FULL-DOSE BREAST INTROPERATIVE RADIOTHERAPY IN THE ELDERLY: A SINGLE CENTER EXPERIENCE

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Aims: To evaluate the outcomes and toxicity after breast conserving surgery (BCS) and full-dose intraoperative radiotherapy (IORT) in patients with age ≥70 affected by early breast cancer (BC).

Methods: From February 2006 to August 2015, 198 patients aged ≥70 years with diagnosis of early BC underwent BCS and full-dose IORT at Papa Giovanni XXIII Hospital (ASST-PG23) of Bergamo. IORT was performed by a dedicated linear accelerator NOVAC 7 HITESYS (NRT, Italy). The single full-dose of 21 Gy was prescribed at 90% at the tumor bed. We evaluated the following outcomes: in-breast tumor recurrence (IBR), defined as any local relapse (LR) within the treated breast, including both true local (in the same quadrant of the primary tumor) and new ipsilateral recurrence (in quadrants other than that primarily involved); distant metastases (DM), defined as any recurrence at the level of organs or structures different from ispilateral or contralateral breast and overall survival (OS), assessed from the date of surgery until death related to breast tumor and to the last follow-up or time of death respectively. For the survival analysis, the start of observation was considered the date of breast surgery.

Results: Median follow up was 5.2 years (range 0-9 years). Median relapse-free survival, disease-free survival and OS was 1,5 years. We evidenced 15 patients (7,5%) with IBR: 11 patients (73%) with true local relapse, 4 (26%) with new ipsilateral recurrences. Twelve patients (6%) had DM: 6 with nodal recurrences and 6 with bone and visceral metastases. Seventeen patients (8,5%) died: 6 patients (35%) for BC. Most patients had post-surgical oedema as acute toxicity and slight scar fibrosis (G1 according to RTOG) as late toxicity.

Conclusions: The use of postoperative RT in the elderly is a matter of debate, particularly due to problems concerning the distance from RT centers and difficulties, such as comorbidities, to attend a daily treatment. However several studies still evidence that complete omission of RT failed in terms of local tumor control also in an elderly patient population. In this contest full-dose IORT in a well-selected group of elderly patients with early BC, in our preliminary analysis, showed to be a valid alternative to the omission of RT for a good local control.

P091

ADJUVANT LEFT BREAST RADIOTHERAPY FOR BREAST CANCER WITH DEEP INSPIRATION BREATH HOLD TANGENTIAL TECHNIQUE

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Aims: Postoperative radiotherapy is the standard treatment for patients with breast cancer as it is able to reduce the risk of recurrence and to improve survival. Together with the improvement of survival of Breast cancer patients, also long-term side effects of radiation treatment have become relevant. Women with left-sided breast cancer have an incrased risk of cardiac toxicity and there is evidence of a dose–response relationship between risk of cardiac morbidity and radiation dose to cardiac volumes. In this study we evaluated the effectiveness of deep insiration breath hold technique (DIBH) to reduce the radiation dose to the heart compared with free breathing (FB).

Methods: Nine patients with left breast cancer have been treated in the radiation unit of the Parma Hospital, from October 2016 to May 2017, with postoperative radiotherapy through DIBH technique. For each patient two TC were acquired: one in FB and one in DIBH by means of Varian RPM respiratory gating system and audio guide. Treatment plans were generated with 3D conformal technique (tangential fields) and a comparison was made of plans in FB and DIBH considering dosimetric parameters of heart (cardiac mean dose,V5,V20,V30) and left lung (V5,V20). Moreover geometric parameters were analyzed in order to eventually find a correlation with the reduction of cardiac doses, and to identify any potential criteria for selection of patients who can benefit most from this technique.

Results: Plans made with DIBH technique showed a significant reduction of mean heart dose, V5Gy, V20Gy and V30Gy ($p<0.01$). The mean heart doses in the FB and BH plans were 3.2 (Gy) and 1.2 (Gy) respectively with a mean dose of 2.0 (Gy) and a 62.5% reduction. Regarding geometric parameters, breast tangential length and para-sagittal cardiac conctact distance (CCDps) significantly correlate at the 0.05 level with mean heart dose reduction. However, the number of patients included in the study must be increased in order to confirm/reject this findings.

Conclusions: According to results already published in other studies, despite the limited number of patients analyzed, our data show how the use of DIBH technique for left breast cancer treatment can decrease the radiation dose to the heart leading to a benefit in the prevention of cardiac morbidity. Moreover this treatment, after proper selection and patient training, was performed safely and regularly.

P092

EARLY CHRONIC TOXICITY OF HYPOFRACTIONATED RADIATION THERAPY FOR 188 EARLY STAGE BREAST CANCER PATIENTS USING TOMOTHERAPY

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Aims: To assess side effects of a hypofractionated scheme including simultaneously integrated boost (SIB) using Tomotherapy (Accuray Inc., Sunnyvale, CA) in Direct modality

Materials and Methods: Patients with invasive breast cancer who underwent breast-conserving surgery treated with hypofractionated scheme using TomoTherapy with Direct modality were evaluated. Whole breast (WB) and boost (BOOST) were irradiated simultaneously to a dose of 45 Gy and 50 Gy respectively in 20 fractions over four weeks. Late toxicity was evaluated according to LENT/SOMA scale. Cosmetic outcome was evaluated using a four-point scale according to Harvard criteria, from the point of view of both patients and physicians.

Table 1. Evaluation of late skin toxicity according to LENT/SOMA scale and cosmetic outcome according to Harvard criteria on 188 patients with a median follow-up of 24 months.

LENT-SOMA	G0	G1	G2	G3
Pain	78.2%	19.1%	2.7%	-
Edema	81.9%	16.0%	2.1%	-
Fibrosis	83.0%	16.5%	0.5%	-
Telangiectasia	98.4%	0.5%	0.5%	0.5%
Lymphedema arm	97.9%	2.1%	-	-
Retraction*	53.2%	33.5%	12.2%	1%
Atrophy	95.7%	3.7%	0.5%	-
Ulcer	100%	-	-	-
Radiological fat necrosis	*YES* 8.5%			
COSMESIS**	***Excellent***	***Good***	***Fair***	***Bad***
Patient's view	36.2%	42.0%	12.2%	3.2%
Physician's view	36.7%	47.3%	9.6%	0.5%

*Retraction evaluation was available for 186 patients. **Cosmesis was evaluated in 176 and 177 by patients and physicians respectively.

Results: One hundred and eighty-eight pts were enrolled. Planning target volume (PTV) coverage and healthy tissues sparing were satisfactory. Median value of V95% (volume of PTV receiving 95% of prescribed dose) was 100% and 99% for PTV of WB and PTV of BOOST, respectively. Median maximum dose to PTV of WB and PTV of BOOST were 113% and 103% of the prescribed dose, respectively. Table 1 shows the percentage of patients with side effects of irradiation of the skin and subcutaneous tissue with a median follow up of 24 months. Neither grade 4 skin ulceration nor soft tissue necrosis was observed. Grade 3 toxicity concerned 1 patient who presented with telangiectasie on the tumor bed. Cosmetic outcome was also recorded.

Conclusions: Toxicity of grade 2 or higher was mild and acceptable. The complained breast retraction was mainly due to surgery. Cosmesis was judged as excellent/good in the majority of patients. Longer follow-up is needed to look at the late-onset breast changes.

P093

PATTERNS OF FAILURE ACCORDING TO MOLECULAR SUBTYPE IN PATIENTS WITH INVASIVE BREAST CANCER TREATED WITH ADJUVANT RADIOTHERAPY AND MODERN SYSTEMIC THERAPY

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Aims: To estimate the impact of molecular subtype on locoregional failure in patients treated with adjuvant radiotherapy and modern systemic therapy.

Methods: we analyzed data of patients with invasive breast cancer treated with adjuvant radiotherapy at our institution from 2005 to 2016. Molecular subtypes were defined as luminal A (LA), luminal B (LB), luminal Her 2, Her 2 and triple negative (TN) based on the 2015 St. Gallen

Consensus Criteria. Survival estimates were calculated according to the Kaplan-Meier method at the end of the follow-up. Differences between groups were evaluated by the log-rank test. Cox proportional regression analysis

Results: 870 patients were evaluated. Molecular subtypes were distributed as follows: 58.5% LA, 21.2% LB, 8.4% luminal Her-2, 3.7% Her- 2, 8.2% TN. 747 patients (85.9%) patients underwent endocrine therapy, 376 patients (43.2%) received adjuvant chemotherapy (antracyclines 70.5% and taxanes 51.3%). Seventy-one patients (8.1%) received trastuzumab immunotherapy . Sixteen (1.8%) loco-regional relapse occurred, 12 (75%) in breast/chest wall area, 2 (12.5%) in the nodal areas, 1 in both chest wall and nodal areas (6.25%). Median follow-up was 4.8 years (range 1-12 yrs). The 10-year local recurrence free survival rate of LA, LB, luminal Her2, Her2 and TN groups were 98.5, 97.1, 96.6, 86.5, 93,3% respectively (p=<0.001). On univariate analysis age < 50 (p=0.03), N+ (p=0.04), high histologic grade (p=0.04) were correlated with local recurrence. At multivariate analysis only high histologic grade (p=0.06) and molecular subtypes (p=0.02) were predictive of local recurrences. The 10-year metastases free survival rate of LA, LB, luminal Her2, Her2 and TN groups were 90.7, 82.4, 91.2, 90.5, 85.4% respectively (p=0.02).

Conclusions: Molecular profile has a significant impact on local and distant failure in patients with invasive breast cancer treated with radiotherapy. Therefore, it should be integrated in adjuvant treatment decisions.

P094

ONLY FOUR FRACTIONS TO DELIVER PARTIAL BREAST IRRADIATION. PRELIMINARY RESULTS OF A PROSPECTIVE PHASE-2 TRIAL

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Aims: A prospective phase II trial was conducted to investigate the feasibility of a novel fractionation scheme to deliver Partial Breast Irradiation (PBI) consisting of 28 Gy in 4 daily fractions (7 Gy/fraction). We report preliminary results of toxicity and clinical outcome.

Methods: The study enrolled patients ≥60 years old and affected by early-stage invasive breast carcinoma (pT1-2, pN0-1a, M0) treated with breast conservative surgery. Treatment volumes and radiation therapy planning were based on NSABP B-39/RTOG 0413 guidelines. The prescribed dose consisted of 28 Gy delivered in 4 daily fractions, 7 Gy/fraction. PBI was delivered with 3-Dimensional External Beam Radiotherapy (3D-EBRT) using non-coplanar fields. Regular follow-up was performed by radiation oncologists, and toxicity was scored with the Common Terminology Criteria version 4.0 scale. Local control (LC), disease-free survival (DFS) and overall survival (OS) were estimated by Kaplan-Meyer method.

Results: 36 patients were enrolled and the median follow-up was 19 months (range:1-34 months). Acute toxicity was very limited: only 1 (3%) patient experienced Grade 1 skin erythema and subcutaneous edema. Late toxicity occurred in 5 (14%) patients. The registered events were Grade-2 dermatitis (3%), Grade-1 and Grade-2 fibrosis (6% and 8%, respectively). One case of subcutaneous fibrosis required surgical biopsy to exclude breast recurrence. No cases of pain or Grade≥3 toxicity were recognized. No patients relapsed locally. One patient developed brain metastases 2 months after PBI and died. The 2-year estimated LC, DFS and OS

were 100%, 97% and 97%, respectively.

Conclusions: PBI delivered in only 4 fractions (7Gy/fraction) showed an excellent acute tolerance. Preliminary results of late-toxicity and clinical outcome demonstrated no excess of side effects or disease recurrence.

P095

ACUTE HAEMATOLOGICAL TOXICITY IN BREAST CANCER PATIENTS TREATED WITH 3D STANDARD OR ACCELERATED INTENSITY-MODULATED POSTOPERATIVE RADIOTHERAPY

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Aims: To evaluate haematological toxicity in two cohorts of breast cancer patients (pts) treated with standard 3D postoperative radiotherapy (control group: CG) or accelerated intensity-modulated postoperative radiotherapy (clinical trial MARA-1).

Methods: Prescribed dose to the breast was 50.4 Gy with sequential 10 Gy electron boost on tumor bed in the CG (n= 130) and 40 Gy with concomitant 4 Gy boost in MARA-1 (n=317). Overall treatment time was of 32 daily fractions for CG and 16 fractions for MARA-1. In CG cohort 85/130 pts (65%) had received adjuvant chemotherapy before radiotherapy, compared to 104/317 (33%) pts in MARA-1 cohort. Complete blood count was performed weekly.

Results: Haematological toxicity was observed in 49/130 (37.7%) pts in CG and in 75/317 (23.7%) pts in MARA-1, respectively (p: 0.0026). As expected, myelotoxicity was more frequent (p: 0.00001) in pts pretreated with chemotherapy (73/189: 38.6%) compared to pts not receiving chemotherapy (51/258: 19.8%). However, haematological toxicity was clinically irrelevant. No myelotoxicity grade > 3 was observed. Grade 2 or 3 toxicity was observed only in 4.6% pts in CG (6/130: 4 leukopenia grade 2, one anemia grade 2, one neutropenia grade 3) vs none in MARA-1. Five out of these 6 pts had received chemotherapy. Anemia or neutropenia grade 2 or 3 occurred in less than 2% of CG pts (2/130). No thrombocytopenia grade > 1 was recorded.

Conclusions: Haematological toxicity in breast cancer pts treated with postoperative radiotherapy (3D standard tecnique or accelerated IMRT) depends on radiotherapy protocol and previous adjuvant chemotherapy treatment. However, myelotoxicity induced by radiotherapy in these pts is mild and does not require regular monitoring during treatment.

P096

RISK ADAPTIVE DOSE PRESCRIPTION FOR SABR IN CENTRALLY LOCATED LUNG LESION: "HOW TO FLY IN NO-FLY ZONE"

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Aims: Stereotactic ablative radiotherapy (SABR) in the treatment of primary early stage non-small cell lung cancer (NSCLC) and lung metastases is considered an emerging therapeutic approach. To date, several clinical data on SABR efficacy derived from treating small, peripherally lung tumors. More recently, initial experiences are evaluating SABR in centrally located lung tumors, using a "risk adapted" dose prescription, in order to reduce the development of 3-5 toxicity. Aim of this preliminary study is to evaluate efficacy and tolerability of SABR in patients with primary or metastatic central lung lesion.

Methods: From January 2012 to September 2016, 45 patients (26 male and 19 female) with 50 centrally located primary NSCLC or oligometastatic patients(defined as patients with ≤5 metastatic sites) received SABR. Median age was 72 year (range 39-83 years). Thirty patients had a diagnosis of NSCLC, while 15 patients were defined as oligometastatic with different histologies. Median internal target volume (obtained by boolean envelope of the gross tumor volume on 4-CT scan) and planning target volume were 6.9 cm3 and 22 cm3, respectively. Median total dose prescription was 60 Gy(range 48-70 Gy), fractionation schedules were included between 4 and 10 fractions and median Biological Equivalent Dose was 105 Gy10 (range 75-119 Gy10). Radiological lung toxicity was reported, while acute and late clinical toxicity were recorded using CTCAE v4.0 scoring system.

Results: Median follow-up was 12 months(range 1-57 months). At 6 months local control was observed in 42 lesions (84%), while distant progression was reported in 31 patients (68%). Analysing clinical acute toxicity, 48 patients reported a grade 0, while no grade 3 were found. For late clinical toxicity only 1 patient had a grade 2 (i.e. cough). At 6 months, radiological lung toxicity was: no radiological changes in 7 patients, mass-like pattern in 9 patients and modified conventio-

nal pattern in 18 patients. In 3 cases, we did not record radiological toxicity at 6 months because patients dead after extra-thoracic progression.

Conclusions: SABR seems to be a safe and effective treatment in central lung lesions. In several cases radiological lung toxicity was not correlated to severe symptoms. These preliminary results justified the benefit of "risk adaptive" dose prescription. A longer follow-up is necessary to confirm the efficacy and tolerability of SABR in the treatment of central lung lesions.

P097

A PRELIMINARY DOSIMETRIC STUDY TO VALIDATE MULTI-SEGMENT PLAN (FIELD IN FIELD) FOR BREAST IRRADIATION USING *IN VIVO* DOSIMETRY (IVD)

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Aims: IVD represents an independent check of the dose able to highlight the reproducibility of the treatment over time and able to help avoidingsystematic errors during dose delivery. Moreover, IVD may be useful to validatea new technique. The aim of this study is to evaluate the accuracyand reproducibility of dose distributions of breast treatments using fie in-field (FIF) technique (TPS Eclipse-Varian) with SOFTDISO (Best MedicalItaly Srl). The FIF technique is a forward planning approach that uses multileafcollimator sub-fields to improve dose uniformity throughout the wholebreast volume.

Method and materials: We acquired the portal image during each session for all beams of seven breast FIF treatment planned. The treatments were delivered with 6MV photon beam by a Varian Clinac 2100 C/D. CT images, RT plan and portal images of patientswere imported in SOFTDISO. SOFTDISO is provided with an analysis module dedicated to the reconstruction of the dose at the point isocenter from the portal images signal. The value of the transit signal is converted to a dose value, Diso, and compared with the value of calculated dose, Diso,TPS. The comparison is performed through the index R = Diso/Diso,TPS. The acceptance criterion was: $0.95 \leq R \leq 1.05$. The daily EPID images were compared to a reference image obtained in the first session of therapy. A further module is dedicated to the gammaanalysis between the reference and daily portal image.

Results: The comparisons showed good Results: The R values for 5 treatments were within 1.5%. In two treatments were within 4%. In particular the R average for all sessions valued was 1.016 } 0.021. The gammaanalysis, performed with 3 mm/5% criteria, yielded $Pg < 1 \geq 93\%$ in 80% of the tests, 20% of the tests supplied $88\% \leq Pg < 1 < 93\%$ due to small setup variations. Conclusions: The IVD assures that the FIF treatment has a good reproducibility during treatment sessions and can replace the standard breast treatment with dynamic wedges.

P098

A RETROSPECTIVE STUDY ABOUT AGE AND SKIN TOXICITY IN BREAST RADIATION THERAPY

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Aims: Radiodermatitis are one of the most important kind of toxicity in breast cancer radiation treatment. Our aim was to determinate an eventual correlation between age and the incidence of radiodermatitis in woman affected by breast cancer who underwent radiotherapic treatment.

Methods : We conducted a retrospective study of the clinical data of 248 patients affected by breast cancer who were treated at our structure from 2009 until 2016; all the patients did an adiuvant radiotherapic treatment with a dose of 60 Gy. We divided the population in two groups according to the patients' age, using the age of 60 years old as discriminating factor for the assignment to each group. We evaluated the skin toxicity using the CTCAE v4.0 rating scale.

Results: The patients group under 60 years old was formed by 127 women while the over 60 years old one by 113. Regarding skin toxicity there were 96 G1 lesions, 37 G2 ones and 7 G3 ones. Using the odd ratio test we saw that the risk for women over 60 years old is only slightly higher than the women in the other group (O.R.= 1,15 C.I. 95%=0.71-1.88).

Conclusions: with aging, the epidermis thins, connective tissue turns by reducing the skin's strength and elasticity and the dermal blood vessels become more fragile. Probably the skin changings due the age can slightly influence the cutaneous repairs systems and make them more prone to this kind of inflammation.

P099

WHOLE BREAST HYBRID-IMRT (HMRT) IRRADIATION WITH SIMULTANEOUS INTEGRATED BOOST TO TUMOUR BED: CLINICAL INTRODUCTION OF AN OPTIMAL CLASS SOLUTION

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Aims: To develop a robust semiautomatic treatment planning approach for whole breast irradiation with simultaneous integrated boost using an hybrid IMRT class solution.

Methods: Twenty-five consecutive patients with left breast cancer were included in the study. All patients received 50Gy (2 Gy/fraction) to the whole breast (PTVbr) and an additional simultaneous 10 Gy (2.4 Gy/fraction) to the tumour cavity (PTVcav) over 25 fractions. Ipsilateral lung, heart and contralateral breast were contoured as organs-at-risk. Healthy tissue was defined as whole body minus PTVbr. Only left sided patients were included in order to evaluate also the heart irradiation. All patients were simulated and treated using the Active Breath Coordinator (Elekta), a spirometer enabling a temporary controlled interruption of patient breathing at the end of inspiration phase. HMRT plans were inversely optimized by combining two open fields with six-eights subfields in two tangential beam. Open fields were setup to include the whole breast with a 2 cm flash region and to carry the 80% of beams weight. HMRT plans were compared with conventional wedged-field tangential plans (WF), field-in-field forward planned tangential plans (FiF) and volumetric modulated arc therapy (VMAT) plans. Dosimetric differences among the plans were evaluated using a Kruskal-Wallis one-way analysis of variance. The Bonferroni correction was applied for pairwise comparisons; an adjusted value of $p<0.0083$ was considered as statistically significant.

Results: No significant differences were found among the four techniques for PTVbr an PTVcav coverage in terms of mean dose, minimal dose (D98%), target coverage (D95% and V95%). The HMRT technique showed statistically significant reduction of healthy tissue irradiation with respect to WF and FiF techniques: V55: 89cc vs 155cc and 143cc; V60: 18cc vs 40cc and 34cc. VMAT supplied the best conformity dose distribution for both PTVs but the worst results for contralateral breast irradiation, ipsilateral lung and heart in the low dose region (V5Gy). With respect to other three techniques, HMRT reported the minimal time for planning optimization and the minimal monitor unit delivery.

Conclusions: HMRT plans resulted in superior target dose conformity and homogeneity with respect to WF and FiF techniques. In addition, due to fast planning time HMRT can be applied for all patients, minimizing the impact on human or departmental resources.

P100

LONG-TERM RECONSTRUCTION FAILURE IN 138 PATIENTS RECEIVING POSTMASTECTOMY RADIATION THERAPY WITH A TEMPORARY EXPANDER OR PERMANENT IMPLANT IN PLACE

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Aims: Immediate breast reconstruction (IBR) is becoming an integral part of breast cancer treatment. Due to increasing indications for post-mastectomy radiotherapy (PMRT), a growing number of patients (pts) receiving PMRT with an implant in place is anticipated. PMRT is well known for having a negative impact on IBR, but recently several papers seem to invalidate these data. The aim of this study is the evaluation of reconstruction failure (RF) in a series of pts receiving PMRT with a temporary expander (TE) or a permanent implant (PI) in place

Methods: Pts undergoing mastectomy and immediate TE/PI reconstruction followed by PMRT between June 1997 and December 2011 were retrospectively evaluated. RF was defined as replacement/loss of implant or conversion to flap. Pts with PI reconstruction were followed-up from the end of PMRT, while who received two-stage TE reconstruction was followed-up from the subsequent replacement of the TE with a PI. All the pts received high-energy (6-18 MV) external beam PMRT with tangential beams to the reconstructed chest wall +/- regional nodes. Standard dose was 45-50.4 Gy in 25-28 fractions

Results: Seventy-two and 76 pts underwent IBRT with TE and PI, respectively. Median age was 46 years; median follow up from surgery was 93 months. RF was evaluated in all the pts with PI except one who removed her implant during PMRT with a median follow up of 103 months (range 6-233) and in 63 TE-pts with a median follow-up of 68 months (range 5-183) since 9 pts never replaced the TE with a PI. Median time from surgery to PMRT was 5 months (range 2-10) and 5 months (range 1-17) in the TE- and PI-group, respectively. Median time from the end of PMRT to the subsequent replacement of the TE with a PI was 8 months (range 2-34). RF occurred in 23/63 (36.5%) TE-pts

after a median time of 24 months (range 1-109) and 45/75 (60%) PI-pts after a median time of 19 months (range 3-146). Details about RF are shown in Tab.1. A statistically significant difference between RF rate in TE and PI groups was observed (chi squared test p=0.0062). Among pts with a replacement of the PI, 6/55 (10.9%) underwent a further surgery with a definitive removal of the PI. Totally 19/138 (13.8%) pts did not keep the PI in place at the last follow up.

Conclusions: In the long run, PMRT after IBR provides an acceptable risk of RF, with better results for TE-group compared to PI-group. A salvage breast reconstruction was possible in most of the pts who had a second RF.

Tab.1 Reconstruction failure (RF) characteristics. Capsular Contracture (CC) was evaluated according to Baker scale.

Type of RF	Tissue expander (TE) reconstruction (pts=63)		Permanent implant (PI) Reconstruction (pts=75)	
	N (%)	Causes	N (%)	Causes
Loss of implant	0		4 (5.3%)	3 baker IV 1 necrosis
Replacement of implant	19 (30.2%)	5 CC Baker IV 3 asymmetry 3 PI rupture 2 CC Baker III 2 PI extrusion 1 surgical diastasis 1 pain 1 radio-dystrophy 1 patient desire	36 (48%)	19 CC Baker IV 13 CC Baker III 4 asymmetry
Conversion to flap	4 (6.3%)	2 infection 1 surgical diastasis 1 PI extrusion	5 (6.7%)	4 CC Baker IV 1 CC Baker IV + PI rupture
	23 (36.5%)		45 (60%)	

P101

FOUR-DIMENSIONAL COMPUTED TOMOGRAPHY IN ACCELERATED PARTIAL BREAST IRRADIATION PLANNING

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Aims: The aim of our study was to evaluate the usefulness of the four-dimensional computed tomography (4DCT) in accelerated partial breast irradiation (APBI) planning.

Methods: At our Institute, we have been treating the index quadrant with external intensity-modulated radiation therapy in a phase III trial. For this study, we selected a sample of 25 patients with left-sided breast cancer and surgical clips at the excision site. Contouring of the target was performed both using three-dimensional computed tomography (3DCT) and 4DCT imaging. On both 3DCT and 4DCT, we recorded the clinical target volume (CTV) and the planning target volume (PTV) and the coordinates of the PTV centroid. We calculated the treatment plans, according to our protocol, using the contours drawn on the 3DCT and 4DCT and evaluated target coverage and sparing of organs at risk (OAR).

Results: Median age of the patients was 63.5 years (range 52-75). The comparison between the 3DCT and 4DCT PTV volumes was not statistically significant (p=0.79). Concerning centroid coordinates, the average absolute differences were 0.1 mm in the latero-lateral, 0.7 mm in the antero-posterior and 0.3 mm in the supero-inferior direction. No statistically significant differences were observed both in PTV coverage and OAR sparing; the 4D PTV contour is adequately covered when the plan based on the 3D contours is used. Target coverage was reduced on average by 1% and no statistically significant difference was observed (p=0.93).

Conclusions: In our experience, no significant differences between PTV volumes, PTV coverage, OAR sparing and centroid position are evidenced when comparing 3DCT and 4DCT plans. Conventional 3DCT-based planning is adequate for APBI.

P102

FIELD-IN-FIELD VERSUS 3D-DYNAMIC WEDGE TECHNIQUES FOR PATIENTS WITH BREAST CANCER: A PRELIMINARY STUDY

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Aims: The aim of the study was to compare the field-in-field (FIF) and the 3D-CRT with dynamic wedge (DW) techniques for breast radiotherapy in terms of dose distribution and reproducibility.

Materials and Methods: Twenty-eight patients with breast cancer from Macerata and Rieti Hospitals were studied (PTV range: 198–2407 cc). For each patient, two plans with opposed tangential fields were prepared: tangential plan with DW and tangential plan with FIF (Eclipse, Varian). Two endpoints were analysed. The first endpoint was a dosimetric comparison between FIF technique with 6MV and 3D technique with DW(mixed energies). The second endpoint was to verify the reproducibility of plans for both techniques: all patients repeated CT scan twice during the radiation treatment. The original plan was recalculated on repeated scans registered with first simulation CT, keeping the same MUs. V95% (% PTV volume receiving 95% of prescription dose), D95% (dose in Gy covering 95% of PTV volume), Dmean, homogeneity index (HI) and conformity index (CI) were used for comparison. The statistic analysis was performed with Wilcoxon test.

Results: Regarding the comparison between FIF and DW, V95%, D95%, and Dmean were higher for FIF technique than DW; HI was lower in FIF technique, indicating a more homogeneous dose distribution within PTV; CI value was between 1 and 2 in both techniques, indicating a good adaptation of the reference isodose to the PTV. Plans calculated on the repeated CTs showed smaller differences with the original plan when using FIF technique. Comparison was made in terms of V95%, D95%, Dmean, HI and CI.

Conclusions: In our preliminary study, FIF technique results in better dose distribution in terms of homogeneity. FIF and DW techniques have the same reproducibility. Further investigations involving an increased number of patients should be performed to determine the impact of FIF technique also on organ at risk toxicities.

P103

PREDICTIVE FACTORS OF EXTENDED NODAL DISEASE IN PATIENTS WITH INVASIVE BREAST CANCER AND SENTINEL LYMPH NODE MACROMETASTASES

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Aims: Data from randomized study trials showed that axillary lymph node dissection (ALND) can be omitted when the sentinel Lymph node biopsy (SLNB) is negative, or involvement is limited to 1 or 2 metastases, given the low risk of axillary relapse. Aim of this study is to identify predictive factors of extended nodal disease (> 3 positive nodes) in breast cancer patients with positive sentinel macrometastases.

Methods: From an institutional database, patients with invasive breast cancer who performed sentinel lymph node biopsy were identified and patients with positive sentinel node biopsy undergoing axillary lymphadenectomy were selected. 2015 St. Gallen consensus criteria were used to define the molecular subtypes (Luminal A, Luminal B, luminal Her2, Her 2, Triple negative). Logistic regression analysis was used to evaluate the impact of molecular status, histopatologic features and patients' age on number of positive nodes at lymphadenectomy.

Results: 578 patients with invasive breast cancer who performed sentinel lymph node biopsy were identified. 120 patients had positive sentinel lymph node and underwent axillary lymphadenectomy (average number of lymph nodes removed:17, range 4-37; average number of positive lymph nodes: 4,32; range 1-23). Only molecular subtypes resulted significantly correlated with a number > 3 of positive nodes (p=0.018; OR=4.181).

Conclusions: Molecular subtype is a predictive factor for extended nodal disease and therefore should be taken into account for regional nodal irradiation indications in cases of SLNB positive disease when ALND has not been performed.

P104

MANUAL CONTOURING OF THE 15 CARDIAC STRUCTURES ACCORDING TO THE ESTRO ATLAS 2017, WAITING FOR EFFECTIVE TOOLS OF AUTOCONTOURING

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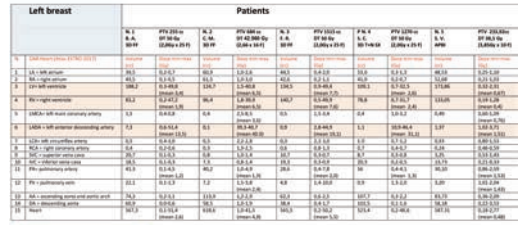
Aims: Verifying the introduction of the manual contouring, in the clinical practice, of the 15 cardiac structures according to the ESTRO 2017 atlas[1]: contouring timing and the observation of OAR's volumes and doses.

Methods: In the first quarter of 2017, after ESTRO atlas publishing, Radiotherapy UOC of San Giovanni Addolorata Hospital started a feasibility study related to the introduction of the 15 cardiac structures contouring. For each patient with breast cancer, medium contouring timing was estimated, volume (cc) of every structure and the irradiation dose (Gy) received, according to the irradiation technique, were measured. 7 patients were contoured, 2 of them with right breast cancer and 5 with left breast cancer. The 2 patients with right breast cancer were treated by APBI technique of IIQ and one with field in field tangential technique. One of the 5 patients with left breast cancer was treated with APBI, the other four were treated with 3D field in field with wedges and mixed energy tecniques. In one case only, even the supraclavicular lymph nodes were treated.

Table 1.



7	LCX= left circumflex artery	1,6	0-0,2	0,58	0,29-0,55
8	RCA = right coronary artery	0,4	0,9-2,9	1,04	0,34-0,76
9	SVC = superior vena cava	6,7	0,6-1,9	12,99	0,23-2,82
10	IVC = inferior vena cava	6,0	0,3-0,8	8,96	0,27-1,60
11	PA= pulmonary artery	28,5	0,1-0,6	58,79	0,23-3,35
12	PV = pulmonary vein	9,1	0,1-1,4	4,74	0,74-1,54
13	AA = ascending aorta and aortic arch	81,1	0-2,6	160,79	0,12-3,05
14	DA = descending aorta	42,8	0-0,2	92,69	0,14-2,62
15	Heart	452,8	0-3,3	629,81	0,10-4,51

Results: The timing needed in the learning phase of the contouring at the beginning was estimated to be about 60-70 minutes, but it was reduced to 45 minutes due to an increasing experience. The volumes of each contoured structure as a range and the dose contribution of every structure are shown in the Table 1.

Conclusions: The experience developed in order to

contour the 15 cardiac structures lead us to search automatic contouring tools to shorten the time needed, currently more suitable for study purpose than for clinical practice. Preliminar data about volumes and doses related to the structures need a reflection in order to develope accurate dose limits, reliable to an increasing of toxicity risk.

Reference

1 Rongrong Zhou et al. Cardiac atlas development and validation for automatic segmentation of cardiac substructures. Radiotherapy and Oncology 122 (2017) 66–71

P105

HYPOFRACTIONATED RADIATION THERAPY IN BREAST CANCER: RETROSPECTIVE ANALYSIS OF OUTCOME AND TOXICITY

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Aims: To report outcome and toxicity in early breast cancer patients treated with conservative surgery and whole breast hypofractionated radiotherapy (HRT) without boost on tumor bed

Methods: We included in this analysis pts treated with breast conserving surgery and HRT with a follow-up of at least 4 years. From May 2007 to May 2012 170 pts with early breast cancer (TNM stage pT1-T2 pN0-N1 up to 3 positive lymph nodes) underwent to adjuvant 3DCRT HRT. 32 pts underwent anthracycline-taxane based chemotherapy before HRT. 145 pts received only hormone therapy and 10 pts received only HRT without no other adjuvant therapy. Total dose delivered to whole breast was 42.56 Gy/16 fx in 164 pts and 42.4 Gy/16 fx in only 6 pts. No pts received sequential or concomitant boost on tumor bed. Late toxicity was recorded according RTOG/EORTC Late Radiation Morbidity Scoring Schema.

Results: Patients median age: 63 years (range 43-85); tumor breast side: 94 right and 76 left. Histology: DCI 142 pts, LCI 18 pts, others 10 pts. 130/170 pts had stage I disease and 40/170 had stage II disease. Median time between surgery and HRT was 106 days (range 41-185). After a median follow-up of 73 months (24-117) 153 pts are still alive. 5 pts died for metastatic disease, 5 pts died for other tumors(2 HN cancer, HCC, NHL and sarcoma) and 7 pts died for other causes. Local recurrence occurred in 3/170 pts (1.76%) after a median of 49 months (range 29-73). 9 pts showed metastatic disease after a median of 41 months (range 9-93). Most common acute toxicicy was skin grade 1 (58%) and grade 2 (34.8%) Only 2 pts presented grade 3 skin toxicity. After 1 month from the end of HRT, only 18.2% pts still had grade 1 skin toxicity. 59 pts presented skin late toxicity (33 pts grade 1 edema, 16 pts grade 1 pigmentation changes, 3 pts telangectasia, 3 pts grade 1 atrophy and 4 pts both edema and pigmentation changes). No > grade 3 events were reported. Only 3 grade 3 fibrosis occurred. No pulmonary or cardiac toxicity was observed. Althoug the series is not homogeneus, there was no significant difference in the incidence of acute or late toxicity in pts that underwent or not to chemotherapy (p=0.8)

Conclusions: In our series HRT is well tollerated and effective, with a good toxicity profile and good cosmetic out come. There is no clear evidence that chemotherapy has an impacto to acute or late skin toxicity. Despite the lack of boost on tumor bed, the rate of local recurrence was only 1.76%

P106

TEN YEAR OUTCOME OF ACCELERATED HYPOFRACTIONATED ADJUVANT WHOLE BREAST RADIOTHERAPY WITH CONCOMITANT PHOTON BOOST AFTER CONSERVING SURGERY FOR EARLY STAGE BREAST CANCER

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Introduction: Accelerated whole-breast radiotherapy (RT) with tumor bed boost in the treatment of early invasive breast cancer has demonstrated equivalent local control, toxicities and cosmesis when compared with standard RT. In Italy, there are still no reports of long-term outcome for hypofractionated radiotherapy to the whole breast after breast-conserving surgery (BCS). We report the 10-year results of a phase II study of hypofractionation adjuvant whole breast radiotherapy with concomitant photon boost after conserving surgery for early stage breast cancer that shortened treatment time to 4 weeks.

Materials and Methods: Data in the medical records of 160 patients (Stage 0-II) were retrospectively reviewed. The patients were treated with accelarated hypofractionated adjuvant whole breast radiotherapy between Between February 2005 and May 2007 at the Ivrea Hospital and were followed for more than 10 years. The basic course of radiotherapy consisted of 45 Gy, to the whole breast in 20 fractions with 2.25 Gy/fraction; an additional boost dose of 0.25 Gy was concomitantly delivered, to the lumpectomy cavity, for an additional dose of 5 Gy. The cumulative nominal dose was 50 Gy. Physician-rated toxicity (Common Terminology Criteria for Adverse Events version 3.0) and cosmetic outcome (CO) were prospectively assessed during yearly follow-up, up to 10 years after radiotherapy.

Results: Follow-up periods ranged from 4 to 118 months; the median follow-up period was 95 months. At 10-year follow-up, overall survival, cause-specific survival, relapse-free survival, and local control were 90.9%, 99%, 95.4%, and 98.8% respectively. Only 7

patients experienced disease recurrence: 5 of them with an axillary nodal relapse; 2 patients with systemic spread. No local relapse occurred. No major toxicities (grade 3 or more) were detected during follow up. Fibrosis was grade 2 in 1% of patients and telangiectasia was grade 2 in 0%. Grade 2 pigmentation changes were detectable in 0% of patients. Breast edema was grade 2 in 2%. Severe late complications were not observed. No major lung and heart toxicities could be detected. Cosmetic result was assessed and scored at 6 months, at 1 year to 10 years: 89% of patients showed excellent or good cosmetic result, and fair-poor in 11%.

Conclusions: In our study, hypofractionated radiotherapy led to excellent results at 10 years. This regimen is a good alternative to 6-7 weeks of conventional whole-breast fractionation with sequential boost and is a good option for most women requiring postoperative WBI.

P107

ROLE OF BNP AND TNI LEVELS AS PREDICTOR MARKERS OF CARDIOTOXICITY IN BREAST CANCER PATIENTS TREATED WITH HFRT

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Aims: We evaluate the measurements of BNP and Troponin I (TnI) as predictors of acute clinical o pre-clinical cardiotoxicity in early breast cancer pts treated with Hypofractionated RT, pointing to dosimetric differences between left and right breast cancer.

Materials and Methods: We enrolled 54 pts (range 56.8-11.4 ys) who underwent conservative surgery and HFRT. Exclusion criteria were: history of ischemic, valvular and hypertensive heart disease; left ventricular ejection fraction <50%; acute or chronic renal insufficiency and liver disease. Hormonal therapy and adjuvant or neoadj CHT weren't exclusion criteria. All pts underwent initial screening pre-RT including cardiological examination, heart disease history, 12-lead ECG, echocardiogram, hemocromium, VES, BUN, creatinine, Na+, K+, blood glucose, LDL, HDL, total cholesterol, triglycerides, uricemia. Blood samples were drawn for BNP and TnI at the enrollment, after the IV and XVI RT fraction and one month after RT completion. RT schedule consisted in a total dose of 42.4 Gy in 16 daily frs delivered by a 6 MV LINAC to the PTV with 2 tangential fields. 21 pts received a subsequent boost to the tumor bed as a total dose of 10 Gy delivered with a direct electron field. Whole heart contouring included the left atrium, left ventricle, right atrium, right ventricle and LAD. DVH, V20, V25, V30, V45, Dmax and Dmean were evaluated.

Results: Pts were divided into 2 Groups: (20) women with right side breast cancer and (34) with left side. All pts had normal values of TnI at time 0 with a median value of 0.55 ng/ml (range 0-6.3). 52pts/54 had normal values of BNP at time 0 with a median value of 32.1 pg/ml (range 10-113).2 pts (1 right side and 1 left side breast cancer) had mildly elevated BNP values (210;304), constantly stable during and after RT. No significant change of TnI and BNP were observed during RT and after 1 month from the end of therapy, without significant differences between left and right breast. At 1 year after RT completion, no patients showed clinical sign or symptoms of cardiac failure, while we recorded left anterior hemiblock in 4 pts and T wave modification in 1 patient

Conclusions:. In our prospective study BNP and TnI levels were constantly in a normal range, in particular in left breast cancer patients. It's mandatory to extend the follow-up, investigating if these data will be confirmed.

P108

HFRT NEUROLOGICAL TOXICITY IN BREAST CANCER PATIENTS TREATED WITH OR WITHOUT ADJUVANT CHEMOTHERAPY: A PILOT MONOCENTRIC EXPERIENCE

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Aims: The aims of this study is to evaluate the incidence of acute skin toxicity, radio-induced brachial plexopathy (RIBP) according to CTCAE and to compare acute toxicity with concomitant Trastuzumab (TST) systemic therapy.

Methods: From October 2016 to May 2017, 11 females affected by ductal breast cancer, were treated with surgery and adjuvant RT. The median age at diagnosis was 61 ys (39-83ys). All cases were discussed in a multidisciplinary meeting. Ten pts underwent to breast conservative surgery plus lymphadenectomy and only one to mastectomy. Two pts were Stage IIB disease, 6 pts St IIIA, 2 pts St IIIB, 1 pt St IIIC. Three pts were Luminal-A (27.3%), 8 pts Luminal-B (72.7%). Two pts had Her2/neu positivity. One pt was treated with NAC; the others with adjuvant CHT with the schedule EC+TXT, time gap between CHT and RT was 2 months (range 1-3). All pts received mild-hypofractionated RT (HFRT): 42.4 Gy in 16 frs, 5 times/w involving the breast and infra-supraclavicular fossa (SCLN) plus boost in lumpectomy area when indicated. PTV was contoured according to RTOG, defined on CT scan. Four pts received a 3D -RT plans, with 3 plans elaboration: ptv breast, ptv SCLN and ptv boost. All of them received a sequential boost of 10 Gy, 2.5 Gy/fr. Seven pts were scheduled for an IMRT-SIB treatment plan, with an elaboration of a single treatment plan involving PTV breast and PTV SCLN (PTV tot) and a concomitant boost of 48 Gy, 3Gy/fr to the tumour bed. According QUANTEC: all pts have DVH heart V25 < 10%. 10 pts a DVH lung V20 < 30%, Dmax to the spi-

nal cord was 6.66 Gy (2.9-16) and to the brachial-plexus 43.9 Gy (42.2-45.9).

Results: Acute toxicity was erythema and moist desquamation. Four pts had a G2 acute skin toxicity, 3 of them were treated with 3D RT, only 1 with IMRT. None of pts refers symptoms related to RIBP. At 4 months FUP pts reported a complete remitted skin erythema. Three pts (27.3%) present a mild lymphoedema of the upper omolateral superior arm that seems to be related to RT. 3 pts (27.3%) had paraesthesia on the irradiated side arm. There was not statistical significance difference between patients treated with TST: only 1 pt had mild lymphoedema and paraesthesia.

Conclusions: It's mandatory to collect a bigger amount of pts to obtain more statistically significant data. Otherwise, in our pilot experience, breast and SCLN HFRT appear to be safe but the development and improvement of paraesthesia must be indagated in a long fup period.

P109

ESTIMATING THE RISK OF LOCOREGIONAL RELAPSE ACCORDING TO MOLECULAR SUBTYPE IN BREAST CANCER PATIENTS WITH 1-3 POSITIVE NODES AFTER POSTOPERATIVE RADIOTHERAPY

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Aims: To evaluate the impact of molecular subtype on locoregional failure in breast cancer patients with 1-3 positive nodes after postoperative radiotherapy.

Methods: From an institutional database we identified 321 patients with 1-3 positive nodes treated with postoperative radiotherapy from 2005 to 2016. Molecular subtypes were defined as luminal A (LA), luminal B (LB), luminal Her 2, Her 2 and triple negative (TN) based on the 2015 St. Gallen

Consensus Criteria. Kaplan Meier log-rank and Cox-regression multivariate analysis were performed to evaluate the relationship between molecular subtypes and locoregional recurrence.

Results: Median follow-up was 4.2 years (range 1-12 yrs). Molecular subtypes were distributed as follows: 57.6% LA, 24.9% LB, 8.7% luminal Her-2, 1.9% Her- 2, 6.8% TN. Two hundred seventy (83.1%) patients underwent breast conserving surgery and fifty-five (16.9%) received mastectomy. All patients received adjuvant radiotherapy to whole breast or chest wall. Sixty-four (19.7%) patients received also radiotherapy to supra-infraclavicular nodes. Luminal A subtype had lowest histologic grades (p=<0.001), lowest extracapsular spread rate (p=0.03). Four (1.24%) loco-regional relapse occurred, 2 (50%) in breast and 2 (50%) in the chest wall area. No difference in local recurrence rate was observed according to molecular subtypes, irradiation of supra-infraclavicular nodes, age, tumor diameter (p=NS). Only the number of positive nodes (1 vs 2-3) was associated with local recurrence risk (p=0.017). Luminal A subtypes had a 10 years metastasis free survival rate higher compared to other subtypes (86.9% vs 64.6%; p=<0.001).

Conclusions: The loco-regional recurrence rate observed was very low. Postoperative radiotherapy even if not associated with supra-infraclavicular nodal irradiation seem to be effective in lowering loco-regional recurrence rate regardless of molecular subtype.

P110

HEART AND CORONARY ARTERY DOSE SPARING IN PATIENTS WITH LEFT-SIDED BREAST CANCER: THREE-DIMENSIONAL CONFORMAL RADIOTHERAPY VS HELICAL TOMOTHERAPY

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Aims: Our study compared heart, left ventricle (LV) and coronary artery dose sparing with three-dimensional conformal radiotherapy (3DCRT) versus Helical Tomotherapy (HT) in women with left-sided breast cancer.

Methods: Tangential field 3DCRT and HT treatments were planned for 20 left-sided breast cancer patients. Computed tomography (CT) scans without and with intravenous contrast (ic) were performed and co-registrated together. Left breast and organs at risk (OARs) were contoured by the same radiation oncologist, who was an expert in breast cancer RT and was trained in coronary artery delineation. Planning organ at risk volume (PRV) for each coronary artery was defined. Particular attention was paid to the left anterior descending artery (LADA) delineation and to PRV-LADA definition.

Results: HT provided the best target coverage and significantly reduced D2% and mean dose (Dmean) to the PRV- LADA, D2% to LV and V25 to the heart. LV Dmean was not significantly higher with HT, while, due to rotational delivery, heart Dmean was. Furthermore, again due to rotational delivery, the dose to PRV of all the other coronary arteries, the contralateral breast and lungs was higher with HT. Only V30 for the left lung resulted lower.

Conclusions: Our data show that HT significantly reduced, LV and LADA doses, while only V25 to the heart was significantly reduced. Moreover with HT a slight dose increase in the other OARs occurred. Further stu-

dies are needed to correlate heart and coronary artery dosimetric findings with in-depth cardiac monitoring.

P111

RADIOTHERAPY TREATMENT IN BREAST CANCER: COSMETIC OUTCOMES FOR ELDERLY PATIENS

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Aims: To evaluate cosmetic outcomes in patients ≥ 65 years with breast cancer.

Materials and Methods: We retrospectively reviewed 107 patients (pts) ≥65 years taken randomly with a history of breast tumor. In our Istitution, between January 2000 and Dicember 2016, 96 pts who underwent quadrantectomy followed by radiotherapy (RT), 7 who underwent mastectomy followed by RT on chest wall and 4 pts nodulectomy followed RT. Of Them: 35 were over 65 years old, 40 were 70-75 years old, 17 were 76-80 years old and 15> 80. Among 107 pts: 40 pts underwent RT and hormonal therapy (OT), 6 pts were treated whit RT and chemotherapy (CT), 58 underwent with RT and CT plus OT and 3 RT alone. After quadrantectomy or nodulectomy 17 pts underwent RT to a total dose of 50 Gy followed by a boost of 10 Gy on tumor bed and 79 pts received 54 Gy (range 50-56Gy) to the whole breast, 4 pts were treated with hypofractionation to a total dose of 42,4 Gy in 16 fractions at 2.65Gy. Pts who underwent mastectomy were treated on chest wall to a total dose of 50 Gy conventional fractionation plus supraclavear (48 Gy total dose). Radiation treatment was provided with conventional three-dimensional conformal radiotherapy (3DCRT) with 6-15 MV photons. Proper hygiene has been suggested in all patients as well as the use of comfortable clothing; pts applied hydrating creams twice a day to prevent the acute skin effects. Patients underwent periodic visits during and after treatment through an integrated multidisciplinary management.

Results: Acute and late toxicity was assessed according to RTOG scale as following: 36 pts had G1 of acute toxicity skin, 15 had G2 and nobody had G3. The preventive use of hydrating creams reduced the skin toxicity. Patients who developed G2 toxicity were easily treated with local steroids for a week. 5 treatment has been interrupted for acute toxicity, but there has been a good compliance of the pts to the treatment. Late skin toxicity understood as the presence of atrophy, burns and necrosis was evaluated at 6,12,24 months. Late sequelae were tolerable: atrophy were the most common side effect whit poor impact on quality of life.

Conclusions: The retrospective randomly study, showed that during radiation therapy is important to the early recognition of the damage through periodic visits and, when necessary, immediate treatment with local steroids for a safe and efficacious treatment.

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CONTRALATER AXILLARY LYMPH NODES METASTASIS (CAM) FROM SECOND PRIMARY/RECURRENT IPSILATERAL BREAST CANCER: CASE REPORTS AND LITERATURE REVIEW

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Aims: CAM in breast cancer is uncommon with an incidence of 1,9-5%. We reported 2 cases of CAM treated in our Hospital.Methods: Case 1: a 61 years old patient (pt) with a history of infiltrating lobular carcinoma of left breast, treated 11 years ago by left breast conserving surgery (BCS) and axillary lymph nodes dissection (ALND) followed by adjuvant chemotherapy (ChT), breast radiotherapy (RT) and hormonal therapy (OT). In 2016 she presented a palpable lesion of ipsilateral breast and controlateral axillary nodes. Core biopsy on breast lesion and fine needle biopsy of right axillary nodes was diagnostic of infiltrating ductal carcinoma (IDC). The pt underwent neoadjuvant ChT, left mastectomy and right ALND with histological diagnosis of ductal carcinoma and 2/15 positive nodes. Case 2: a 63 years old pt with a history of left breast IDC treated 11 years ago by BCS and ipsilateral ALND, followed by adjuvant ChT, locoregional RT and OT. In 2016 she presented a new lesion in the left breast discovered by a screening mammography and multiple contralateral nodes discovered by a Positron Emission Tomography (PET). Left mastectomy and ALND was performed with histopatological report of IDC of the breast and 5/18 positive nodes. Postoperatively, she was treated with adjuvant ChT and OT. For both cases, staging with a PET showed no distant metastases. The Pubmed database was searched between 2007 until May 2017 using the following terms: controlateral axillary metastases, breast cancer, lymph nodes. Results: Six articles were included in the finally analysis that evaluated the management of CAM in pts presented a secondary/recurrent ipsilateral breast cancer. A total of 35 pts were described, ranging from 1 to 14 per publication. ALND was performed in 18 pts (51%) of all pts, in 14 of witch (78%) it was combined with regional RT. Axillary RT only was performed in 11 pts (31%) and 6 pts (17%) had no axillary treatment at all. In our hospital we treated both pts with right high axilla and supraclavicular nodes RT using 3DC-RT for a total dose of 50 Gy delivered in 25 fractions. Conclusions: Management of CAM is controversial because the significance of contralateral axillary tumor involvement at the time of secondary primary ipsilateral breast diagnosis is not clear. After an extensive multidisciplinary consultation ,according to literature review, we treated our pts as having early-stage disease with aberrant lymphatic drainage rather than metastatic disease.

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THE USE OF EICOSAPENTANOIC ACID (EPA), WITH GAMMA-LINOLENIC ACID (GLA) AND VITAMINS (VITAMINS A, C AND E), CAN PLAY ROLE IN PREVENTING SKIN TOXICITY IN BREAST CANCER PATIENT TREATED WITH RADIOTHERAPY

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Aims: The study wanted to compare the addiction of oral eicosapentanoic acid (EPA), gamma-linolenic acid (GLA) and vitamins (vitamins A, C and E) , in the cosmetic outcome in the breast cancer (BC) patients (p.) treated by radiotherapy (RT) with historical cosmetic results of our Department

Methods: From January to April 2017, thirty-nine BC p. (pT1–3a, pN0–1a, M0,R0), treated with conservative surgery (± adjuvant chemotherapy) followed by endocrine treatment, who underwent to RT, received oral supplementation with W-care - lipids EPA - GLA and vitamins A, C and E- In our institute, RT is performed at whole breast and at lumpectomy site with hypofractionated regimen and concomitant boost, at dose \fx of 225 & 250 cGy in twenty daily fractions, or ,alternatively ,with the standard treatment at dose\fx of 200cGy for 25\30fx. Our RT technique allows the reduction of the hot \ cold regions and the better control of dose homogeneity, obtained with modified tangentially fields and field-in-field technique, reducing normal tissue (NT) injury. In the study, the drug (W-care) was subministered once a day the week before and twice a day during RT for 45 days. Early and late-occurring NT effects were assessed weekly and at the end of RT by p. , with Short satisfaction questionnaire, from E.O. assessments of redness measurement, Radiation Dermatitis Severity score or presence of moist desquamation, CTVAE score, and from Digital images photographs. Furthermore, the use of soothing cream was one of the surrogative endpoint used for to compare these pastients with the historical group. Four BC p. discontinued W-care for unpleasant taste or low compliance after two week of treatment, only 10 out of 39 patients were required to use the usual topic protection against radiation induced dermatitis.

Results: All p. received RT for a total radiation dose of ≥50 Gy. There were no interruption of RT treatment, due to skin toxicity or to drug intolerance. All p were satisfied of the cosmetic outcomes. In the present group , the following acute skin toxicity scores were observed: grade 0:35%; grade 1:65%; grade 2, 3, 4:0%. in the historical group, the scores were: grade 0, 2%; grade 1, 64%; grade 2, 32%; grade 3, 2%; and grade 4, 0%. No > gr 1 toxicity was observed in the present study, and a significantly lower rate of occurrence of skin topic treatment was recorded when compared with previously group (27% vs.95%).

Conclusions: Though with the use of the innovative medical technology we reduced the incidence of severe radiation dermatitis, the radiation-induced skin reactions are still a significant complication. By the use of the nutraceutical supplementation with W-care (EPA, GLA and vitamins A, C and E) we recorded an important reduction of radiation dermatitis severity in this small set of breast cancer patients. Further analysis is needed to evaluate the impact on late effects

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LEFT VENTRICLE AND LEFT ANTERIOR DESCENDENT ARTERY DOSE CONSTRAINTS AND HEART TOXICITY IN BREAST CANCER PATIENTS TREATED WITH HYPOFRACTIONATED RADIOTHERAPY (HFRT) AND SYSTEMIC THERAPY

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Aims: The aim of this study is to evaluate cardiotoxicity in patients treated with CHT and RT and establish a correlation between heart safe dose to left ventricle and left anterior descendent artery (LAD).

Materials and Methods: We start a study protocol in collaboration with cardiologists in order to evaluate cardiotoxicity in pts irradiated on the left breast. 54 pts in which RT adjuvant was indicated (±adjuvant therapy), were enrolled from March 2014 to June 2016. 16 pts underwent conservative surgery, neo or adjuvant CHT and HFRT. All pts were addressed to: cardiological examination, ECG, echocardiogram, CBC, VES, BUN, creatinine, Na+, K+, blood glucose, LDL, HDL, total cholesterol, triglycerides, uremia. Exclusion criteria were any heart dysfunction, renal insufficiency and liver disease. ECGs were performed at the enrollment, 1 and 12 months after the end of the treatment. Blood samples were drawn for BNP and Troponine I (TnI) at the enrollment, after the IV and XVI RT fraction and one month after RT completion. 15 pts were scheduled for adjuvant CHT, 1 neoadjuvant CHT. 4/15 pts received TST-CHT schedule due to HER2 positivity. All pts received EBRT, 7 with right side and 9 with left side breast cancer. RT schedule consisted in a total dose of 42.4 Gy in 16 daily frs. 14 pts received a sequential electron boost of 10 Gy/4frs. Heart contouring included the left atrium, left ventricle, right atrium, right ventricle, LAD and were evaluated V20, V25, V30, V40, Dmax and Dmean trough DVHs.

Results: All pts had a normal pre-RT TnI value with a mean of 1.15 pg/ml (range 0.01-4.6). BNP pre-RT mean 47.7ng/ml (range 14.3-113.4) and there was no statistical significant difference with TST scheduled pts. No significant change of TnI and BNP were observed during RT and after 1 month from the end of therapy, without significant differences between left and right breast. None patient showed a clinically RT-related cardiac failure. 1 left side pt had a left anterior hemiblock on the ECG without symptoms 1 year after RT.

Left Ventricle Dmean in our left breast irradiated pts cohort was 1.77 Gy (range 0.72-4.26). LAD Dmean in left side breast cancer pts HFRT treated was 1.81 (range 1.81-27.7)

Conclusions: A well developed 3DRT lead to reduce the Dmax to OARs, focusing on heart structures, main cause of morbility. This reflects a mild or none toxicity also in pts treated with systemic therapy. Still to fulfil a longer fup to enhance a long term toxicity study.

P115

ADJUVANT HYPOFRACTIONATED RADIOTHERAPY FOR EARLY BREAST CANCER

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Aims: The purpose of the study was to evaluate the acute and late side effects of skin, cosmetic result, and disease control in patients with breast cancer who received adjuvant radiotherapy hypofractionated.

Methods: From april 2014 to march 2017, in our center, were treated 55 women with breast cancer who had undergone conservative surgery. The median age was 65 (range 49-82). All the patients had a histological of invasive ductal carcinoma, 39 (70%) in stage T1 and 16 (30%) in stage T2. All women were treated with conformal 3D external beam radiotherapy for a total dose of 42.40 Gy, with 2.65 Gy fraction dose and for 5 days a week.

Results: All women completed radiotherapy. 48 patients (88%) presented acute toxicity of Skin of Grade 1 and 7 patients (13%) presented acute toxicity of Skin of Grade 2. In a 9.4 months average follow-up was observed in 3 patients (5%), whit a ample breast, late skin toxicity. Was osserved in 1 patient (1,8%) distant recurrence and no local disease was observed in any patient.

Conclusions: In our study we didn't find any significant acute skin effects such to invalidate the therapeutic choice. Was observed low incidence of late skin toxicity with satisfactory cosmetic outcome. Hypofractionated adjuvant radiotherapy has been proved to be an appropriate treatment choise for control desease. However a longer follow-up and a larger number of patients are needed to confirm these results

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DOSE TO PELVIC BONE MARROW DEFINED WITH FDG-PET PREDICTS FOR HEMATOLOGIC NADIRS IN ANAL CANCER PATIENTS TREATED WITH CONCURRENT CHEMO-RADIATION

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Aims: To test the proof of principle that irradiated volume of pelvic active bone marrow (ACTBM), as detected by 18FDG-PET, may be a predictor of decreased blood cell nadirs in anal cancer patients undergoing concurrent CT-RT and to identify subregions within the pelvis involved in the occurrence of acute hematologic toxicity.

Methods 44 patients submitted to IMRT and concurrent CT were analyzed. Several bony structures were defined: pelvic and lumbar-sacral (LSBM), lower pelvis (LPBM) and iliac (IBM) bone marrow. ACTBM was characterized employing 18FDG-PET and defined as all subregions having Standard Uptake Values (SUVs) higher than SUVmean. All other regions were defined as inactive BM (INACTBM). On dose-volume histograms, dosimetric parameters were taken. Endpoints included white blood-cell-count (WBC), absolute-neutrophil-count (ANC), hemoglobin (Hb) and platelet (Plt) nadirs. Acute toxicity was scored according to RTOG scoring scale. Generalized linear and logistic regression models were used to find correlations between dosimetric variables and blood cell toxicity.

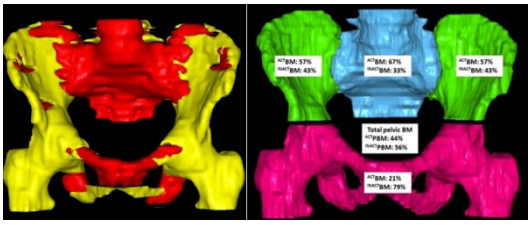

Figure 1.

Results: ACTBM mean dose had a statistically significant correlation with WBC (β=-1.338;p=0.020), ANC (β=-1.65; p=0.048) and Plt (β=-0.031;p=0.024) nadirs. On the contrary, no correlation was found between INACTBM mean dose and any blood cell nadir. ACTBM V10 had a significant correlation with WBC (β=-0.062;p=0.004) and ANC (β=-0.038;p=0.015) nadirs. ACTBM V20 was significantly correlated to WBC (β=-0.044;p=0.017), ANC (β=-0.027;p=0.039) and Plt (β=-1.570;p=0.050) nadirs. ACTBM V30 had a significant correlation with WBC (β=-0.033;95%CI:-0.064/-0.002;p=0.036) and Plt (β=-

1.720;p=0.010) nadirs. ACTBM V40 was significantly correlated to WBC (β=-1.490;p=0.040) nadir. With respect to subregions within the pelvis, WBC nadir was significantly correlated to ACTLSBM mean dose (β=-1.852;p=0.009), V10 (β=-2.153;p=0.002), V20 (β=-2.081;p=0.003), V30 (β=-1.971;p=0.023) and to ACTIBM V10 (β=-0.073;p=0.016). ANC nadir found to be significantly associated to ACTLSBM V10 (β=-1.878; p=0.025), V20 (β=-1.765; p=0.030). No significant correlation were found between dosimetric parameters and > G3 hematologic toxicity.

Conclusions: 18FDG-PET is able to define active bone marrow within pelvic osseous structures. ACTBM is a predictor of decreased blood cells nadirs in anal cancer patients undergoing concurrent CT-RT. Lumbar-sacral bone marrow dose seems to be the strongest predictor.

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CAN INCREASE ONCOLOGICAL OUTCOMES OF GASTRIC CANCER WITH POSTOPERATIVE RADIOTHERAPY: A META-ANALYSIS

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Background: The management of gastric carcinoma has been extensively studied but data on survival are still equivocal.

Objective: To assess the effects of radiotherapy combined postoperatively with chemotherapy on the increase of overall and disease free survival.

Data Sources: Computerized bibliographic searches of MEDLINE and CANCERLIT (1970–2016) were supplemented with hand searches of reference lists. Study selection: Studies were included if they were randomized controlled trials (RCTs) comparing postoperative radiochemotherapy to postoperative chemotherapy or to surgery alone, and if they included patients with resected, histologically-proven, gastric carcinoma without metastases. Ten RCTs, 4 of postoperative radiochemotherapy versus surgery alone (708 patients), 6 of postoperative radiochemotherapy versus postoperative chemotherapy (1020 patients), were analyzed.

Data extraction: Data on population, intervention, and outcomes were extracted from each RCT, in accordance with the intention to treat method, by three independent observers, and combined using the DerSimonian method and Laird method.

Results: Postoperative radiochemotherapy compared to postoperative chemotherapy or surgery alone significantly reduces the 3-year and 5-year overall survival (RR 0.89; 95%CI 0.81-0.97 and RR 0.83; 95%CI 0.77-0.91,respectively) and 3-year and 5-year disease free survival rate (RR 0.82; 95%CI 0.71-0.95 and RR 0.80; 95%CI 0.65-0.98, respectively).

Conclusions: In patients with resected gastric cancer, regardless surgical procedure, postoperative radiochemotherapy increases overall survival and disease free survival.

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PATIENTS WITH LOCALLY ADVANCED RECTAL CANCER (LARC): PREDICTIVE FACTORS OF NODAL RESPONSE TO NEOADJUVANT RADIO-CHEMOTHERAPY (RTCT)

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Aims: Preoperative RTCT followed by total mesorectal excision (TME) is the standard of cure in patients (pts) with LARC. After neoadjuvant RTCT the rate of complete pathologic response (pCR) range between 15%-30% and many studies are trying to find predictive factors of response in order to select pts who could benefit from intensified loco-regional treatments or organ-preserving options. The primary endpoint of this retrospective analysis was to identify predictive factors of nodal response to neoadjuvant RTCT, which could be used in the next future for treatment decision making.

Methods: We analyzed retrospectively the data of 119 pts affected by LARC (100% cT3-T4 and 90,7% cN+) treated with neoadjuvant RTCT (50.4 Gy in 28 FF + capecitabine 1650 mg/mq/day) followed by TME, between January 2008 and April 2014, in Pisa University Hospital. Based on MR-images, we analyzed nodal characteristics at diagnosis (clinical nodal stage, number of nodes with lower diameter ≥5mm and their distance from mesorectal fascia) trying to correlate these factors with the pathological nodal response. We also analyzed the time between surgery and the end of RTCT (> or < 8 weeks) and its correlation with nodal response.

Risults: All pts completed the planned radiotherapy and underwent surgery. The mean time between the end of RTCT and surgery was 8,6 weeks (range: 4,7-15,1). Twenty-five pts (21%) had metastatic nodes at the pathological examination; twenty of them (80%) were clinically staged as N+ by our calculation (nodes ≥5mm at pelvic MR). The analysis showed a strong correlation with one of the parameters analyzed: the number of nodes ≥ 5mm either as a continuous variable (p= 0,004) or as a dichotomous variable (number of nodes <3 vs ≥4; p<0,0001).

Conclusions: Know predictive factors of pathological response in pts affected by LARC treated with neoadjuvant RTCT could be important to decide to modify the locoregional treatments itselves. We decided to focusing our study on the analysis of predictive factors of nodal response only; based on our results, we could assume that pts with a greater number of large

nodes at diagnosis (≥5mm) are more likely to have positive lymph nodes at histological finding and could therefore benefit from an increase in loco-regional treatments. In our study we did not find a correlation between the interval RTCT-surgery and the nodal response, probabily because this parameter was too homogeneous in our cohort of pts.

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SIB-IMRT VERSUS CONVENTIONAL RT FOR ANAL CANCER: A MATCHED PAIRED ANALYSIS

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Aims: To evaluate clinical outcomes of a simultaneous integrated boost- intensity modulated radiotherapy (SIB-IMRT) approach in patients with non metastatic anal cancer compared to those of a set of patients treated with 3-dimensional conformal radiation and sequential boost (CRT).

Materials and methods: A retrospective cohort of 190 anal cancer patients consecutively treated between March 2007 and October 2015 at 2 academic centres with concurrent chemo-radiation employing either SIB-IMRT or CRT was analysed. The SIB-IMRT group consisted of 87 patients, treated with 2 cycles of Mitomycin and 5-Fluorouracil using a SIB-IMRT based schedule of 42-45 Gy/28-30 fractions to the elective pelvic lymph nodes and 50.4-54 Gy/28-30 fractions to the primary tumor and involved nodes, based on pre-treatment staging. The CRT group comprised 103 patients, treated with Mitomycin or Cisplatin and 5-Fluorouracil or Capecitabine concurrent to CRT with 36 Gy/20 fractions to a single volume including gross tumor, clinical nodes and elective nodal volumes and a sequential boost to primary tumor and involved nodes of 23.4 Gy/13 fractions. We determined colostomy-free survival (CFS) and overall survival (OS), loco-regional recurrence and distant metastases rates for each radiation modality. Cox proportional-hazards model addressed factors influencing OS and CFS. Propensity score-matched analyses were performed to compare SIB-IMRT and CRT.

Results: Median follow-up for the entire patient group was 32 months. Average overall treatment time was 42 days in the SIB-IMRT group and 59 days in the CRT group. Patients treated with CRT had significantly higher stage and lower grading. The overall survival at the time of analysis was 74%, similarly for the 2 groups. Three-year colostomy-free survival was 66% for all patients, with no significant difference between the two groups (61% for SIB-IMRT and 74% for CRT, Log-Rank 0.85). The cumulative incidence of colostomies showed that the majority of events occurred within 18 months in both groups. We found no significant difference in terms of outcomes by univariate analysis and a propensity score analysis adjusted for disparities between the groups.

Conclusions: Results of this analysis indicate that 3-year clinical outcomes of SIB-IMRT are similar to CRT. Even if highlighting the retrospective observational nature of the study, these data support the routinary use of SIB-IMRT in clinical practice for anal cancer patients submitted to concurrent chemo-radiation.

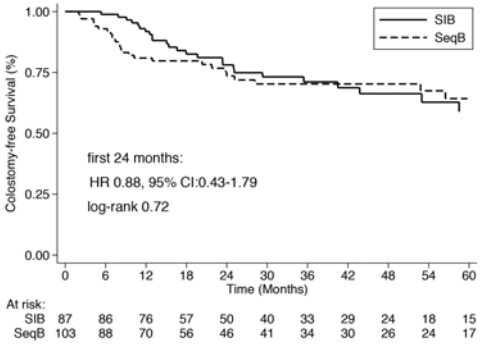

Figure 1.

P120

POTENTIAL PREDICTIVE BIOMARKERS TO CHEMORADIATION TREATMENT RESPONSE IN LOCALLY ADVANCED RECTAL CANCER: A METABOLOMIC STUDY

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Aims: Blood or urinary metabolomics is a promising biomarker discovery platform due to their minimally invasive characteristics. Aminoacids and acylcarnitines were misured as indirect markers of fatty acid and protein catabolism, with the aim to identify potential biomarkers of tumor response to neoadjuvant chemoradiotherapy (CRT) in patients affected by locally advanced rectal cancer (LARC), with attention to the identification of specific pathways that could be targeted for personalizing treatments.

Methods: Between March 2013 and September 2014, 18 patients with LARC were treated with neoadjuvant CRT at the Radiation Oncology Unit of SS Annunziata Hospital. Sera, (7.0 µL) collected during routine chemistry tests before treatment (T0), at day 14

(T14) and at day 28 (T28) of CRT, were subjected to a targeted tandem mass spectrometry (MS/MS) analysis for the detection of acylcarnitines and aminoacids.

Results: At T0 three of 21 aminoacids significantly differentiated responder patients (RP) from no-responder (NRP) ones: methionine, tyrosine and histidine. At T14 proline, valine and alanine resulted significant in differentiating RP and NRP. At T28 only valine continued to remain statistically different. By analysing acylcarnitines, no differences were measured for the exception of free carnitine that significantly differentiated RP in respect to NRP already at T0 time point.

Conclusions: Prospective detection of response to preoperative CRT could provide a personalizing treatment strategy in effort to improve survival outcomes and to decrease treatment morbidity. In our pilot study we focused attention on a pool of metabolomic substances that seem able to predict response, before CRT and during CRT, differentiating RP versus NRP patients. These preliminary data will be validated in an ongoing independent cohort of LARC patients.

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ADAPTIVE INDIVIDUALIZED HIGH-DOSE NEOADJUVANT RADIOTHERAPY IN HIGH RISK RECTAL CANCER: PRELIMINARY RESULTS OF A PHASE II STUDY

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Aims: Aim of this study was to evaluate the pathological response of locally advanced rectal cancer (LARC) after adaptive neoadjuvant intensified radiation therapy (RT) with concomitant and sequential boost.

Methods: Patients with high risk biopsy proven LARC were included. Primary end-point was pathological complete response (pCR). Secondary objectives included acute/late toxicity and predictive value of [18F]FDG-PET/CT. The sample size was calculated based on the two-stage design by Simon. All patients performed [18F]FDG-PET/CT at baseline (PET0) and after 2 weeks during RT (PET1). Since now, only 4 patients performed [18F]FDG-PET/CT before surgery (PET2). IMRT was delivered concurrently with capecitabine-based chemotherapy in all patients. Tumor volume (TV) was delineated using a gradient-based delineation method and the maximal standardized uptake values (SUVmax) were calculated. The dose to rectum, mesorectum and pelvic lymph nodes was 45 Gy (1.8 Gy /fraction). A concomitant SIB was delivered to GTV (defined on PET0) +2 cm margin with a total dose of 50 Gy (2 Gy/fraction). A subsequent sequential boost was delivered to GTV (defined on PET1)+5mm margin with a total dose of 5 Gy in 2 fractions (2.5 Gy/fraction) for a total dose of 55 Gy. Pathological response was expressed based on pTNM and Dworak tumor regression grading and toxicities were scored according to the CTCAE v4.03 scale.

Results: Nine patients (8 males, median age 60 years) were enrolled. The median SUVmax of the rectal lesions was 12.9 (range: 5.6-45) at PET0, 9.7 (range: 5.6-20.4) at PET1 and 5.5 (range: 0-5.9) at PET2, respectively. TV measured by PET was 28.1 mL (range: 1.2-90.9) at PET0 and 11.6 mL (range: 0.7-62.4) at PET1, respectively. Median SUVmax percent reduction and median TV percent reduction during RT was 33% (range: 0-54%) and 64% (0-86%), respectively. Among patients undergoing PET2, median SUVmax percent reduction compared with PET0 was 50% (range: 47%-100%) and 34% (range: 21%-100%) compared with PET1. The only patient with positive lymph-node at PET0 responded completely to lymph-node at PET1, while rectal lesion showed a stable uptake. PET2 was completely negative. To date, this is the only resected patient (11 weeks after RT) with complete clinical response (cCR) and pCR. No acute grade ≥ 3 toxicity was recorded.

Conclusions: These preliminary results shown that an adaptive strategy based on [18F]FDG-PET/CT can be feasible to reduce the target volume of a sequential boost.

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PRELIMINARY RESULTS OF ANAL CANAL MOTION EVALUATION FOR MAGNETIC RESONANCE (MR) GUIDED RADIATION THERAPY

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Aims: A major concerns in the treatment of rectal cancer aiming for sphincter preservation is represented by organ function preservation, if sphincter saving surgery is applied. Intrafraction motion can influence the volume of anal canal irradiated. Defining intrafraction movement of such structure can both affect the definition of ITV, and allow a personalized OAR gating delivery when MRI-guided radiation therapy is administered. Purpose of this study was to quantify the intra-fraction displacement of the anal canal in order to optimize the treatment for rectal cancer.

Methods: Rectal cancer patients treated at Gemelli ART with both VMAT and hybrid MRI tri-cobalt treatment unit underwent simulation with on-board 0.35-T MRI with MRIdian radiation therapy system. Sagittal cine MR images were acquired along the medial axis by a true fast imaging with steady-state free precession sequence. The system allow to set tracking points (TP) on the visualized imaging that record any displacement of the selected anatomic point over cine acquisition time (both monitoring only without dose delivery and while treatment administration). Three TP were set at the level of the superior border (TP1), center (TP2) and inferior border (TP3) of anal canal, respectively. Three consecutive sets of cine MR images were acquired for each patient analysed. The displacement of the tracking points along the cranio-caudal (CC) and anterior-posterior (AP) directions were recorded. In particular: movements exceeding 1, 2 and 3 mm were considered; shifts lasting less than 1% of the monitoring time were considered negligible and correlated to the shifts recorded for the bony landmark.

Results: Anal Canal motion was assessed in five patients, for 3 observation each. Maximum Craniocaudal (CC) displacement (mean value) was: 0.39 (TP1), 0.35 (TP2) and 0.37 (TP3) cm. Median CC displacement (mean value) was 0.01 for TP1, TP2 and TP3. The mean displacement actually impacted over 1 mm for 35% (TP1), 21.6% (TP2) and 18.8% (TP3) of the evaluated time, reducing to over 2 mm for 12% (TP1), 4% (TP2) and 2% (TP3) of the evaluated time.

Conclusions: These preliminary results support the hypothesis that intra-fraction anal canal motion could have an impact on the dose distribution for low rectal cancer. Moreover, applying a MR-based gating on OAR seems feasible and potentially useful. Final details will be presented.

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STEREOTACTIC BODY RADIATION THERAPY (SBRT) FOR UNRESECTABLE LOCALLY ADVANCED PANCREATIC CANCER: CLINICAL OUTCOMES ON 100 PATIENTS

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Aims: To assess the efficacy of stereotactic body radiotherapy (SBRT) in patients with inoperable locally advanced pancreatic cancer (LAPC).Methods: Patients with unresectable LAPC with maximum tumor diameter ≤ 5cm, without limph node disease and without distant metastasis were treated with SBRT, after multidisciplinary board evaluation. Prescription dose was 45Gy in 6 fractions. Primary end-point was freedom from local progression (FFLP). Secondary end-points were OS, PFS and toxicity. Local control was defined according to RECIST criteria. Acute and late toxicity was scored according to the NCI Common Terminology Criteria for Adverse Events (CTCAE) v3.0.

Results: Between January 2011 and December 2016, 100 patients with LAPC were treated with SBRT. Median FUP was 86 months. FFLP was 82% and 76% at 1 and 2 years, respectively. At univariate ($p<0.03$) and multivariate analysis ($p<0.001$), lesion size was significant for LC. Median PFS was 7 months. Median OS was 11 months. Chemotherapy administered before SBRT ($p< 0.005$) and FFLP ($p<0.002$) were significantly correlated with OS. Grade 3 gastrointestinal toxicity was detected in 2% of patients.

Conclusions: SBRT is an effective and safe local therapy for selected patients with LAPC. Our results suggest that the stereotactive treatment may be a promising therapeutic option in the multi-modality treatment of these patients.

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POST-OPERATIVE HYPOFRACTIONATED IMAGE-GUIDED INTENSITY-MODULATED RADIOTHERAPY IN CHOLANGIOCARCINOMA.

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Aims: To evaluate feasibility of post-operative hypofractionated image-guided intensity modulated radiotherapy (Hypo-IG-IMRT) in patients (pts) with peri-ilar and distal cholangiocarcinoma.

Background: we previously tested Hypo-IG-IMRT in pts with locally advanced pancreatic cancer. The dose of 44.25 Gy in 15 fractions (fr) to the tumor was feasible and safe (Int J Radiation Oncol Biol Phys, Vol. 87, No.5, 2013).

Methods: pts with histologically proven peri-hilar and distal cholangiocarcinoma after surgery were eligible. Simulation consisted in contrast-enhanced computed tomography (ce CT) or FDG CT/PET (CTPET) or when possible four-dimensional ce CT/PET (4D c-e CTPET), Clinical Target Volume (CTV) consisted in surgical bed and regional lymph-nodes and highly suspected PET uptakes. For Klatskin tumor, CTV included the surgical margin and hepatic hilum. For distal cholangiocarcinoma CTV included the anastomosis between the biliary tree and the small intestine. R1 site

was identified by pathological data and surgeon indications. The planning target volume (PTV) was defined with standard margins, except in pts who underwent 4D ce CT a margin of 5 mm was added to internal target volume. Median dose of RT was 44.25 Gy (40-48) in 15 fr on PTV and was delivered with VMAT or Tomotherapy. Concomitant chemotherapy (Cht) consisted in capecitabine .

Results: From 11/2010 to 09/2016, 24 pts were treated. Characteristics of pts: median age: 69 years (45-83), 12 M and 12 F, median KPS: 90. Eighteen pts had Klatskin disease, 6 pts common and distal bile duct disease. Treatment: All pts underwent surgery (19 pts R1). Three pts received neoadjuvant Cht. Seventeen pts received concomitant Cht . Ten pts underwent ce CT and CTPET simulation, 6 pts 4D ce CTPET and 8 pts ce CT. PET was positive in 8 pts. Acute Toxicity: all pts were evaluable. G1-G2 toxicity: 2 pts diarrhea, 14 nausea/vomiting, 9 abdominal pain, 3 cholangitis, 2 gastric ulcer. One pt had G3 gastro-duodenitis. Late toxicity: All pts were evaluable, no toxicity ≥ G2 occurred.

Responses: 24/25 pts were evaluable. Eleven pts had PD (4 local and distant PD, 4 only distant and 3 only local progression). 3y local progression, disease progression, and OS (from start of RT) resulted 57%, 37%, 50% respectively.

Conclusions: Post-operative Hypo-IG-IMRT delivering 44.25 Gy in 15 fr is feasible with good toxicity profile even with concomitant capecitabine in patients with peri-hilar and distal cholangiocarcinoma.

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PATIENTS' SELECTION FOR RADIOCHEMOTHERAPY IN BORDERLINE RESECTABLE AND LOCALLY ADVANCED PANCREATIC CANCER: REPORT FROM THREE PROSPECTIVE MONO-INSTITUTIONAL PHASE II STUDIES

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Aims: An accurate diagnosis followed by multimodality therapy is essential to achieve long-term survival patients with pancreatic cancer. We have proposed a model to select better patients for neoadjuvant treatments.

Matherials and Methods: From 2008 through 2017 84 patients (F:41; M:43) with borderline resectable or unresectable PDAC were accrued in three consecutive prospective studies of radiochemotherapy (RCT) with or without induction chemotherapy (IC). In all cases an accurate pre-treatment staging including CT scan, EUS, FDG-PET/CT and laparoscopy with peritoneal washing was performed. After induction chemotherapy and approximately 4 weeks after the completion of RCT, a re-evaluation was performed regarding tumour response and resectability with clinical examination, laboratory test, tumor markers, CT scan, FDG-PET/CT scan and laparoscopy.

Results: The median age of patients was 68 years (range 36–75 years). According to the results of the pretreatment workup, twenty patients (23.8%) had metastatic disease and were therefore excluded from the protocols. Patients who underwent induction chemotherapy (Gem-Ox or FOLFIRINOX schemes) were evaluated for clinical response after 2 months by using CT scan and PET-CT scan. Nine patients experienced disease progression, three patients refused to continue the protocols. Fifty-two patients received concomitant RCT and were evaluated for clinical response. The median follow-up for all patients was 25 months (range, 6.1 to 81 months) .Twenty-four patients (46%) underwent surgical radical resection, with negative margins. No patient died due to perioperative complications. For the whole group, the median PFS was 18.1 months. Two-year and three-year LC were 79% and 62%, respectively. Median OS was 16.2 months. One-year OS, two-year OS and three-year OS were 74%, 35% and 26%, respectively. Patients who underwent resection had a significantly longer median OS compared with non resected patients (37.6 months vs 13 months, $p = 0.02$). The median PFS for resected patients was 33 months compared with 11.2 months for non resected patients ($p = 0.005$). The median PFS for patients treated by upfront RCT was 10 months compared with 20 months for patients treated by IC followed by RCT ($p = 0.001$).

Conclusions: Our diagnostic workup, including CT scan, FDG-PET/CT scan and laparoscopy could be a model useful to clinicians who treat pancreatic cancer to improve patients' selection and clinical outcomes.

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NEOADJUVANT CHEMORADIOTHERAPY IN RESECTABLE PANCREATIC CANCER: A SYSTEMATIC REVIEW

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Introduction: Interest for neoadjuvant therapy in resectable pancreatic cancer (PC) is growing due to the disappointing results of standard therapies based on upfront surgery followed by adjuvant treatments. Aim of this systematic review is to analyze the current evidences of literature on the impact of neoadjuvant chemoradiation on outcome of patients with resectable PC.

Methods: A systematic review of literature from

2000 to 2017 on Pubmed and Scopus was performed. We included retrospective and prospective studies published in English enrolling more than 25 patients. Overall survival was the primary endpoint. Secondary endpoints included local control, acute and late toxicity, perioperative complication, response rate, R0 resection rate, and pCR rate.

Results: A total of 16 studies including 1411 patients met the selection criteria. Median local failure rate was 12% (range: 0-29.7%). Out of operated patients, median R0 resection rate was 92% (range: 68-100%). Only 9 papers reported pCR rate with a median value of 3.8% (0-17.6%). Median survival in patients with resected PC was 27 months (range: 11.7-50.2 months) compared to patients not undergoing surgery (median: 9.5 months; range: 5.5-11.0 months). Median acute GI ≥ G3 toxicity rate was 19.2% (range: 3.0-40.7%).

Conclusions: Neoadjuvant therapy is feasible and relatively safe, able to improve R0 resection rate and median OS, with a positive impact on local control. The role of this therapy is still debated and controversial and only prospective randomized controlled trials with adequate sample size will clarify the real benefit of neoadjuvant therapy in resectable PC.

Table 1.

Author; year	Pts	Dose (dose/ fraction) Gy	Concurrent chemotherapy	Induction Adjuvant chemo	Acute GI toxicity G≥3 (%) [scale]	Resected patients (%)	R0 resections (%)	pCR (%)	Local failures (%)	Median survival (months)		5-year survival (%)	
										ALL	RES	ALL	RES
Pisters PW et al. 2002	37	30 (3) + 10 (RT) 10-15	Paclitaxel	NR	29.7	57.0	68.0	0.0	0.0	12	19	3-year 11.0	3-year 28
Evans DB et al. 2008	86	30 (3)	Gem	1 Gem dose before CRT, 4 Gem doses after CRT	10	74.0	89.0	1.0	11.0	22	34	27.0	36
Talar S et al. 2008	32	40 (2)	5-Fu + CDDP or Gem	Not delivered	5Fu-CDDP 11, Gem 12	75.0	NR	NR	12.5	10.2	20.5	3-year 22.0	3-year 29.1
Varadhachary GR et al. 2008	90	30 (3)	Gem	4 Gem-CDDP doses before CRT, 1 Gem dose after CRT	25.3	66.0	96.0	0.0	25.0	17.4	31	NR	NR
Le Scodan R et al. 2009	41	50 (2)	5-Fu + CDDP	Not delivered	36.6	63.0	81.0	3.8	4.0	9.4	11.7	NR	NR
Turrini O et al. 2009	102	45 (1.8)	5-Fu + CDDP	Not delivered	5.0	61.0	92.0	13.0	13.0	17	23	16.0	15.0
Turrini O et al. 2010	34	45 (1.8)	Docetaxel	Not delivered	5.0	50.0	100.0	17.6	0.0	15.5	32	20.6	41.0
Barbier L et al. 2010	88 (Tot. 173)	45 (1.8)	5-Fu + CDDP Rebus	Not delivered	NR	13	NR	NR	10	15	21.5	2	9
Papalezova KT et al. 2012	144	45 + 5.4 (1.8)	Infusional 5-Fu or capecitabine	Adjuvant Gem (33.0%)	NR	53.0	75.0	10.0	12.0	15	27	NR	21.0
Takahashi H et al. 2013	188	50 (2)	Gem	Gem after CRT, + liver perfusion CT after surgery	3.0 0	87.0	99.0	NR	15.0	NR	NR	34.0	57.0
Kharofa J et al. 2014	36 (Tot. 69)	50.4 (1.8)	Gem or Capecitabine	NR	NR	83	NR	NR	NR	20.1	20.1	NR	NR
Tzeng CW et al. 2014	115 (Tot. 167)	30 / 50-50.4	Gem / 5Fu Gem	Gem-CDDP	NR	83	89.5	NR	NR	28	35.2	21	29
Roland CL et al. 2015	222 (Tot. 397)	30 or 50.4	Gem 5-Fu Capecitabine	Gem before CTR	NR	100	92	[illegible]	29.1	NR	NR	26.1	NR
Shi et al 2015	102 (Tot. 248)	50.4 (2)	Gem	Gem before CRT +5Fu WHF and Gem or Gem alone after surgery	NR	100	98	NR	NR	19.3	30.2	NR	NR
Golcher et al. 2015	33 (Tot. 66)	55.8 (1.8) or 50.4	Gem + CDDP	Not delivered	[illegible]	57.57	89.47	NR	NR	25	NR	NR	NR
Kalfbeek K et al. 2016	68	50.4 (1.8)	Gem or Capecitabine	Gem-Erlotinib-CDDP Other Before CTR	NR	87	97	3.3	NR	31.5	41.0	NR	NR

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NEOADJUVANT CHEMO-RADIOTHERAPY IN CURATIVE TREATMENT FOR LOCALLY ADVANCED ESOPHAGEAL CANCER: A 11-YEARS SINGLE INSTITUTION EXPERIENCE

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Aims: We present our 11-years experience in the treatment of patients with esophageal and gastroesophageal junction (GEJ) cancer with neoadjuvant intent.

Materials and Methods: From December 2005 to January 2017, 47 patients with locally advanced esophageal and GEJ cancer were treated with neoadjuvant intent in our institution. All patients underwent complete physical and clinical examination, esofagogastroduodenoscopy and CT (PET/CT was performed in 72% of the cases and only 1 patient required a diagnostic laparoscopy). Most of them were male, with a good performance status, mean age 61 y (range 43-75). The most common site of the disease was the lower esophagus (almost 40%); in 10 cases the disease involved the GEJ. Low grade squamous cell carcinoma was the most frequent diagnosis, often involving the adventitia (>70%) and the local nodes (cN1/2 >60%). Patients and disease characteristics are summarized in Table 1.

Results: all patients were treated with chemoradiotherapy with neoadjuvant intent (except 1 patient treated only with radiotherapy). The most prescribed fractionation schedule was 1.8/50.4 Gy (mean total dose was 49 Gy, range 41.4 - 54) while concomitant chemotherapy was usually CDDP+5FU based (administered the 1st and 5th week of RT). Almost all the patients completed the scheduled treatment without interruption: serious adverse effects were rare (9% of G4 blood disorders and 11% of G3-G4 dysphagia according to CTCAE v4.0). Nutrition support was needed in 48% of the patients with a mean loss of weight of 5% (35% of the patients didn't lose any weight). 74% of the cases underwent surgery: half of them showed a complete pathological response at the histological report; 20% of them showed a sistemic progression of the disease after chemoradiotherapy. Local control was almost 75% at 1 year while overall survival was 65% at 5 years.

Conclusions: neoadjuvant chemoradiotherapy is an effective part of a multimodal approach in the treatment of esophageal and GEJ cancer with curative intent, is well tolerated and indeed leads to a complete pathological response in 55% of the cases. Unfortunately 15% of the patients don't undergo surgery due to a systemic progression of the disease, which means that a very careful selection of the patients is still required.

Table 1. Patients' and disease characteristics.

Gender	%	Site	%	cT	%	cN	%
Male	81.4%	Cervical	4,7	T1	2,3	N0	39,5
Female	18.6%	Upper thoracic	9,3	T2	20,9	N1	34,9
IK at diagnosis		Mid thoracic	25,6	T3	72,1	N2	25,6
100-90	53.5%	Lower thoracic	39,6	T4a	4,7		
80-70	44.2%	EGJ	20,9				
60	2.3%						

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VOLUMETRIC MODULATED ARC THERAPY FOR UPPER ABDOMINAL TUMORS: A DOSIMETRIC COMPARISON WITH INTENSITY MODULATED RADIOTHERAPY AND 3D-CONFORMAL RADIOTHERAPY TECHNIQUES

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Aims: To compare volumetric modulated arc therapy (VMAT) with intensity-modulated radiotherapy (IMRT) and 3D-conformal radiotherapy (3DCRT) in their ability to spare organs at risk (OARs) and to cover Planning Target Volume (PTV) in upper abdominal cancer treatments.

Methods: A total of 17 patients treated with adjuvant radiotherapy at our institution were included in this retrospective study. Seven patients were treated for pancreatic cancer, 8 for gastric cancer and 2 patients for cholangiocarcinoma. These treatments were planned using 3DCRT, conventional step-and-shoot 7-fields IMRT and single arc VMAT, and 6 MV photon beams. As regards VMAT plans, they were generated using 10 MV photon beams, too. Conformity index (CI), Homogeneity index (HI) and Gradient index (GI) were evaluated. Other parameters were: monitor units (MU), actual delivery time, PTV coverage and OARs doses. All generated plans consisted of a prescription total dose of 50.4 Gy to PTV (28 fractions) with the objective to deliver the prescribed dose to >95% of the PTV with a dose range ± 10%.

Results: The VMAT and IMRT plans showed better PTV coverage and OARs sparing in comparison to the 3D-CRT technique. Particularly kidneys and liver sparing was improved with VMAT and IMRT (V12=48% and V30=18%, in VMAT and IMRT plans versus V12=55% and V30=39% in 3DCRT plans, for kidneys and liver respectively). VMAT exhibited a better mean CI (0.62±0.05) and mean GI (0.15±0.04) than other techniques - IMRT: mean CI (0.57±0.05), mean GI (0.14±0.04) and 3DCRT mean CI (0.39±0.05), mean GI (0.12±0.04). No differences were observed in HI between the three techniques. MU and treatment delivery time were reduced in VMAT treatments (420 MU and 1.5 minutes versus 500 MU and 10 minutes, for VMAT and IMRT respectively). No significant variation ($p < 0.005$) was found between 6 and 10 MV VMAT plans.

Conclusions: Our study showed a better OARs sparing with VMAT and IMRT for upper abdominal treatments. The improvement of CI and GI in association with the reduction of MU and treatment delivery time confirmed the advantages of VMAT in comparison with other techniques. Since no significant differences were found between the use of 6 or 10 MV in VMAT plans, 6 MV should be preferred to minimize diffuse radiation and avoid neutron activation.

These preliminary results should be confirmed in larger and prospective studies to evaluate the overall treatment plan quality and to understand the clinical relevance of these benefits.

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CHEMORADIOTHERAPY FOR OESOPHAGEAL CANCER FOLLOWED BY SURGERY STUDY (CROSS): SINGLE CENTER EXPERIENCE

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Aims: Multimodal approach is the recommended strategy for locally advanced oesophageal and junctional cancer (OC). CROSS is one of the standard regimens for the treatment of this disease. The purpose of our study was to evaluate the role of volumetric-modulated arc therapy (VMAT) in the neoadjuvant chemoradiotherapy management of advanced medium and distal oesophageal cancer in terms of toxicity and response to treatment.

Methods: From November 2012 to December 2016 consecutive fit patients (ECOG-PS) with resectable, locally advanced (T3-4,N0 and AnyT,N+ M0) OC were enrolled to receive neoadjuvant CROSS regimen. All patients underwent FDG-PET scanning before and after induction chemoradiotherapy. A pathologic uptake was observed in all patients. Patients showing no progression over neoadjuvant treatment were evaluated for oesophagectomy.

Results: The analysis included 62 patients, with a median age of 65 years (range of 40 - 81) and a generally low ECOG-PS (0-2). No cases of pulmonary or cardiologic toxicity > G2-G3 was registered. Fifteen (24.1%) patients had disphagia G2. Nine patients (14.5 %) did not receive a complete CROSS regimen. Thirteen patients (20.9 %) did not undergo surgery due to progressive disease (7 pts), unfitness (3) and death occurring during neoadjuvant treatment (3: 2 myocardial infarction and 1 aortic dissection). Fifty-one patients (82.2 %) underwent oesophagectomy. The sensitivity of CT and PET/CT were 94% and 95% respectively in predicting pathological response. A clinical partial or complete response was observed in 92% of the cases (radiological/metabolic) and was confirmed after surgical intervention (67% partial or complete and 27% stable response). Tumor down-staging was recorded in 67% of patients and nodal down-staging in 50%.

Complete pathological response was recorded in 13 cases (20.9 %).

Conclusions: VMAT was applied in the context of neoadjuvant chemoradiotherapy for the treatment of medium and distal oesophageal carcinoma with satisfactory results in terms of tolerance and toxicity.

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FDG-PET/CT IMAGING FOR STAGING AND TARGET VOLUME DELINEATION IN VOLUMETRIC-MODULATED ARC THERAPY (VMAT) OF ANAL CARCINOMA

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Adding an integrated PET/CT scan to the staging workup has a significant impact on therapy planning, identifying those patients who need higher-dose RT to the metastatic nodal and those with otherwise occult metastatic disease. We include integrated PET/CT in the pretreatment staging workup and target volume delineation of 30 patients with anal cancer candidates for curative radio-chemotherapy.

Methods: Thirty patients, 12 M/18F, (median age:53years with range: 52-84 years) with biopsy proven squamous anal cell carcinoma were treated using the volumetric-modulated arc therapy (Vmat). Tumor stage included: 13% I, 30% II, 7% IIIA, 50% IIIB. T1-4N0-3M0 anal cancer patients received 5FU and MMC days 1and 25 of radiation treatment. Simulation was performed by PET/CT imaging with patient in treatment position. The GTV and the CTV changed in site, shape and in size based on PET/CT imaging. The treatment plan was designed to deliver in one process with simultaneous integrated boost (SIB) a dose of 54 Gy to the planning target volume (PTV 54) based on the gross disease (T and N pet+ or >3 cm) in a 2.16 Gy-daily fraction, 5 days a week. At the same time, the subclinical disease N<3cm (PTV50) was planned to receive 50 Gy in a 2 Gy-daily fraction and elective nodal (PTV45) to receive 45 Gy in a 1,8 Gy-daily fraction.
Results: PET/CT fused images led to change the stage in 10/30 cases (33%):
3 cases from N0 to N2 and N3,
2 from N1 to N2 or N3,
3 from N1 to N0,1 from N3 to N2 1 from N2 to N1
Conclusions: Anal cancer is FDG-PET avid.
FDG-PET/CT has a potential relevant impact in staging and target volume delineation of the carcinoma of the anal canal.
-Clinical stage variation occurred in 33% (10/30) of cases with change of doses to GTV-N pet+/-.
-PET upstages 20% (6/30)and PET downstage 13% (4/30) changes the dose -RTP (RT treatment planning).
PET can aid in anal cancer staging and identification of residual disease, recurrent/metastatic disease but warrants further prospective studies.

P131

ACCURACY OF DIFFUSION-WEIGHTED MAGNETIC RESONANCE IMAGING IN RESTAGING LOCALLY ADVANCED RECTAL CANCER AFTER PREOPERATIVE CHEMORADIATION.

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Aims: To analyze diffusion-weighted magnetic resonance imaging (DW-MRI) for treatment response assessment in locally advanced rectal cancer (LARC).

Methods: This is a retrospective study. We analyzed patients with histologically proven rectal adenocarcinoma, stage II-III disease, who underwent surgery following neoadjuvant chemoradiotherapy (nCRT). All patients were referred for a DW-MRI protocol prior and after nCRT.

Results: Between May 2013 and March 2017, 33 patients with stage II-III rectal cancer, underwent surgery after completed nCRT. Only 16 patients underwent DW-MRI prior and after nCRT. DW-MRI was performed in a median of 6 weeks (range: 4-8 weeks) after nCRT. All patients underwent surgery after a median of 2 weeks (range: 2-4 weeks) after restaging with DW-MRI. After nCRT, DW-MRI showed a downstaging of disease in every case, clinical complete response was observed in no case. After surgery two patients had patological complete response (pCR), that was not recognized at the DW-MRI. Complete nodal response was correctly predicted in 7 patients (44%) by DW-MRI, but we observed an DW-MRI T overstaging in every case. In none of the patients the surgical plan was changed after the restaging DW-MRI.

Conclusions: This study was limited by its small sample size and retrospective nature. DW-MRI could be useful for discriminating between the pCR patients and the no-pCR patients, in order to achieve sphincter sparing surgery or wait and see strategy in selected cases, but further studies are necessary to identify the optimal MRI parameters combination to predict tumor response and the optimal timing to perform DW-MRI after nCRT to identify the maximal response to treatment.

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VOLUMETRIC MODULATED ARC THERAPY (VMAT) IN THE NEOADJUVANT OR EXCLUSIVE TREATMENT OF ANORECTAL CANCER: DATA FROM A SYSTEMATIC REVIEW

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Aims: To review the available data from clinical outcome studies concerning the use of VMAT techniques in exclusive or neoadjuvant chemoradiation anorectal cancer setting. The rationale is closely related to the higher normal tissues sparing, dose escalation possibility and faster delivery of VMAT compared to 3D-CRT or IMRT.

Methods: A systematic review based on PRISMA methodology of papers reporting clinical studies on VMAT was carried out in December 2016 using the National Library of Medicine (Pubmed/MEDLINE). The following words were searched: "volumetric arc therapy"[All Fields] OR "vmat"[All Fields] OR "rapidarc"[All Fields]) AND "radiotherapy"[All Fields] AND Clinical Trial [All Fields]. Only article published in English were considered. Clinical data on volumetric arc therapy of anorectal cancers were extrapolated from the review and represent the object of this analysis.

Results: Seven clinical studies (3 prospective and 4 retrospective) from 2010 to 2016 reported data on 227 anorectal cancer patients treated by VMAT (Table). All of them were chemoradiation studies in the neoadjuvant [1-3] or exclusive setting [4-7], with a number of patients ranging from 11 to 81. The most represented technique was the 2 arcs VMAT SIB one [3-5,7], but image guided delivery was pursued in only 3 papers [3,4,7]. Acute toxicity G≥3 was recorded by CTC scale and was mostly gastrointestinal but with a large variability, while late toxicity G≥2 was reported only in [2,4]. With a follow up range of 15.3-61 months clinical outcomes were reported in [1-5] and local control rate, disease free and overall survival were reported in [3-7].

Conclusions: the available studies provided further lines of evidence supporting the implementation and use of SIB-VMAT on a routine basis for treatment of anorectal cancer in combination with concurrent chemotherapy due to lower rates of acute organ toxicity and promising trends in LC and DFS. More caution should be reserved when a dose escalation protocol is foreseen.

Table 1. VMAT-SIB in anorectal cancer

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[18F]FDG-PET/CT HAS NOT A PREDICTIVE VALUE IN PATIENTS AFFECTED BY RECTAL CANCER TREATED WITH NEOADJUVANT CHEMORADIOTHERAPY

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Aims: To assess the role of [18F] FDG-PET/CT parameters in relation to tumor characteristics, tumor response and prognosis in a series of locally advanced rectal cancer (LARC) treated with neoadjuvant chemoradiotherapy (CRT).

Methods: 100 patients treated with neoadjuvant CRT followed by radical surgery were enrolled. Main outcome measures: maximum standardized uptake value (SUVmax), SUVmean, metabolic tumor volume (MTV), and total lesion glycolysis (TLG) of the baseline [18F] FDG-PET/CT were calculated. The correlation of PET parameters with tumor staging, tumor regression grade (TRG), and survival was analyzed.

Results: According to TRG classification, 16 patients (16 %) were classified as TRG1 and 84 (84%) as TRG2–5. Mean values and SD of SUVmax, SUVmean, MTV, and TLG are reported in Table 2. MTV (p=0.04) and TLG (p=0.03) were significantly higher in the T4 than in the T3 cases. None of SUV parameters of the primary tumor correlated with lymph-

node involvement as defined at initial clinical staging. From logistic regression model, primary tumors with SUVmax, SUVmean higher than median values were statistically associated with T4-stage (OR 5.2; 95% CI 1.0-27.2; OR 5.3; 95% CI 1.0-27.7). [18F]FDG-PET parameters of non-responders (TRG2-5) were not significantly different from responders (TRG1), although each value was higher in TRG2-5 than in TRG1. None of the PET parameters resulted statistically associated with TRG. The median follow-up time of the whole series was 32 months (range 12-116 months). At the time of analysis, 8 patients had died (8%), 6 out of 8 died of metastatic progression disease. Twenty-four patients (24%) developed "loco-regional" or at "distance" relapse. All but one of them were classified as TRG2-5 at the histological analysis: 10 developed a loco-regional recurrence (41.7%) and 14 liver and/or lung metastasis (58.3%). None SUV parameters were significantly correlated to tumor progression.

Conclusions: Our data demonstrate specific PET parameters cannot be used as a surrogate marker of rectal tumor regression grade after neoadjuvant CRT. Despite a relative short follow-up time and a low rate of tumor relapses, the large number lesions studied suggest those with higher SUV uptake or MTV are not the most at risk of recurrent disease or tumor death.

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SECOND PELVIC RECURRENCE OF RECTAL CANCER SUCCESSFULLY TREATED WITH A RE-REIRRADIATION (3RD RADIATION COURSE)

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Aims: In case of recurrence, re-irradiation of previously irradiated patients may increase the rate of salvage radical resection. Due to the delivered high dose of re-irradiation an emerging concern is the incidence of radiation-induced lumbosacral plexopathy, therefore a re-reirradiation is never considered. This report describes a third irradiation of a lesion adjacent the lumbosacral plexus using a highly selective technique, sparing it almost completely.

Methods: A 53-year old woman treated in 2008 for a locally advance rectal cancer recurred in 2011 and underwent reirradiation and surgery. In December 2015 a MRI showed a single local recurrence infiltrating the muscle right next to the right lumbosacral plexus and close to the cauda equine. It was decided to re-reirradiate the single lesion. The total dose deriving from the previous treatment plans was assessed by non-rigid image registration, using the dedicated tool implemented in MIM 6.1.7 (MIMvista Corp., Cleveland, US-OH). The treatment was performed with Cyberknife (Accuray, Sunnyvale, CA) with a schedule of 20 Gy in 5fractions (4Gy per fraction). The dose was prescribed to 70% isodose and target coverage was 97%.

Results: Two months after the treatment, MRI and the clinical examination were performed. MRI showed a decreased signal and a stable disease in term of dimensions.

Conclusions: This case report suggests that pelvic re-reirradiation might be a possibility in very carefully chosen cases of rectal cancer patients, using very selective treatment modalities

P135

TUMOR DELINEATION BY CT-MRI CO-REGISTRATION FOR PREOPERATIVE RADIOTHERAPY IN LOCALLY ADVANCED RECTAL CANCER: INTER AND INTRA OBSERVER AGREEMENT

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Aims: In the treatment of locally advanced rectal cancer (LARC), the intensification of preoperative radio-chemotherapy is becoming crucial as a way of increasing response rates as well as for the development of new organ-preservation approaches. Dose escalation programs are providing promising results but this approach requires optimization of boost volume definition. T2 weighted (T2w) magnetic resonance (MRI) imaging is the gold standard for rectal cancer staging and the diffusion-weighted sequence (DWI) allows for the best definition of the lesion. We compared the rectal gross tumor volume (GTV) delineated on computed-tomography (CT), T2w MRI and DWI MRI images to evaluate inter- and intra-observer agreement.

Methods: LARC patients (pts) underwent CT without mdc for radiotherapy treatment planning and subsequently T2w and DWI (b = 1500 s / mmq) MRI axial sequences. CT and MRI were acquired in the prone position and pts had the same bladder preparation for both procedures. Rigid CT-RM co-registration of image series was obtained. Four independent observers (ob) with different skill levels and experience delinea-

ted the GTV on CT, T2w and DWI MRI images. Conformity index (CI) was calculated between each ob-pair per patient per technique and between each technique-pair per patient per ob. Reliability between techniques and between ob was assessed using the intraclass correlation coefficient (ICC).

Results: Twenty consecutive pts were enrolled, 17 of whom were evaluable. CT, T2w MRI and DWI MRI mean GTV volumes in cm^3 were 45.61, 36.64 and 36.56, respectively for ob one; 44.34, 35.58 and 43.92 for ob two; 51.54, 35.58 and 38.74 for ob three; 42.08, 35.46 and 35.33 for ob four. ICC among ob for TC, T2w MRI and DWI MRI volumes were 0.75, 0.79 and 0.94 respectively and this reliability were confirmed by the comparison between ob-pair. Mean CI for TC, T2w MRI and DWI MRI between ob-pair were 0.57, 0.58 and 0.72; mean CI for ob one, two, three and four between modality-pair were 0.31, 0.34, 0.31 and 0.29 respectively. Mean difference of urinary bladder volume between CT and MRI was 25 cm^3 but this did not affect CI.

Conclusions: MRI, mostly DWI series, showed high agreement among different ob and therefore could be useful for the definition of GTV in LARC. Studies with a larger number of pts are needed to assess whether such agreement is significant. It remains difficult to determine whether there is a better imaging for defining the true tumor volume.

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THE ROLE OF PET/CT IN THE TREATMENT OF ANAL CANAL CARCINOMA (ACC) WITH VOLUMETRIC MODULATED ARC (RAPIDARC, RA) THERAPY AND CONCOMITANT CHEMOTHERAPY: A MONO-INSTITUTIONAL EXPERIENCE

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Aims: This study was intended to determine the role of PET/CT in the treatment of anal canal carcinoma (ACC) with volumetric modulated arc (RapidArc, RA) therapy and concomitant chemotherapy.

Methods: A retrospective analysis has been conducted on 102 patients treated with RA since 2009. After CT-simulation with contrast and CT-PET simulation with FDG, the treatments were prescribed with SIB technique with 59.4 /61.6 Gy to the primary tumor and nodes CT-PET positive and 49.5/50.4 Gy to the elective nodes in 33/28 fractions.

Results: Median age of patients was 65 yrs; 90% had Stage II-III. All patients were staged with CT total body scan with contrast, pelvic MRI wit contrast and trans anal endoscopy/ultrasonografy. In all 102 patients CT-simulation with contrast and FDG CT-PET simulation with images-match was performed . Pathologic uptake was observed in all patients. For the definition of anal canal tumor localization, we considered as positive any focal uptake of FDG superior to the background activity. For nodal involvement we considered as positive, regardless of size, any increased uptake in the iliac region (external iliac, internal iliac and common iliac), the obturatory fossa, the mesorectal region , the inguinal node and the presacral nodes. In case of extra-pelvic findings, we reported as positive any increased uptake in lymph nodes greater than 10 mm in the longest diameter when located in the lomboaortic, retroperitoneal, retrocrural, mediastinal or supraclavicular regions. In 33/102 (32.3 %) patients the FDG CT-PET simulation was helpful to prescribe an additional dose to the pathological lymph nodes. There were no changes to the PTV tumor. In 16/102 (15.7%) cases the modification of the PTV node involved inguinal lymph nodes. In these cases, inguinal ultrasound confirmed the PET. In 4/102 (3,9%) cases distant metastases were detected, thus determining the change of therapeutic strategy.

Conclusions: Compared to conventional imaging, PET/CT allows a better definition of nodal status in one third of cases, thus modifying the strategy and possibly the treatment planning of patients affected by anal cancer.

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FEASIBILITY OF A COMBINATION OF 90Y/177LU-RADIOPEPTIDE THERAPY (PRRT) AND EXTERNAL BEAM RADIATION THERAPY (RT) IN NEUROENDOCRINE TUMORS (NETS): PRELIMINARY REPORT ON 25 CASES

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Aims: PRRT with 90Y-DOTATOC (YD) and 177Lu-DOTATATE (LuD) demonstrated up to 35% objective responses in NETs and acceptable toxicity profile. Given their rather indolent behavior, multiple treatments are sequentially applied and RT is frequently proposed as oligometastatic or palliative setting. Aim of this study is to assess whether the combination of PRRT and RT arise concern about tolerability.

Methods: Over 807 pts receiving PRRT (1997-2014) in our Institute, 17% underwent also RT (14% after PRRT, 3% before PRRT). Among these, 25 pts had dosimetry and clinical data of PRRT+RT. The primary NETs were: pancreas (12), lung (7), others (6), and multiple metastases were located in liver (24), bone (13),

others (14). Bone metastases were treated with 3D conformal RT, while oligometastases with image-guided intensity modulated radiotherapy (IMRT), volumetric modulated arc therapy (VMAT) or stereotactic RT. Treatment plans were optimized accounting for the dose received by the organs at risk (OARs) during PRRT (kidneys, K and red marrow, RM). Dose to the liver (L) was also evaluated. Doses to OARs and tumor were assessed and toxicity investigated (CTCAE v4). OARs for RT depended on the tumor site.

Results: The table shows median (range) details on activities and doses to OARs for PRRT and for RT. Large dose variability was observed in PRRT due to individual metabolism (tumor: 1-42 and 1-56 Gy/GBq for YD and LuD). Dose to kidneys by RT was negligible but in only 1 pt, (4-8 Gy) without K toxicity. Another pt had grade I kidneys toxicity. No severe red marrow toxicity was observed (14 pts grade I-II; 3 none). Median follow-up was 3.5 (0.2-12.3) years. 7 patients died.

Conclusions: PRRT and RT have generally different OARs with the great potential to increase the dose to the tumor without increasing toxicity, especially in red marrow and liver. However, most often RT irradiates bone and liver mets, potentially delivering non negligible doses to the kidneys, red marrow and liver, once summed to the doses delivered by PRRT (Figure d). Dosimetry for combined PRRT and RT deserves multidisciplinary discussion, being aware of the large variability of PRRT doses due to individual metabolic behavior. Our results indicate that combined PRRT and RT have a great potential and could represent a base for future prospective studies.

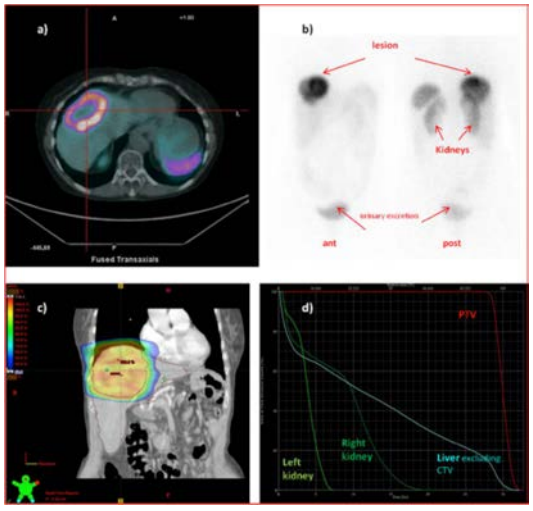

Figure 1. Dosimetry of adjuvant RT (30 Gy, 10 fractions, VMAT) in a patient with liver mets (200 ml) from pancreatic NET, after relapse to PRRT (27.9 GBq of LuD). Mean doses were: for PRRT, k=17 Gy, RM=1.1 Gy, L=1.4 Gy, clinical target volume (CTV)= 230 Gy; for RT: K_{right}= 8.3 Gy, K_{left}= 3.8 Gy, liver-CTV=12.8 Gy, CTV=30 Gy. Both treatments were well tolerated (RM grade I; K, L absent). a) fused SPET/CT image (axial) and b) planar whole body (anterior, posterior) images of LuD; c) isodose distribution in a coronal plane; d) Dose Volume Histograms for the planning target volume (PTV) and OARs. The patient is alive with no toxicity at 5 yr follow-up.

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PET GUIDED AND FFF DELIVERED STEREOTACTIC BODY RADIOTHERAPY FOR LIVER METASTASIS: A RISK-ADAPTED DOSE PRESCRIPTION STRATEGY.

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Aims: Stereotactic body radiotherapy (SBRT) is an emerging treatment option for unresectable liver metastasis (LM). An accurate treatment planning with risk-adapted dose prescription and the identification of specific constraints for organs at risk (OARs), daily Cone Beam CT (CBCT) as image-guidance, could allow an effective and safe treatment delivery. The diagnostic accuracy of 18F-FDG PET-CT as imaging pre and post SBRT could be a really useful tool. Moreover flattening filter-free (FFF) mode is a promising opportunity to reduce treatment time and related patients positioning uncertainties during delivery. Aim of the present study was to report feasibility and efficacy of PET guided FFF-SBRT in LM treated in our Cancer Care Center.

Table 1 Summary of patients' and lesions' characteristics.

Patients' and lesions' number	22 and 41
Mean age (range) [years]	69 (37-89)
Gender (M:F)	14:8
Primitive cancer (lesions' number)	
Colorectal	16
Esophagus	9
Lung	8
Pancreas	4
Ovary	3
Breast	1
Mean lesions diameter (range) [cm]	2 (1-6)
Mean lesions volume (range) [cm^3]	
CTV	6 (1-71)
PTV	25 (6-147)
Mean volume of healthy liver (range) [cm^3]	1117 (812-2129)
Relapse/Progression site (patients' number)	
Liver in field	6
Liver out field	11
Other	10

Methods: Between 10/2014 and 02/2017, 41 LM in 22 patients underwent SBRT. Clinical target volume (CTV) was identified on CT scan and 18F-FDG PET-CT performed in all patients before treatment. An additional margin of 3-5 mm was added for planning target volume (PTV). Dose-volume constraints for duodenum and stomach were D1cc <36Gy and D3cc<36Gy, respectively. A healthy liver volume >800cm3 was guaranteed in all cases, and to reduce interfraction liver deformations, abdominal compression was used. In order to respect OARs dose-constraints a risk-adapted dose prescription strategy was adopted, choosing between schedules with biologically effective dose (BED) <70Gy or >70Gy, according to ICRU83. SBRT was delivered with volumetric modulated arc technique (VMAT) using RapidArc and FFF mode. Daily CBCT

was performed. The patients were evaluated for acute toxicity and at 3, 6 and 12 months for late toxicity and treatment response with 18F-FDG PET-CT.

Results: Patients' and lesions' characteristics are summarized in Table 1. At median follow up of 12 months (range 2-30), 15 of 22 (68%) patients are alive. Dose with BED >70Gy was prescribed in 83% of cases. At 3 months complete response (CR), partial response (PR), stability disease (SD) and progression disease (PD) was observed in 66%, 27%, 3% and 4%, respectively. At 6 months 46% CR, 3% PR and 22% PD were reported; at 12 months 27% CR and 7% PD. No ≥G3 acute and late toxicity were found.

Conclusions: Risk-adapted dose prescription, image-guided and FFF mode were an effective and safe SBRT strategy for LM. Further clinical evaluations, including the role of 18F-FDG PET-CT, are warranted.

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NEOADJUVANT CHEMOTHERAPY AND VMAT RADIOTHERPY WITH SIMULTANEOUS INTEGRATED BOOST (V-SIB) FOR LOCALLY ADVANCED RECTAL CANCER. OUR EXPERIENCE

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Aims: To evaluate feasibility, tolerance and impact on local control in neoadjuvant chemotherapy and VMAT radiotherapy with simultaneous integrated boost (V-SIB) for locally advanced rectal cancer. This technics allowed us to increase the dose in the Tumor site.

Materials and Methods: From January 2015 to December 2016, 18 Patients (pts) affected by locally advanced rectal cancer were treated with Neoadjuvant Chemotherapy (capecitabine) and V-SIB followed by radical surgery in our center. All the cases were discussed in a multidisciplinary meeting. All patients had rectal adenocarcinomas, 13 G2 and 5 G3 at pretreatment biopsy. All patients had endoscopy and RM. The majority of patients had also an Endoscopic Ultrasound. At staging 2 patients had T3N0, 9 T3N1, 6 T3N2 and 1 T4aN1. All patients received 45 Gy in 25 fraction on whole pelvis, 1,8 GY for fraction, and an integrated boost on mesorectum, to a total of 50 Gy in 5 pts, 2 Gy fraction, and 52.5 Gy in 13 cases, 2,1 Gy. All patients had radical surgery after a median of 79 days (range 68 – 118 days). 16 patients had radical anterior rectal resection, 2 pts a "Miles" surgery.

Results: after neoadjuvant treatment 11 pts had G0-1 rectal toxicity, 5 pts G2. In 2 cases treatment was interrupted. In one case per G3 local toxicity in a frail patient, In one case we founded lung progression during treatment (initial PET classified M0). No genitourinary toxicity was recorded. At surgery 4 pts had a T0N0 (4/18 22%), 2 T1N0 (11%) 6 T2N0 (33%), 1 patient T2N1, one patient had initial T3N0 and T2N1a at surgical specimen. 12/16 patients had a complete response on nodal site initially N+. One patient had a liver metastasis resection diagnosed during liver intraoperative ultrasound, not visible at pre treatment staging.. During follow up one patient ad a gastric cancer (primary, total gastrectomy, NED after a total of 16 month). One patient T3N1 had a T1N0 at surgery but a local recurrence after 14 month. The patient with lung progression during treatment had also liver metastasis 6 month after initial treatment, and died after 17 month. No patients had post treatment permanent toxicity.

Conclusions: our data suggests the feasibility of the treatment with V-SIB, because it results in a non-aggressive management, with good results in desease local control. For our short follow up and thesmall number of cases in the study we are not able at now to consider impact of our treatment on Desease Free and overall survival.

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STEREOTACTIC BODY RADIATION THERAPY IN LIVER DISEASE

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Aims: The liver is a common site of metastases. At moment the curative management of unresectable hepatic tumors represents a major task. Aim of this study is to investigate the treatment outcomes, Local Control (LC), Progression Free Survival (PFS), Overall Survival (OS) and toxicities of patients with secondary and primary liver disease treated with Stereotactic Body Radiation Therapy (SBRT).

Methods: From December 2007 to March 2016, 43 patients with 58 lesions in the liver not eligible for surgical resection were included in this study. Metastatic tumors comprised the majority of patients (86%), Hepatocellular Carcinoma (HCC) represented the 5% and Intrahepatic Cholangiocarcinoma the 9% of all patients. Forty lesions (69%) were treated with one fraction: 20 Gy in 1 case, 23 Gy in 20 cases and 30 Gy in 19 cases. Fifteen lesions (26%) were treated with 3 fractions: total dose 42 Gy in 1 case, 45 Gy in 10 cases, 54 Gy in 4 cases. Three lesions (5%) were treated with 5 fractions: total dose of 40, 38 and 30 Gy respectively.

Results: Median follow-up time for all patients was 16 months (range, 1-106 months) and 24 months (range, 8-106 months) for living patients. LC was reached in 47 out of 58 (81%) treated lesions. The progression-free survival at 12 and 24-months was respectively 42% and 36%. The median time to progression was 8 months. Median overall survival was 20 months (CI: 95%, 8-32 months), with 12 and 24-months rates of 74% and 46%, respectively. At last follow-up twenty-eight (65%) were died, the treatment was well tolerated and all patients completed therapy without treatment interruptions. The toxicity was not more than Grade 2

according to the CTCAE v.4.

Conclusions: The SBRT is an alternative treatment for unresectable primary or secondary liver disease. The outcomes in terms of LC are good. However, long term survival results poor. The toxicity is acceptable, with low rates of toxicity, and low Grade of toxicity. In conclusion, the SBRT in the liver is feasible, effective and a safe option of treatment.

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ROLE OF SBRT IN PATIENTS WITH UNRESECTABLE PANCREATIC CANCER

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Aims: Pancreatic cancer remains a disease with a poor prognosis. In most cases patients (pts) affected by pancreatic cancer are unable to undergo surgical resection which is the only potentially curative treatment option. Chemoradiation is a standard of care treatment for pts with locally advanced unresectable disease, but local failure rates are high with conventionally fractionated radiotherapy. Stereotactic body radiotherapy (SBRT) represents a promising local approach with a good rate of local control (LC) and low toxicity. The aim of this study is to evaluate the effectiveness and the safety of SBRT in terms of LC, toxicities and overall survival (OS).

Methods: Between December 2012 and February 2017, 37 pts were treated with Hypofractionated Image Guided-Volumetric Modulated Arc Therapy (IGRT-VMAT) for unresectable pancreactic cancer at the diagnosis (29 pts) or for local recurrence after surgery (8 pts). Target was contoured using mdc enhanced CT. In 17 pts PET/CT scan was used to better define the treatment volume. OARs were defined according AAPM 101 and dose constraints used were: Dmax duodenum 24Gy (<0,035cc), Dmax Spinal Cord 18Gy, Dmax Aorta 30Gy (<0,035 cc), Dmax Stomach 24Gy (<0,035cc), Dmax Bowel 27 Gy (<0,035cc) and Liver V15<700cc. VMAT treatment was delivered by 6MV beam modulator Linac with 4mm MCL. Patient set-up at isocenter position was controlled before each fraction by Cone-Beam CT. Median delivered dose was 36Gy/3fx prescribed to the 70% isodose line (dose at the isocenter 51,43Gy). Target volume ranged from 8,04 and 145,21cc (median 73,35cc). 19 pts received Gemcitabine chemotherapy before SBRT and 7 after SBRT. Toxicities were assessed by CTCAE4.0 criteria and results were evaluated 2 months after the end of SBRT and every 3 months successively using CT and/or PET/CT.

Results: Median follow-up was 7,8 months (range 2-51,2). LC ratio was 86,5% (1 complete response, 27 partial response and 4 stable disease). 5 pts presented local progression. 13 pts developed early metastatic disease. No grade 2 or higher acute or late toxicity was observed. OS was 58%, 31% and 10% at 3, 6 and 12 months respectively (median OS 7,4 months).

Conclusions: In our experience SBRT for unresectable pancreatic cancer is safe and a high rate of LC can be achieved with low toxicity. Furthermore, another advantage of SBRT is the short course of radiation treatment giving pts with poor prognosis the opportunity to have a better quality of life in their remaining time earlier.

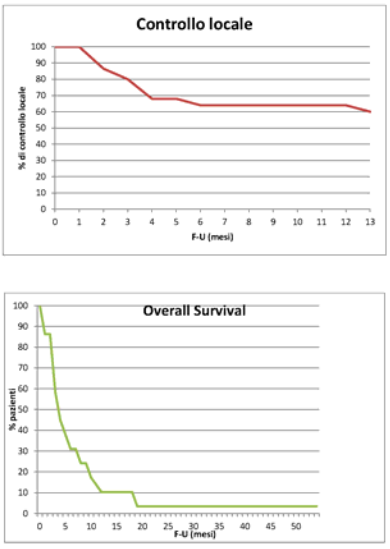

Figure 1.

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NEOADJUVANT RADIOCHEMOTHERAPY IN LOCALLY ADVANCED RECTAL CANCER: VALUE OF IMAGING IN PREDICTING CLINICAL OUTCOMES

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Purpose. Correlation between imaging (PET-TC and magnetic resonance) and pathological response after neoadjuvant concurrent radiochemotherapy, followed by surgery. We report our experience at S. M. Goretti Hospital in these last years.

Materials and Methods: From January 2007 to December 2014 we treated 47 patients diagnosed with locally advanced rectal cancer. 15 patients were females and 32 males. Median age at diagnosis was 65 years (range 47-83). Clinical stage was as follows: 16 pts stage IIA (T3N0) and 31 pts IIIB (T3-4 N1). All patients received a pre and post treatment staging including colonoscopy and computer tomography. Perfusion computer tomographyin was performed in the first 11 pts. A Magnetic Resonance and a PET-TC simulation was performed in the last 30 pts. All patients received a dose of 50-50.4 Gy in 1.8-2 Gy per fraction to the pelvic area. Concomitant chemotherapy was based on pro-

tracted intravenous infusion 5 FU (220 mg/mq) in 19 pts, capecitabine (825 mg/mq twice daily) throughout radiotherapy coursein 23 pts, and in 5 pts Cisplatin 60 mg/mq-5 FU 1000 mg/mq 1-4 days q28. Surgery was performed 6-8 weeks after radiotherapy course.

Results: After a median follow-up of 76 months (range 25-116 months), 43 patients were still alive and free of disease, 4 pts died of local progression of disease and systemic metastases, after 18, 19, 28 and 36 months of follow-up. Sfincter saving surgery was performed in 50% of patients eligible for abdominal perineal resection. Complete pathological response was reported in 11 patients (pCR: 23%) and correspons to a clinical complete response, as assessed by PET-TC parameters. The treatment was well tolerated, moderate acute and late toxicity (G1-2 according to RTOG scale) were reported. No patient suffered a performance status worsening during the scheduled treatment.

Conclusions: These results sugests that preoperative radiochemotherapy is a well tolerated and effective treatment and PET-TC parameters correlate clinical and pathological response.

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HELICAL TOMOTHERAPY IN UPPER GASTROINTESTINAL TRACT CANCER: IMPACT OF TECHNIQUE IN TREATMENT INTERRUPTION

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Aims: As showed in literature, prolonged radiation treatment time (RTT) is associated with worse survival in several tumor types. This study evaluates the impact of Image Guided-Intensity Modulated Radiation Therapy (IG-IMRT, Helical Tomotherapy) in toxicity-related treatment interruption in upper gastrointestinal tumors.

Methods and materials: From May 2013 to March 2017, 40 patients (pts) (26 M; 14 F) with upper gastrointestinal cancers (8 esophageal, 5 gastric, 22 pancreatic and 5 hepatobiliary) underwent radiation treatment in our institution. Patients received concomitant capecitabine based chemo-radiation (CHT-RT) or induction gemcitabine based chemotherapy followed by concomitant CHT-RT with definitive, neoadiuvant or adiuvant intent. All patients were treated with IG-IMRT Helical Tomotherapy with different doses and fractionations. We calculated Radiation Therapy Treatment Time (RTT) and classified it according to McMillan study in: standard (45Gy/25 fr: 32-38 days; 50,4Gy/28 fr: 28-42 days; 36Gy/12 fr:21-23 days) and prolonged (45Gy/25 fr: >38 days; 50,4Gy/28 fr: >42 days; 36Gy/12 fr: >23 days). We assessed treatment interruption and its relative toxicity according to RTOG acute radiation morbidity criteria.

Results: Median RTT was 36 days, range 21-60. Standard RTT was performed in 24 patients (60%) and prolonged in 10 patients (25%). 6 pts (15%) definitively suspended treatment due to worsening performance status (4 patients) and disease progression (2 patients). Among prolonged group average treatment interruption days was 6 (range 3-17). Interruption was related to haematological toxicities, abdominal pain and weight loss requiring replanning.

Conclusions: IG-IMRT with Helical Tomotherapy provides optimal target coverage minimizing treatment-related toxicity and, consequently, treatment interruptions in upper gastrointestinal cancer. Longer follow-up is needed to assess the impact of RTT on local control and overall survival

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PANITUMUMAB SEQUENTIAL PALLIATIVE RADIOTHERAPY IN THE TREATMENT OF ADVANCED RECTAL COLON CANCER

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Aims: Panitumumab is a monoclonal antibody indicated for the treatment of patients with metastatic colorectal cancer which expresses the epidermal growth factor receptor (EGFR) after the failure of the chemotherapeutic regimens containing fluoropyrimidine, oxaliplatin and irinotecan, in the case that tumors present the non-mutated KRAS gene (wild-type). We wanted to test the safety and the efficacy of a sequential chemotherapical and radiotherapical treatment with panitumumab in 5 patients affected by locally advanced large intestinal adenocarcinoma with pain and colonrectal bleeding.

Methods: Five patients with symptomatic locally advanced rectal cancer were treated with two panitumumab chemotherapy cycles and subsequently they were also subjected to pelvic palliative radiotherapy with a 39 Gy DT in 13 fractions, followed by another 3 panitumumab chemotherapy cycles.

Results: All patients have completed their radiotherapy treatment with a marked improvement of symptoms. The magnetic Resonance in the follow-up demonstrated a reduction of the neoplastic mass

Conclusions: Radiotherapy is the primary treatment for locally advanced rectal colon cancer. Panitumumab chemotherapy did not lead to an increase in toxicity. All patients have showed a reduction of their symptoms and a response in terms of the rectal heteropathy's reduction.

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ADJUVANT CHEMORADIATION WITH 5-FU, CAPECITABINE OR GEMCITABINE IN PATIENT WITH DUCTAL PANCREATIC CANCER

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Aims: Evaluate outcome and prognostic factors in patients treated with adjuvant chemoradiation after pancreatic resection.

Methods: Between June 2007 to December 2015, 96 patients underwent adjuvant radiotherapy and concurrent chemotherapy with 5- fluorouracil (26%), capecitabine (61%) or gemcitabine (13%). Complete pancreatic resection was performed in 8% of patients, tail resection in 18 % of patients and head/body resection was performed in 74% of patients. The pathological stage was as follows: 7% stage I, 67% was stage II, 25% was stage III and 1% was stage IV.

Results: The median follow up was 27 months. Mean overall survival was 22,3 months. The most common toxicity (in capecitabine or 5-FU patients) was grade 1-2 GI toxicities, gemcitabine caused frequent haematolgical toxycities, reported in 44% of cases. Grade 3 and grade 4 of toxicities were observed in 13 and 2 patients respectively. Grading, stage and postoperative chemotherapy were significant prognostic factors for survival and relapse.

Conclusions: Adjuvant conformal radiotherapy and concurrent chemotherapy is a recommended, feasible and well-tolerated treatment and may be beneficial for patients.

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SORAFENIB AND RADIATION THERAPY FOR THE TREATMENT OF ADVANCED HEPATOCELLULAR CARCINOMA: A CASE REPORT

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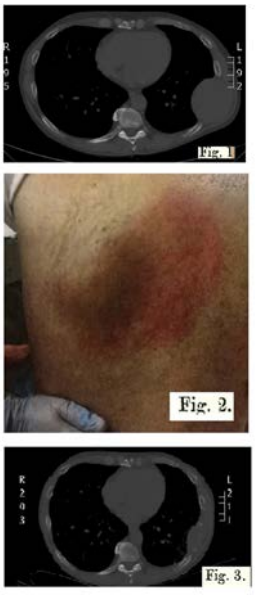
Aims: Hepatocellular carcinoma (HCC) is the third highest cause of cancer-related death worldwide and its incidence is increasing. Although lung and bone is the most common site of extrahepatic metastases from hepatocellular carcinoma (HCC), the optimal treatment for such metastases has not been established. External beam radiotherapy (EBRT) is becoming a useful local control (pain, infiltration).Sorafenib is the only systemic treatment that improves survival in advanced disease, however, prognosis remains dismal. We report a case of combination of radiation therapy and Sorafenib for advanced HCC and resulting response and toxicity.

Methods: A 60-year-old male presented with thoracic pain and temperature, on a background of alcohol use and no chronic active hepatitis infection.A palpable left posterior chest wall mass, was noted on physical examination.He had an ECOG PS of 2-3 and required Oxycodone 10 mg daily for pain control.CT scan confirmed a left pleura mass (8 x 63 x 64 cm), interesting chest wall,with involvement of VI-VII-VIII ribs,and a diffuse infiltrate process involving nearly the entire VI segment of the liver (Figure 1). His baseline bloods confirmed a Grade 2 transaminitis but otherwise normal liver reserve (Child–Pugh A); FP at diagnosis was >2200. A mass biopsy was performered, and the hystologic results was haepatocaellular carcinoma. We prescribed 30 Gy in 10 fractions (3 Gy per fraction) to the mass at the chest wall and started concurrently Sorafenib

Results: After a week,the patient developed symptoms of hand foot syndrome (edema,burning sensation,especially over palmoplantar surfaces) and erythema in the irradiated area-G2-(Figure 2). At the physical examination the chest lesion was reduced(4.5 cm vs 8 cm). We decided to stop radiotherapy and Sorafenib and finally palliative radiation dose,delivered to the lung lesions,was 21 Gy. After 10 days we revalue the clinical presentation: patients presented no pain and erythema was G1. Repeat imaging after 3 months of intermittent Sorafenib confirmed a marked decrease in the size of the tumor mass at the chest wall with segment VI of the liver appearing completely atrophic and evidence of re canalization of the left portal vein (Figure 3); FP continues to fall consistent with ongoing response.The patient had a marked clinical response with decreased pain and improved performance status (ECOG PS 1).

Conclusions: Concomitant Radiotherapy and Sorafenib show a good response to treatment,but might present a high toxicity,particulary in irradiated skin.



Figures 1,2,3.

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IFRT VS ISRT: DOSIMETRIC EVALUATION OF TREATMENT VOLUMES AND ORGAN AT RISK IN LYMPHOMAS

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Aims: Target volumes and OAR's dose evaluation in Lymphoma treatment planning: IFRT vs ISRT.

Methods: In our department we evaluate patients affected by NHL/HL before the beginning of chemotherapy; at that time we also acquire a CT scan performed in treatment position. At the end of the scheduled chemotherapy patients perform another CT scan that will be fused with the first one for definitive treatment planning, also considering restaging diagnostic CT and PET-CT. From 2012 to 2016, 24 patients were planned using this approach. We select 3 cases. For each patient, two 3D-CRT plans were made: one based on IFRT and the other on ISRT approach, both to deliver 30Gy/15fr on the initial sites of disease (PTVII) and an additional boost of 6Gy/3fr on residual disease (PTVI). For ISRT we consider cranium-caudal limits in pre-chemo CT and later-lateral limits in post-chemo CT. The prescription dose for PTV was calculated based on constraints for lung sum (V20<32%, MLD<20Gy), heart (V30<46%, Dmean<26Gy) and thyroid (Dmean). Plan evaluation was made by TPS Oncentra Exernal Beam v4.5.2.

Results: CASE#1 (mediastinum, bilateral neck and axilla): PTVII 2079.1 vs 1396.4cc for IFRT and ISRT respectively; Lung: V20 49.5% vs 39.5% for IFRT and ISRT respectively; MLD 19.8 vs 17.5Gy for IFRT and ISRT respectively. Heart: V30 78.3% vs 29.9% for IFRT and ISRT respectively and Dmean 30.3 vs 14.8Gy for IFRT and ISRT respectively. Thyroid: Dmean 35.1 vs 29.2Gy for IFRT and ISRT respectively. CASE#2 (bilateral neck, mediastinum): PTVII 1376.8 vs 651cc for IFRT and ISRT respectively; Lung: V20 35.3% vs 24.1% for IFRT and ISRT respectively; MLD 14.4 vs 9.9Gy for IFRT and ISRT respectively. Heart: V30 84.5% vs 8.9% for IFRT and ISRT respectively and Dmean 30.9 vs 7.4Gy for IFRT and ISRT respectively. Thyroid: Dmean 32.3 vs 32.5Gy for IFRT and ISRT respectively. CASE#3 (mediastinum): PTVII 713.6 vs 412.7cc for IFRT and ISRT respectively; Lung: V20 38.2% vs 25.6% for IFRT and ISRT respectively; MLD 15.6 vs 11.5Gy for IFRT and ISRT respectively. Heart: V30 74.8% vs 36.1% for IFRT and ISRT respectively and Dmean 29.3 vs 25.5Gy for IFRT and ISRT respectively. Thyroid: Dmean 1.1 vs 0.4Gy for IFRT and ISRT respectively.

Conclusions: We conclude that the use of ISRT reduces OAR's radiation exposure. In addition the fusion between the first and the second CT simulation can improve the accuracy of contouring.

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RADIOTHERAPY AFTER AUTOLOGOUS SELF CELL TRANSPLANT IN RELAPSED/REFRACTORY HODGKIN LYMPHOMA; OUTCOME AND RISK STRATIFICATION BASED ON THE GHSG PROGNOSTIC SCORE

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Objectives: To retrospectively asses outcome and toxicity of consolidation involved-field radiotherapy (IFRT) after high-dose chemotherapy plus autologous self cell transplant (HCT-ASCT) in recurrent or refractory Hodgkin lymphoma (HL), and to evaluate whether the German Hodgkin Study Group (GHSG) risk model improve prognostication in this setting.

Methods: The analysis was conducted in 30 patients who underwent HCT-ASCT for recurrent or refractory HL and subsequently received consolidative IFRT at a single institution from 2002-2015. Our policy was of adding IFRT in patients with positive PET scan before ASCT (23/30 patients, 77%), and/or irradiating sites of bulky disease at relapse (11/30 patients, 37%). Of the 30 patients, 8 (27%) patients had stage IV HL. Median interval from ASCT to IFRT was 2.5 months (range, 1-14 months), and the median IFRT dose was 35 Gy (range, 25-44 Gy). Patients were stratified into 4 risk groups according to the presence of 5 easily available clinical risk factors identified by the GHSG; (1) stage IV disease; (2) time to relapse ?3 months; (3) ECOG-PS ?1; (4) bulk ?5 cm; and (5) inadequate response to salvage chemotherapy. Group-stratified Kaplan-Meier PFS curves were estimated and compared using the log-rank test, starting from the date of completion of IFRT.

Results: The median follow-up was 34 months (range, 1-132 months), and the 2-year PFS in the entire series was 60%. Only 6 patients failed in the IFRT site, corresponding to a in-field control rate of 79% at 2 years. Four patients out of the 24 who had medistinal radiation developed pulmonary toxicity (one patient experienced grade 2 radiation pneumonitis, 1 patient developed fatal pneumonitis, and two patients had bacterial pneumonia). The 2-year PFS in 4 risk groups of the risk score were: 86%, 83%, 50%, 30%, and 29%, for 0 risk factors (n=8), 1 risk factor (n=6), 2 risk factors (n=2), and 3-5 risk factors (n=14), respectively. The difference between the PFS curves was statistically significative (p=0.008).

Conclusions: Consolidation IFRT after ASCT in HL is effective for selected patients. Based on the 2-year PFS in each of the GHSG risk groups, our data indica-

ted that the groups with 0-1 risk factors are most likely to benefit from consolidation IFRT.

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DOSIMETRIC EVALUATION OF CARDIAC STRUCTURES AND BREAST IN EARLY STAGE HODGKIN LYMPHOMA TREATED WITH IMRT BUTTERFLY RADIOTHERAPY

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Aims: Patients affected with early stage Hodgkin's lymphoma (LH) show long-term survival after a combined modality treatment approach. Thus, it is important to assess the risk of long-term complications after therapy such as cardiovascular disease and breast cancer, especially in young people. In this study, we retrospectively analyzed the dose received by different cardiac substructures and breasts using intensity-modulated radiation therapy (IMRT) "butterfly" technique (BT).

Materials and Methods: We selected 5 female patients (mean age 28,4±7.3) with stage IIA mediastinal LH and bulky disease at diagnosis, treated with involved-site radiotherapy (IS-RT). Syntregra software (Philips Medical Systems) was used to merge planning CT scan with pre-RT contrast enhanced CT scan. Treatment plans were performed with TPS Pinnacle, planning a total dose of 30Gy in 15 fractions. We contoured the clinical target volume and organ at risk (OR), specifically spinal cord, right (R) and left (L) breasts, lungs, whole heart and the following cardiac substructures: right and left atrium, right and left ventricle, aortic, pulmonary, mitral and tricuspid valves, left main, left anterior descending, left circumflex and right coronary arteries. IMRT plans were generated using 5 coplanar beams (3 anterior 330°- 0°- 30° and 2 posterior 160°-210°) BT. One patient with gigantomastia (each breast 2500cc in volume) was planned modifying BT inverting field direction (2 anterior and 3 posterior beams) to reduce breast exposure. We analyzed PTV coverage (mean dose -Dmean- and V95% -percentage of volume receiving 95% of prescription dose-), and doses to normal structures (Dmax, Dmean, percentage of volume receiving 30Gy -V30-, 25Gy-V25-, 20Gy-V20- and 5Gy -V5-).

Results: We met the following PTV coverage: V95%= 95,3 ± 2,1% and Dmean =29,9 ± 0,2Gy. Dosimetric parameters for cardiac substructures and other OR are reported in table. For R and L breast in the patient with gigantomastia, Dmean was 1,0Gy and 1,9Gy, V30 was 0,0% and 0,0%, V25 0,0% and 0,5%, V20 0,8% and 2,0%, V5 3,5% and 9%, respectively.

Conclusions: Compared to AP-PA standard technique, IMRT BT achieves adequate target coverage with better conformity. New objectives during IMRT optimization should be introduced in order to spare different cardiac substructures identified in literature as implicated in cardiovascular late toxicity. We further suggest optimization in breast tissue especially in patients with high breast volume.

Table 1A: Maximum and mean dose to organs at risk

Organ at risk	Maximum dose (Gy) ± SD	Mean dose (Gy) ± SD
Heart	29,8 ± 1,7	5,0 ± 2,2
Left ventricle	17,7 ± 10,7	3,2 ± 1,5
Right ventricle	22,1 ± 8,2	2,9 ± 2,2
Left atrium	28,7 ± 1,2	10,3 ± 3,5
Right atrium	29,3 ± 2,1	8,4 ± 7,5
Aortic valve	21,1 ± 7,3	15,8 ± 8,8
Pulmonary valve	25,1 ± 7,3	18,7 ± 8,9
Mitral valve	3,1 ± 2,8	2,4 ± 1,5
Tricuspid valve	5,8 ± 8,2	3,7 ± 3,9
Left main coronary a.	24,3 ± 5,8	20,6 ± 7,9
Left anterior descending a.	18,0 ± 10,0	4,1 ± 2,8
Left circumflex coronary a.	19,8 ± 9,2	14,2 ± 8,9
Right coronary a.	21,9 ± 10,5	17,0 ± 11,0
Left Breast	22,5 ± 7,7	1,4 ± 1,05
Right Breast	27,8 ± 5,0	1,8 ± 1,3
Total lung	31,2 ± 0,9	7,6 ± 2,2
Spinal cord	27,9 ± 0,2	-

Table 1B: Mean percent volumes of organs at risk receiving 30, 25, 20 or 5 Gr

Organ at risk	V30 (%)	V25 (%)	V20 (%)	V5 (%)
Heart	0,0	4,1	7,7	18,0
Left ventricle	0,0	0,2	0,8	8,1
Right ventricle	0,0	1,2	2,3	12,4
Left anterior descending aorta	0,0	3,2	2,8	19,1
Left Breast	0,0	0,6	1,4	5,1
Right Breast	0,0	0,8	4,5	7,6
Total lung	0,2	6,6	12,5	42,1
Spinal cord	0,0	15,2	29,2	48,9

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EFFICACY AND SAFETY OF LOCAL RADIOTHERAPY WITH NEW TARGET THERAPIES IN PATIENTS WITH MULTIPLE MYELOMA

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Aims: This study evaluated the efficacy and safety of radiotherapy for osteolytic bone lesions in multiple myeloma (MM) concurrently delivered with new target therapies.

Methods: We selected a total of 31 patients, 17 male and 14 female, affected by MM, treated with Radiotherapy (RT) with a dose of 30 Gy delivered in 10 daily fractions, from 2010 to 2016. All of these received different concurrent novel agents as Bortezomib and/or Talidomide. Treatment sites were as following: 5 cervical rachis (16.13%) , 20 dorsal rachis (64.51%), 4 lumbosacral rachis (12.90%), 1 femoral diaphysis (3.22%) and 1 humerus (3.22%). We evaluated pain response, radiotherapy toxicity and haematologic toxicity.

Results: The median age at MM diagnosis was 66.29 years (range 37-76), while median age at radiotherapy treatment was 67.71 years (range 41-84), All patient completed RT without interruptions. Twenty/3 patients received bortezomib (74.19%), 6 patient Talidomide (19.35%) and 2 patient Bortezomib and Talidomide (6.45%) concurrently with radiotherapy. Pain relief (NRS scale) was observed in 30 of 31 patients (96.77%). The median NRS score before RT was 6.96 (range 1-10) versus 2.92 (range 0-9) after RT,

the p-value is <0.00001 with the significant levels of p<0.05. In 30 of 31 we also observed a decrease of corticosteroid and other killpain treatments. No hematologic toxicities of any grade was observed in 100% of treated patients, while we observed RT toxicity (grade 1 by RTOG) in 6 patients (1 nausea, 1 diarrhea, 4 dysphagia) due to treatment site (mostly at dorsal rachis).

Conclusions: Radiotherapy and concurrent new target therapies was safe and well tolerated in all our MM patients. All MM patients showed an important pain decrease and, in particular, no adverse events were recorded.

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TBI IN ALLOGENEIC BONE MARROW TRANSPLANTATION: RESTROSPECTIVE CLINICAL ANALYSIS OF A STANDARD TECHNIQUE REGARDING OUTCOME, DOSIMETRIC AND LOGISTIC PARAMETERS AS A BENCHMARK FOR COMPARISON TO A RECENTLY DEVELOPED VOLUMETRIC ARC (VMAT) APPROACH

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Aims: To evaluate the clinical and dosimetric results of total body irradiation (TBI) with a standard open-field technique and to estimate the relative merit of a volumetric-arc (VMAT) technique compared to the traditional one. Primary end-point was clinical outcome regarding efficacy and lung toxicity with standard TBI after both myeloablative and nonmyeloablative conditioning. Secondary endpoints were dosimetric and logistic/economic factors to serve as a benchmark for a comparison to a VMAT-based approach.

Methods: From 2008-2016 at the Dept. of Radiotherapy, Policlinico Modena 35 pts were conditioned for allogenic transplants for different hematological malignancies. Induction chemotherapy (iChT) varied between patients. After iChT, 22/35 pts (65%) were in complete response (CR); 9/35 pts (26%) had progressive disease (PD); 2/35 pts (6%) were in partial response (PR). Only 1/35 (3%) was treated in first relapse. All patients underwent allogenic transplants. 18/35 pts (51%) received TBI as myeloablative treatment (MA-TBI), with a total dose of 12 Gy at 2 Gy per fraction, twice daily. 17/35 pts (49%) received non-myeloablative TBI (NMA-TBI), 9 of which received a total dose 4 Gy at 2 Gy per fraction, twice daily and 8 patients received 2 Gy in one single dose.

Results: Over both conditioning paradigms, after transplant, 29/35 pts (83%) were in CR. 6/35 (17%) who did not respond to therapy, died. 21/35 (60%) pts are alive at analysis and 19 of these pts are disease free.. Acute and subacute lethal toxicity was observed as febrile neutropenia for 1/35 pts (3%, after NMA-TBI) and pneumonia for 3/35 pts (8%, two of which after MA-TBI). Lung dose never exceeded 10 Gy and dose rate was below 20cGy/min in all patients. For MA-TBI the average treatment time at first fraction was 106 min, for NMA-TBI 52 min and 36min for follow-up fractions. Literature data regarding VMAT suggest significantly shorter treatment times (<60min and <30min min for first and consecutive fractions of MA-TBI) can be achieved with similar dosimetric results albeit with a higher instantaneous lung dose rate (100-120cGy/min).

Conclusions: Dosimetric and toxicity results with standard TBI were favourable and in line with literature data. The overall treatment time, however, was longer than what can be achieved with VMAT with similar dosimetric characteristics. VMAT would result in a more comfortable set-up for the patient patient and faster overall execution if pulmonary toxicity remains low despite higher instantaneous dose rates.

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DOSIMETRIC AND CLINICAL OUTCOMES OF INVOLVED-FIELD RADIOTHERAPY FOR EARLY-STAGE LYMPHOMA WITH MEDIASTINAL INVOLVEMENT

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Aims: To evaluate the dosimetric and clinical outcomes of involved-field radiotherapy (IF-RT) for patients with early-stage lymphoma with mediastinal involvement.

Methods: Patients with early- stage Hodgkin's lymphoma and non Hodking's lymphoma involving the mediastinum were reviewed. All patients received polichemotherapy followed by IF-RT. Three-dimensional conformal radiotherapy (3D-CRT) plans were generated. The dose-volume histograms of the target volume, heart and cardiac cavities, left coronary artery and lungs were evaluated. During the follow up patients underwent periodic cardiologic controls, which included echocardiogram. Toxicity was reported using the Common Terminology Criteria for Adverse Events version 4.02.

Results: Eighteen patients with early-stage disease with mediastinal involvement (14 Hodgkin's lymphoma and 4 Non Hodgkin's lymphoma) treated from December 2008 to October 2016 were retrospectively reviewed. The median age was 27 years (range 16-79). 14 patients had Stage IIA disease and 4 patients had Stage IIB. One patient had a bulky mediastinum at presentation and 12 patients had involvement of both the mediastinum and either cervical or axillary nodes. The median dose to the planning target volume (PTV) was 30.6 Gy (range 19.8-46.8). The mean V20 to the lungs

was 12% (range 1-36). The mean V25 to the whole heart and mean dose were 8.5% (range 0-29) and 6,2 Gy (range 0-16), respectively. The mean V25 to the left atrium was 16.2%(range 0-55). The mean V30 to the left and right ventricle were 0.27% (0-4,8) and 1.95%(0-25), respectively. The mean maximum dose to the left coronary artery was 19.3 Gy (range 1,2-31). At the median follow up of 50 months (range 5-103), we found 2 recurrences and 1 patient dead for disease. At the time of this analysis 16 patients are alive without disease. One patient developed an acute G1 esophagitis (CTCAE 4.2) and 1 patient experienced a reduction of ejection heart fraction. No other late toxicities were reported.

Conclusions: IF-RT ensures a good outcome, with mild toxicity in patients with early-stage mediastinal lymphoma. Longer follow-up will be needed to accurately determine late effects.

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MODERATELY HYPOFRACTIONATED RADIOTHERAPY IN POSTOPERATIVE PROSTATE CANCER: A MONO-ISTITUTIONAL EXPERIENCE

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Aims: To report the outcome of moderately hypo-fractionated radiation therapy in patients with prostate cancer after radical prostatectomy using intensity-modulated radiation treatment with simultaneous integrated boost (IMRT-SIB).

Methods: From April 2011 to April 2016, 121 high risk patients were included in this study. High risk was defined by positive surgical margins, pathological stage T3b, positive lymph nodes and/or detectable PSA after surgery. All patients underwent adjuvant treatment and were treated at Sant'Orsola-Malpighi Hospital in Bologna. All patients received 66 Gy to the prostate bed in 30 fractions (2.2 Gy per fraction). Pelvic nodes irradiation was prescribed to 62.8% of patients (54 Gy in 30 fractions). Acute toxicity was recorded and evaluated according to RTOG (Radiation Therapy Oncology Group) criteria and late toxicity according to the RTOG-EORTC (European Organization for Research and Treatment of Cancer) scale.

Results: No cases of grade ≥ 3 acute gastrointestinal and genitourinary toxicity were recorded. Grade 2 acute gastrointestinal and genitourinary toxicity was recorded in 3.3% and 6.6% of patients, respectively. Five-year grade 3 late gastrointestinal and genitourinary toxicity was 0% and 2.1%, respectively. Overall 5-year biochemical relapse-free survival (bRFS) was 87.4%.

Conclusions: Adjuvant moderately hypofractionated IMRT-SIB treatment, enabling a reduction in the overall treatment time, shows a favorable acute and late toxicity profile and promising results in terms of relapse-free survival.

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U0126 MEK/ERK INHIBITOR INCREASES PROSTATE CANCER CELLS RADIOSENSITIVITY IN VITRO AND IN VIVO BY DOWNREGULATING MEK/ERK/C-MYC AXYS AND AFFECTING DNA REPAIR SIGNALS

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Prostate cancer (PCa) is the most commonly diagnosed cancer among men in western countries. Radiotherapy (RT) is considered as the first-line treatment for localized PCa because of its non-invasiveness. It is generally accepted that the primary therapeutic effect of RT is the induction of DNA damage in the irradiated cells. However, PCa cells often show resistance to RT and the molecular mechanisms responsible for radioresistance are largely unknown. MAPK signal transduction pathways respond to extracellular and intracellular cues by activating specific cellular signaling cascades to regulate cell cycle, growth, proliferation, differentiation and survival. Uncontrolled activation of MAPKs as well as of DNA-damged repair mechanisms have been related to PCa radioresistance but no data have been yet collected on the role of MAPKs as potential therapeutical radiosensitizing target. This study was designed to examine whether the ERK pathway affects intrinsic radiosensitivity of PCa cancer cells. Exponentially growing human PCa, PC3, LnCap, and 22Rv1 cell lines were used. The specific MEK/ERK inhibitor, U0126, reduced the clonogenic potential of the three cell lines, and was affected by radiation. U0126 inhibited phospho-active ERK1/2 and reduced DNA protein kinase catalytic subunit (DNA-PKcs) suggesting that ERKs and DNA-PKcs cooperate in radioprotection of PCa cells. Interestingly we found that ERK1/2 inhibition drastically affected the expression of c-Myc, one of the most important oncogene shown to control PCa onset and progression. The PC3 cell line xenotransplanted in mice showed a reduction in tumor mass and increase in the time of tumor progression with U0126 treatment

associated with reduced DNA-PKcs, an effect enhanced by radiotherapy. Thus, our results show that MEK/ERK inhibition affect transformed phenotype and enhances radiosensitivity of PCa cells, suggesting a rational approach in combination with radiotherapy.

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MAY SALVAGE RADIATION THERAPY (SRT) HAVE STILL A ROLE IN LOCO-REGIONAL MACROSCOPICALLY 18 F-CHOLINE PET/ MULTIPARAMETRIC MRI POSITIVE RELAPSED PROSTATE CANCER? RESULTS FROM AN ITALIAN MULTICENTRIC RETROSPECTIVE ANALYSIS

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Aims: Even if all recent Guidelines recommend SRT after Radical Prostatectomy as soon as the PSA rises above 0.20 ng/ml, still nowadays several patients (pts) experience loco-regional macroscopic relapse.Aim of our study is to retrospectively evaluate the role of SRT +/- concomitant androgen deprivation therapy (ADT) in pts with macroscopic PCa loco-regional relapse.

Methods: From 2001 to 2016, 102 pts with local macroscopic relapse underwent SRT +/- concomitant/adjuvant ADT in 4 different Italian Centers (Modena, Roma "Tor Vergata", L'Aquila, Terni). Mean age was 72years. At time of first diagnosis 66pts had pT2 PCa, 12 pT3a, 20 pT3b and 1 pt pT4 according to TNM AJCC Stratification (in 3pts initial staging was not available). Only 7pts had abdominal node involvement. Gleason Pattern Score was <7 in 29pts,=7 in 56 and >7 in 15pts (unknown data in 2pts). At time of SRT 28pts had a PSA value <1.0, 50 1.1-5 and 24pts >5 ng/mL. Before being submitted to SRT 57pts were staged with 18F-Choline CT-PET, 34pts with Pelvic MRI while 15pts had both to help with for a better RT planning. At the end of restaging 92 had just prostatic bed relapse, 4 nodal Involvement and 6pts had both. Due to clinical stage and PSA value, 51pts were submitted to first line ADT before RT, while 6pts had received two or more ADT lines. SRT was delivered in association to ADT in 61pts and in 41 it was continued in an adjuvant approach(Mean Duration 16 months).

Results: At a median FUP of 44.8 months all pts but 14 were alive. All pts were treated with high dose RT+/- concomitant ADT.Median RT dose to PTV1(site of relapse)was 72 Gy(range 62-79 Gy).Target volume encompassed prostatic bed+macroscopic lesion in 70pts,while in the other 32pelvic abdominal RT was performed(in 24pts with prophylactic intent,in 8pts using a boost on positive nodes).Three- and 5-year actuarial OS were 96.0% (ES±2.3%) and 83.7% (ES±4.3%), respectively.Three- and 5-year Biochemical Free Survival were 79.9%(ES±4.3) and 72.4%(ES±53) respectively while Metastasis Free Survival 85.6%(ES±4.0%) and 83.7%(ES±4.3%). Seventeen pts experienced distant recurrences:bone lesions were found in 13pts, extra-pelvic nodes in 5pts and liver mts in 1pt.Only 2pts had G3 late genitourinary side effects.

Conclusions: Our results of high dose SRT +/- ADT in macroscopic PCa relapse demonstrate an excellent profile in terms of oncological outcomes confirming once more the important role of SRT even in this unfavourable subset of pts.

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COMBINED, INTENSIFIED AND MODULATED ADJUVANT THERAPY IN PROSTATE CARCINOMA: A PHASE II TRIAL

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Aims: Prostate cancer patients at high risk of loco-regional recurrences may benefit from postoperative radiotherapy (RT) following radical prostatectomy (EORTC trial 22911). However, despite an improvement in biochemical relapse-free survival (bRFS), the risk of recurrences remained high for those patients. We postulated that adjuvant androgen deprivation therapy (ADT), radiation dose escalation, and selective pelvic irradiation for patients at risk for regional failures may improve the outcome. The combined-intensified-modulated-adjuvant (CIMA) as described may improve survival through a reduction of loco-regional and systemic failures.

Methods: A phase II trial was designed to test the hypothesis that CIMA treatment may improve 5-year

bRFS by 15%. Patients less than 80 years old, with a histological diagnosis of prostate adenocarcinoma without distant metastases, stage pT2-4 N0-1, no previous treatments and an ECOG performance status of 0-2 were selected. All patients had at least one of these pathologic features: extracapsular extension, positive surgical margins, or seminal vesicle invasion. Radiation dose to the tumor bed ranged from 64.8 to 70.2 Gy. Pelvic lymph nodes were treated to 45 Gy in selected patients at risk of regional failures (57%). Selected patients at risk for distant metastases (69.1%) received hormonal therapy.

Results: One-hundred-twenty-three patients were enrolled in the study and completed the planned CIMA treatment. At a median follow-up of 67 months (range: 48.0-98.0 months), actuarial 5-year bDFS was 92.9%. Actuarial 5-year local control and metastasis-free survival (MFS) were 98.7% and 96.1%, respectively. Actuarial 5-year overall survival was 95.1%. Actuarial 5-year MFS were 98.8% and 86.8% in patients with Gleason score 7 or less and above 7, respectively (p=0.01). Only 2.4% and 3.3% of patients developed grade 3 acute gastrointestinal (GI) and genitourinary (GU) toxicity, respectively. 5-year survival free from grade ≥ 2 GI and GU toxicity was 96.7% and 88.6%, respectively.

Conclusions: In selected patients at risk of recurrences following RP, CIMA was well tolerated and improved bRFS. Patients with a high Gleason score (>7) had an increased risk of developing distant metastases despite hormonal therapy. These patients may benefit from chemotherapy in future prospective trials.

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HYPOFRACTIONATED POST-OPERATIVE IMRT IN PROSTATE CARCINOMA: A PHASE I/II STUDY

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Aims: To report the outcome of hypofractionated radiation therapy after radical prostatectomy (RP) for prostate cancer (PCa) using intensity-modulated radiation treatment with simultaneous integrated boost (IMRT-SIB).

Methods: One hundred and twenty four patients with PCa at high risk of relapse after RP or diagnosis of biochemical relapse were included in this phase II study (adjuvant: 106 patients, salvage: 18 patients). All patients received 62.5 Gy to the prostate bed (PB) and 45 Gy to pelvis nodes in 25 fractions. Androgen suppressive therapy was prescribed based on NCCN risk categories. Acute and late toxicities were recorded and evaluated according to RTOG (Radiation Therapy Oncology Group) criteria and RTOG-EORTC (European Organization for Research and Treatment of Cancer) scale, respectively.

Results: Median follow-up was 30 months (13-92). Besides one patient with grade 4 acute genitourinary (GU) toxicity, no further cases of grade ≥ 3 acute gastrointestinal (GI) or GU toxicity were recorded. Grade 2 acute GI and GU toxicity was recorded in 24.2% and 18.2% of patients, respectively. Cumulative actuarial incidence of GI and GU grade ≥ 2 toxicity was 1.1% and 7.3% respectively. Five-year biochemical relapse-free survival (bRFS) was 86.5% (adjuvant: 87.9% vs salvage: 79.5%).

Conclusions: After RP, hypofractionated IMRT-SIB treatment, enabling a reduction in the overall treatment time, showed a favorable acute and late toxicity profile and encouraging results in terms of relapse-free survival.

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STEREOTACTIC BODY RADIATION THERAPY (SBRT) IN THE MANAGEMENT OF OLIGOMETASTATIC KIDNEY CANCER: A NEW CHANCE OF CURE?

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Aims: The rate of kidney cancer has been increasing by 1.7% annually for the past 10 years, comprising approximately 3.9% of new cancers. Renal cell carcinoma (RCC) is the most common kidney cancer, with an overall 5-year survival rate of 45%. Kidney cancer can metastasize, most commonly to lungs, lymph nodes and bones. Our aim is to analyze control of disease, survival and toxicity of patients treated with Stereotactic Body Radiation Therapy (SBRT) on extracranial metastases from kidney cancer.

Methods: from 2004 to 2016, sixty-four patients and 81 lesions were treated with SBRT. Median age was 66 years old, and majority of the patients were affected by RCC, in particular clear cell type were represented in

75% of cases. Six patients (9,4%) were affected by transitional cell kidney cancer. Median time to development of distant metastasis was 41.1 months (range 0 – 387) while median time to SBRT was 54.5 months. Thirty-nine (47.6%) of the treated distant metastasis were located in the lungs and 25 (30.5%) lesions were represented by lymph nodes. Forty-eight patients were treated on one lesion, 15 patients on 2 lesions and 1 patient on 3 lesions simultaneously. Median dose for SBRT was 45 Gy in a median dose per fraction of 8 Gy (range 4 – 25 Gy). Median Biological effective dose (BED) was 82 Gy .

Results: With a median follow-up of 16.7 months, all patients completed the planned treated. Overall clinical benefit rate was 97,6%. Best local response was classified as complete response in 28 lesions, partial response in 35 lesions and stable disease in 16 lesions. Local control (LC) rates at 1- and 2- years were 89% and 86%. At univariate analysis, RCC (p=0.048; HR 4.41, 95% CI 0.883 – 22.025) and the use of systemic treatment administered before SBRT (p=0.017; HR 0.221, 95% CI 0.057 – 0.856) impact on LC. At multivariate analysis, only chemotherapy before SBRT was significant on LC (HR 0.135 95% CI 0.023 – 0.695). Median Overall survival (OS) was 81 months. OS at 1, 2 and 5 years were 98%, 90%, and 73%. Age (p=0.011; HR 4.424 95%CI 1.266 – 15.457), and histology (p= 0.00; HR 13.037, 95%CI 3.384 - 52.324), were prognostic for OS. Treatments were well tolerated with 8 patients reporting Grade 1 and one patient reporting Grade 2 acute toxicity. Four patients treated on lung reported in the late setting grade 1 and grade 2 pneumonitis.

Conclusions: Oligometastatic patients from kidney cancer can benefit from SBRT as an effective and safe treatment.

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SALVAGE IMAGE-GUIDED INTENSITY MODULATED OR STEREOTACTIC RE-IRRADIATION FOR LOCALLY RECURRENT PROSTATE CANCER: MONO-INSTITUTIONAL UPDATE OF 64 PATIENTS

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Aims: To assess the potential clinical benefits of external beam re-irradiation (re-EBRT) delivered to either the prostate or prostatic bed for local recurrence after radical or adjuvant/salvage radiotherapy (RT).

Methods: Patients (pts) with biochemical failure and evidence of isolated local relapse of prostate cancer (PCa) after radical/salvage EBRT or brachytherapy (BRT) that received image-guided (IG) re-EBRT in the European Institute of Oncology between November 2009 and November 2016. Biochemical failure was defined as two consecutive rising PSA level >0.2 ng/ml post radical prostatectomy and according the Radiation Therapy Oncology Group (RTOG) and American Society for Radiation Oncology Phoenix Consensus after primary RT. Biopsy was not mandatory if all elements were univocal (PSA evolution,PET and MRI findings). Patients with distant metastasis at the time of re-EBRT were excluded. Re-EBRT was delivered with IG-IMRT and stereotactic technology including Rapid Arc®, VERO® and CyberKnife® to a total dose of 15-32 Gy in 2-10 fractions.Toxicity was evaluated using RTOG/EORTC criteria. In this analysis the updated data of some pts published by Zerini et al (2015) were included.

Results: This analysis included data of 64 pts. Median age was 73 years (range=52.6–90.4). Only one patient experienced an acute genitourinary (GI) event ≥3 represented by transitory macroscopic hematuria, and in one patient was registered late GI toxicity ≥3 consisted in permanent reduction in bladder capacity. No pts experienced grade ≥ 3 rectal and intestinal events. At the median follow-up of 26.8 months (3.1–85.1), progressive disease was observed in 40 pts (62.5%). (Table 1). In all cases, clinical progression followed biochemical progression. Mean and median time-to-progression are 17.8 and 13.8 months, respectively (range=2-65.6). At the last follow-up, 31 pts (48.4%) show no evidence of disease, 26 pts (41%) are alive with biochemical or clinical disease and 1 have been lost at clinical follow-up. Six pts (9%) died: 4 of disease progression, 1 for another type of tumor and 1 for unknown cause.

Conclusions: Re-EBRT delivered with modern techniques IMRT-IGRT, is a safe,feasible and noninvasive treatment for locally recurrent PCa offering satisfactory tumor control (4 out of 10 pts are free of progression and other salvage treatments at 2 years) without significant acute and chronic complications.A longer follow-up and greater series of pts treated are needed to assess the late toxicity rates

Table 1. Type of progression

Patients n°	Outcome (median follow-up 26.8 months)
15	Biochemical relapse alone
12	Clinical local relapse (in field) + biochemical relapse
2	Locoregional relapse (out field)+ biochemical relapse
11	Metastatic relapse + biochemical relapse

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IS ELECTIVE PELVIC RADIOTHERAPY STILL USEFUL IN CLINICALLY NODE-NEGATIVE PROSTATE CANCER? A LONG-TERM ANALYSIS

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Purpose/Objective: Whole pelvic radiotherapy (WPRT) role remains highly controversial in prostate cancer. Aim of this long-term analysis is to update data, already published,[1] to select patients that can benefit of WPRT.

Methods and Materials: High- and very high-risk patients(T3 or T4 and/or GS 8-10 and/or PSA>20 ng/mL) were analysed. Lymph-nodal Involvement (LNI) risk was assessed through Roach equation.[2] Prone or supine immobilization were used respectively in WPRT and Prostate Only RT(PORT). CTVs were: CTV1 prostate (7020/1.8 cGy fx until 1999 and then 73.8/1.8 cGy fx), CTV2 seminal vesicles(55.8/1.8 cGy for cT1-T3a and 64.8/1.8 cGy for cT3b-T4), CTV3 pelvic nodes(4500/180 cGy fx). PTVs derived from 1 cm to corresponding CTV. Long-term androgen deprivation therapy was prescribed. Late toxicity was graded according to the CTC v4.03. Statistical analysis was performed using R statistical software 3.2.4.

Results: Among the 358 patients enrolled between 1994 and 2007, 319 high-risk ones were selected: 20 patients treated by 2D RT until 1999, and 299 by 3D RT from 2000; 147(46.1%) treated with WPRT and 172(53.9%) with PORT. Median age at diagnosis was 70 for WPRT(42–80 years) and 72 for PORT(56–83 years) group. The two groups were heterogeneous for age (p=0,0017). With a median follow-up of 128 months, the 10-year bDFS, DFS, DSS and OS rates were respectively 64%, 75%, 91% and 83%, with a median OS of 127 months. No statistically significant differences were found among PORT or WPRT group, including disease stage, Gleason score, or PSA level at diagnosis and also in the subgroup analysis considering Roach formula LNI risk assessment with different cut-off(15%, 20%, 25%, and 30%)in terms of bDFS, DFS OS, age<70 (p=0.077). Only OS showed a better prognosis for WPRT, significant in 15% and 20% nodal-risk groups, but not confirmed by univariate analysis. Grade 3 late toxicity, either gastrointestinal(GI) or genitourinary(GU), was very low(0,63% and 0,94%, respectively);GI grade 4 toxicity was reported in only one patient. Any statistically significant difference was reported between WPRT vs PORT,neither in terms of GU(p = 0,81) or GI(p = 0,15) toxicity.

Conclusions: This long-term analysis failed to demonstrate a benefit for elective WPRT compared to PORT. The retrospective nature, small sample, long-time of accrual, with different doses and techniques, were some study limitations. On-going trials and new studies are encouraged to create performing tools for patient selection.

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THE ROLE OF IALURIL SOFT GELS• IN REDUCING ACUTE URINARY TOXICITY DURING MODERATE HYPOFRACTIONATED RADIOTHERAPY IN POST-PROSTATECTOMY SETTING: A PRELIMINARY EXPERIENCE

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Aims: To evaluate the role of Ialuril soft Gels® in reducing acute genito-urinary (GU) toxicity during moderate hypofractionated radiotherapy in postoperative prostate cancer patients treated with Volumetric Modulated Arc Radiotherapy (VMAT).

Methods: Eligible patients were < 85 years old, with an ECOG performance status of 0–2, histologically proven adenocarcinoma of the prostate without distant metastases, and pathological stage pT2–4 N0-1, with at least one of the following risk factors: capsular perforation, positive surgical margins, seminal vesicle invasion and/or postoperative PSA > 0,2 ng/mL. Patients were prospectively recruited and randomized (1:1) to receive RT alone or RT combined with Ialuril soft Gels®. GU toxicity was evaluated according to CTCAE v4.0. GU acute toxicity was assessed during and within 90 days after the treatment.

Results: From July 2016 and April 2017 60 patients previously submitted to RP, received adjuvant (34 patients) or salvage (26 patients) post-operative radiotherapy (RT). Patient's characteristics are detailed in Table 1. Forty-eight patients, among the 60 treated, as a result of surgery, had already developed basal GU toxicity as follow: G2 22/60 (37%), G1 26/60(43%). In patients treated with Ialuril soft Gels® the following acute GU toxicity was reported during and within 30 days after RT: G0 24 (80%), G1 4 (13%), G2 2(7%), G3 0; G1-G2 toxicity was represented by urgency, dysuria and urinary retention. In the arm without Ialuril soft Gels®: G0 8(27%), G1 13 (43%), G2 8 (27 %), and G3 1 (3%). G1-G2 toxicity were represented by urgency, dysuria and urinary retention. G3 toxicity consisted of severe dysuria. A significantly statistical difference was

found between two groups in terms of acute GU toxicity (p=0.00018).

Conclusions: Ialuril soft Gels® reduced significantly acute GU toxicity compared to patients that did not receive Ialuril soft Gels®. This medical device could be useful in PC patients during hypofractionated RT in post-operative setting. Further studies are warranted.

Table 1. Patients' characteristics.

	Ialuril arm	No Ialuril arm
N. of patients	30	30
Age (year) median (range)	63 (49-75)	66 (51-82)
PSA pre-RT median (range) ng/ml	0.065 (0-6.6)	0.04 (0.005-10.3)
TNM stage		
pT1	0/30	0/30
pT2	11/30	7/30
pT3a	12/30	12/30
pT3b	7/30	11/30
pT4	0/30	0/30
pN0	14/30	18/30
pN1	4/30	7/30
pNx	12/30	5/30
Surgical margin		
R0	11/30	18/30
R1	19/30	12/30
RT Intent		
Adjuvant	18/30	16/30
Salvage	12/30	14/30

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PHASE II STUDY WITH FFF LINAC-BASED SBRT IN FIVE CONSECUTIVE FRACTIONS FOR LOCALIZED PROSTATE CANCER: PRELIMINARY REPORT

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Aims: Stereotactic Body Radiation Therapy (SBRT) has been recently considered an option in selected prostate cancer(PC) patients. Usually, PC SBRT has been delivered every other day to favor normal tissues recovery. Flattening Filter Free(FFF)delivery is a modality able to reduce treatment time, decreasing positioning uncertainties. Aim of the present phase-II study is to evaluate feasibility, side effects and biochemical control of FFF-SBRT delivered in 5 consecutive days.

Methods: The study, approved by Ethical Committee, started on 03/2014.Inclusion criteria were:age ≤ 80 years, performance status ≤ 2, histologically proven adenocarcinoma, low-intermediate risk, no distant metastases, no previous surgery other than TURP, no other tumors, a pre-SBRT IPSS score ranged between 0 and 7. The schedule was 35Gy for low risk and 37.5Gy for intermediate risk PC in 5 fractions, delivered in 5 consecutive days. SBRT was delivered with volumetric modulated arc therapy (VMAT) and image-guidance by Cone beamCT (Varian TrueBeam,Palo Alto USA). Toxicity assessment was performed according to CTCAEv4.0. Hormonal-therapy was prescribed according to risk classification.

Results: At the time of the analysis, 52 patients were recruited in the protocol and treated. Median age was 73 years (55-83 years), median follow-up was 25 months (range:3-40). According to risk-category, 34/52 patients were low-risk and 18/52 were intermediate risk. Median initial PSA was 5.9 ng/mL (range 1.8-15.7). Median Gleason Score was 6(6-7). IPSS pre-SBRT was registered for all patients, with a median value of 4.5(range 0-7). All patients completed the treatment as planned. Acute genitourinary(GU) toxicity was:G0 36/52(69%), G1 11/52(21%), G2 5/52 (10%). Acute rectal (GI) toxicity was:G0 43/52(83%), G1 8/52(15%), G2 1/52(2%). No acute toxicities > G3 were recorded. At the time of the analysis late GU and GI toxicities were as follows: GU-G0 43/52(83%), GU-G1 7/52(13%), GU-G2 2/52(4%); GI-G0 48/52(92%), GI-G1 4/52(8%).The median value of IPSS post-SBRT was 3(range 0-20).No late toxicities≥G3 were recorded. Biochemical control was 98% according to Phoenix criteria.

Conclusions: The present FFF-SBRT phase-II study for low-intermediate PC delivered in 5 consecutive days showed to be feasible and well tolerated as well as other series with the same technique and fractionation delivered every other day (Alongi *et al*. Radiation Oncology 2013). Longer follow-up is needed to assess late toxicity profile and clinical outcomes.

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MULTIMODAL TREATMENT FOR HIGH-RISK PROSTATE CANCER: RESULTS OF A PROSPECTIVE PHASE II TRIAL

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Aims: To evaluate the safety and oncological outcomes of intensity-modulate radiation therapy (IMRT), adjuvant chemotherapy (CHT) with Docetaxel and long-term androgen deprivation therapy (ADT) following radical prostatectomy (RP) and extended lymphadenectomy (PLND) in high-risk prostate cancer patients (pts).

Methods: Inclusion criteria were: 1)age >18 and <75years; 2)any pT3 GS ≥7b N+/- R+/- or pT2c GS ≥8 N+/- R+; 3)M0 before and after surgery; 4)ECOG: 0-1; 5)normal liver and renal function; 6)WB>4000, Hb>10 g/dl, plt>100000. Exclusion criteria were: 1) uncontrolled inflammatory intestine chronic disease, severe

infection, peripheral neuropathy or prior cancer treatment within 5 years before enrollment; 2)bilateral orchiectomy, history of pelvic radiation, local treatment for prostate cancer or ADT before surgery. ADT was started within 3 months from surgery and was prescribed for 2 years. IMRT with concurrent Docetaxel was initiated not before 4 months from RP/PLND. 65 Gy to the prostatic bed and 57.2 Gy to the pelvic lymph nodes (in case of pN+) in 26 fractions were delivered. Weekly intravenous Docetaxel (30 mg if body surface area (BSA) was ≤ 1.8 m2 and 40 mg for BSA > 1.8 m2) was administered. Acute and late Genito-Urinary (GU) and Gastro-Intestinal (GI) toxicities were scored according to the CTCAE, v3.0. Biochemical and clinical recurrence-free survival were explored with the Kaplan-Meier method.

Results: Overall 42 patients were included. Pts characteristics are summarized in Table 1. Related to IMRT, acute toxicities were recorded for the GU (grade ≥2 in 8 [19%] pts) and the GI (grade ≥2 in 6 [14.3%] pts). No grade ≥ 4 acute GU toxicity or grade ≥ 3 acute GI toxicity were observed. The late grade ≥2 GU toxicity was registered only in 2 (4.8%) pts; no late grade ≥2 GI toxicity was observed. CHT toxicity was observed in 5 (11.9%) pts. Continence after RP/PLND and post-IMRT/CHT was achieved in 29 (69%) and 27 (64.3%), respectively. After a median follow-up of 3.4 years, PSA relapse and clinical recurrence were observed in 7 (16.7%) and 4 (9.5%) pts. Actuarial overall survival was 93.6%. No pts died for prostate cancer during the follow-up. Actuarial biochemical and clinical recurrence-free survival were 70.7% and 84%, respectively.

Conclusions: Multimodal therapy for high-risk prostate cancer seems feasible, well tolerated and effective in terms of oncological outcome. Nevertheless, this results need to be confirmed on a larger series.

Table 1. Pts characteristics.

Patients perioperative Characteristics	n= 42
Age, years, median (IQR)	62 (56-66)
PSA at diagnosis, median (IQR)	15.5 (8.0-22.3)
cT stage	
cT2c	22 (52.4%)
cT3	23 (47.6%)
cN+	2 (4.8%)
Biopsy GS	
7b	10 (23.8%)
8	17 (40.5%)
9	15 (35.7%)
pT stage	
pT2c	6 (14.2%)
pT3a	10 (23.9%)
pT3b	26 (61.9%)
pN+	16 (38.1%)
GS	
7b	2(4.8%)
8	11 (26.2%)
9	29 (69.0%)
Positive surgical margins	26 (61.9%)

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CURATIVE RADIOTHERAPY IN MUSCLE-INVASIVE BLADDER CANCER PATIENTS, OUR EXPERIENCE

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Aims: To evaluate clinical results in selected bladder cancer patients treated with curative radiation therapy.

Materials and Methods: We reviewed clinical records of bladder cancer patients treated in three Radiotherapy Centres of Sicily (Papardo Hospital and Policlinico G. Martino in Messina and Policlinico Rodolico in Catania) from March 2013 to March 2017 who were suitable to radical cistectomy. The toxicity was evaluated with RTOG acute and late morbidity scoring.

Results: Twenty three patients (5 female and 18 male) were evaluable. The median age was 84 years (range 55-97). All patients were submitted to TURB (transurethral bladder resection) both to define the istotype and to debulk. 5/23 patients had cT1G3; 8/23, cT2G3; 5/23, cT2G4; 3/23, cT3G3; 2/23, cT4a. Chemotherapy was administered in 7/23 patients: 2/23 had local chemotherapy instillation; 3/23 had neoadiuvant chemotherapy; 2/23 had concomitant radiochemotherapy. The radiotherapy techniques used were: IMRT in 4/23 patients, IMRT-IGRT in 3/23 patients, VMAT in 1/23, 3DCRT in 5/23 patients and 3DCRT-IGRT 10/23 patients. The median delivered dose was 62Gy (range 36-66 Gy), with a fraction dose of 200 cGy in 18/23 patients, 210 cGy in 3/23 patients and 180 cGy in 2/23 cases The median follow-up was 14 months (range between 2- 44 months), only one patient was lost at follow up. In 2/23 patients radiation therapy treatment was interrupted at 36 Gy and 54 Gy from G3 toxicity. A complete response was observed in 19/22 (86.3%) patients and a partial response in 1/22 (4.6%) patients. The recurrence was observed in 1/22 patient after 6 months and in 1/22 after 18 months treated with a radical cystectomy for a total of 9.1% of patients. Genitourinary acute toxicities were: G0 in 3/22 patients, G1 in 8/22 patients, G2 in 4/22 patients, G3 in 7/22 patients. Gastrointestinal G1 toxicity was observed in 4/22 patients. No late toxicities was reported. The median survival was 14 months.

Conclusions: In conclusion the radiotherapy treatment is an excellent therapeutic option in patients with bladder cancer suitable to radical cystectomy with a 86.3% of complete response and acceptable toxicity.

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ROLE OF MULTIPARAMETRIC MRI IN THE LOCAL STAGING OF PROSTATE CANCER AND ADVANTAGES OF FUSION IMAGING FOR RADIATION TREATMENT PLANNING

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Aims: To evaluate the effectiveness of multiparametric MRI for a better locoregional staging and the radiation treatment planning in prostate cancer.

Methods: Between April 2010 and April 2016, 170 patients with histologically-proven prostate cancer underwent before radiation treatment a multiparametric MRI (Mp-MRI). The protocol is based on T2 TSE sequences, diffusion weighted imaging (DWI/ADC), and dynamic contrast material-enhanced imaging (DCE). Mp-MRI significantly improves the accuracy of tumor localization and for pretreatment planning and provides highly accurate local staging information. Diffusion weighted imaging (DWI) is a sequence which enables the quantification of random Brown¬ian motion of water molecules in tissue and it can be quantitated in terms of the ADC on diffusion-weighted MR images. In prostate carcinoma, water's molecules motion is restricted because of their high cellular density, resulting in decreased ADC. DCE MR imaging is a fast dynamic imaging that can depict the vascularity of the tumor. Usually, prostate cancer appears as an early and rapidly enhancing lesion with fast washout of contrast material in comparison with that of normal prostate tissue: the presence of rapid washout is highly indicative of prostate cancer. MRI were also registered with the CT simulation for a better delineation of the target and Organs at Risks (OAR). Correct radiological staging, is of main importance for target volume definition and dose prescription in highly-conformal curative radiotherapy (RT)

Results: All patients presented alterations in the T2 sequences. DWI/ADC and DCE confirmed the lesions evidenced to T2 sequences in 146 and 120 patients, respectively. DWI/ADC was able to find more alterations than T2 sequences in 11/24 cases without perfect correspondence. DCE was capable to find more alterations than T2 sequences in 6/50 cases without perfect correspondence. In 106/170 patients MRI staging modify risk class prevalently from low intermediate to high-risk. In all cases MRI helps to better delineate volumes contouring respect CT simulation alone. MR imaging allows excellent delineation of the contours of the prostate and surrounding structures.

Conclusions: We confirm that Multiparametric MRI (T2-weighted, DWI and DCE sequences) is able to overcome the limitations of conventional MRI sequences. The use of mp-MRI has increased the accuracy of localization and staging of prostate tumors and resulted in a substantial shift in tumor stage in > 60% of patients underwent to curative Radiotherapy. The accuracy in the staging of disease helps us to "tailor" the treatment protocol based of risk class.

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LATE TOXICITY PROFILE OF HYPOFRACTIONATED PROSTATE CANCER RADIOTHERAPY

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Aims: To evaluate late rectal and urinary toxicity in patients with localized prostate cancer treated with hypofractionated radiotherapy.

Methods: From 2003 to 2016 we treated 217 pts with localized prostate cancer; 105 pts had low risk disease and received 60 Gy in 20 daily fractions to the prostate and 45 Gy in 15 fractions to proximal seminal vescicles. 112 had intermediate risk prostate cancer and received 54.3 Gy in 15 fraction and 43.44 Gy in 12 fractions 3 week to the prostate and to the seminal vescicles respectively. 3D conformal radiotherapy was used; 26 pts (25%) in the low risk group and 37 (33%) in the intermediate received daily cone beam CT. After a median follow up of 81 months (144-18 months) we made a retrospective late toxicity analysis according to the Radiation Therapy Oncology Group criteria.

Results: G1 late urinary toxicity occurred in 10 pts (9.5%) and 15 pts (13%) and G1 rectal side effects in 5 (4.7%) and 8 pts (7%) in the low and intermediate risk group respectively. 2 patients in the first group (2%) and 2 patients in the second one (1.7 %) had late urethral stricture requiring TURB. G2 late gastrointestinal toxicity was observed in 1 (1%) and 2 pts (1.7%) respectively. Pts with late toxicity > G2 didn't receive daily IGRT.

Conclusions: Regarding late adverse events, hypofractionated radiotherapy seems to be safe and well tolerated. Daily IGRT is useful in order to reduce late toxicity rates.

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METASTATIC KIDNEY CANCER: MONO-INSTITUTIONAL RETROSPECTIVE ANALYSIS OF PATIENTS TREATED AT FLORENCE UNIVERSITY HOSPITAL

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Aims: Metastatic kidney cancer is a heterogeneous disease, and several factors can influence outcomes in patients treated in this setting. We aimed to evaluate outcomes and explore prognostic factors in patients with metastatic Renal Cell Cancer (mRCC) treated in our Institution.

Methods: Patients with mRCC treated between 2011 and 2017 were retrospectively reviewed. All underwent systemic treatment according to common clinical practice. Clinical outcomes were 1st line Progression free survival (PFS) and Overall Survival (OS). Prognostic impact of the following factors was analyzed: baseline performance status (PS), number of metastatic sites, presence of visceral vs bone lesions, time to metastatic disease, response to first line, tumor grade, Xp11 translocation, surgery, first line therapy performed (pazopanib vs sunitinib), and use of an immune checkpoint inhibitor after a first-line regimen failure. Survival analysis was performed using the Kaplan-Meier method and compared with the log-rank test. Prognostic factors were investigated with univariate and multivariate analysis according to the Cox model. A p value ≤ 0.05 was considered statistically significant.

Results: 41 patients (33 males and 8 females) were retrospectively analyzed. Average age was 59.9 years (range 27-80). Thirteen (32%) patients were found with distant metastases at diagnosis. In the remaining patients mean time to distant recurrence was 59.6 months (range 1.5 - 312). 5-years OS and 5-years PFS were 77.4% and 17.4%, respectively. A PS> 2 and time between diagnosis and metastatic recurrence were significantly related to OS (p 0.0001 and p 0.021, respectively). HR for death was 0.4 (95% CI 0.03-0.57, p 0.017) in patients with time to distant metastases $\geq$ 31,5 months. Local surgery and surgery on metastatic sites did not influence OS in metastatic patients at diagnosis (p=0.49 and p=0.48, respectively). PS>2 was the only independent prognostic factor for PFS (50 vs 17.8%, p=0.0001).

Conclusions: Our experience showed that only PS and time to metastatic disease significantly affected explored outcomes. No prognostic factor showed impact on outcomes, including 1st line treatment. These results further suggest the need of prospective studies to explore disease features and differentiate between subsets of patients. Due to the low number of patients treated with immunotherapy, further experience is needed to explore these new agents in real clinical practice.

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PRELIMINARY RESULTS OF EARLY-SALVAGE RADIOTHERAPY TRIAL IN PATIENTS AT INTERMEDIATE RISK AFTER RADICAL PROSTATECTOMY (THE EASY-TRIAL)

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Aims: To describe preliminary data about a protocol based on close PSA monitoring after radical prostatectomy and early salvage radiotherapy in no metastatic patients at intermediate risk of biochemical and/or clinical relapse.

Methods: Selected histologically proven prostate cancer patients undergoing radical prostatectomy with or without lymphadenectomy and one of these pathological features: pT2-R1, pT3a-R0, pT3a-R1, pT3b-R0 and pN0 and undetectable PSA level after surgery. PSA test every two months was performed and 68Ga-PSMA PET/CT was planned in patients with increased PSA. Patients with two consecutive postoperative raised PSA or at least 1 postoperative PSA > 0.2 ng / ml and negative 68Ga-PSMA PET/CT for extra-pelvic disease localization will be treated with salvage radiotherapy. No hormonal therapy performed before or after prostatectomy is allowed.

Results: From October 2016 to April 2017, 68 patients < 80 years old were enrolled: 18, 34, 13, and 3 were pT2-R1, pT3a-R0, pT3a-R1, and pT3b-R0, respectively. To date only 1 case of biochemical relapse was recorded (PSA: 0.31 ng/ml at the second PSA evaluation).

Conclusions: Longer follow-up and larger series will allow to evaluate the role of early salvage strategy and its efficacy in terms of biochemical relapse free survival.

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THE ROLE OF 18F-CHOLINE (FCH) PET/CT FOR THE PREDICTION OF LONG-TERM RESPONSE TO RADICAL RADIOTHERAPY (RT) IN PATIENTS WITH LOCALIZED PROSTATE CANCER (PCA)

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Aims: This study aims to determine if metabolic parameters provided by FCH PET/CT are able to predict the long-term response to radical radiotherapy (rRT) in patients with localized PCa.

Methods: Between 2011 and 2016, from a monocentric database, we retrospectively reviewed pre-treatment FCH PET/CT scans of 36 patients who underwent RT for the definitive treatment of localized PCa. For each PET/CT scan, different metabolic parameters were assessed, such as maximum standardized uptake value (SUVmax), average SUV (SUVavg), metabolic tumor volume (MTV), total lesion choline kinase activity (TLCKA) and FCH multifocality. In all patients, the value of PSA before RT (PSAp) was recovered. All patients underwent rRT for a total equivalent dose of 78-80 Gy, with a standard or hypofractionated schedule (2 Gy or 2.5Gy /fraction). Patients were classified as disease free (DF) if the increase of PSA value after RT was less than 2 ng/mL respect to PSA nadir value, conversely with an increase of PSA higher than 2 ng/ml they were classified as recurrent (not disease free, NDF). Only patients with at least 1-year follow up, after rRT, were enrolled in this study.

Table 1.

Variables	DF (n=30)	NDF (n=6)	P value
Median SUVmax (range)	6.1 (0.2-29.6)	10.3 (0.3-22.7)	0.110*
Median SUVavg (range)	3.6 (0.1-6.3)	4.9 (0.2-9.4)	0.050*
Median MTV (range)	6.9 (0.03-167.9)	19.5 (3.9-49.1)	0.757*
Median TLCKA (range)	15.9 (0.1-169.2)	44.8 (4.6-462.2)	0.022*
Median PSAp (range)	11.8 (4.5-54.8)	18.7 (2.2-88.7)	0.011*
Multifocality, n (%)			
No	19 (63.3%)	1 (16.7%)	0.036**
Yes	11 (36.7%)	5 (83.3%)	

**t-Student test; **chi-square test*

Results: In all 36 patients, median (range) values of SUVmax, SUVavg, MTV, TLCKA, and PSAp were 6.6 (0.2-29.6), 3.62 (0.1-9.4), 7.79 (0.03-167.9), 20.1 (0.1-462.2) and 12.7 ng/mL (2.2-88.7 ng/mL), respectively. Moreover, 16 (43%) patients had a multifocality FCH uptake in prostate gland. After 1-year of follow-up, 30 patients were considered as DF and 6 patients were considered as NDF. All metabolic parameters were lower in DF than NDF patients (Table 1), in particular TLCKA, SUVavg and FCH multifocality. At multivariate logistic regression analysis, only multifocality resulted a predictor of rRT failure (OR: 9.98; 0.88-11.26; p=0.063).

Conclusions: High values of TLCKA result predictive of poor outcome after 1-year follow-up for patients with a multifocal intraprostatic lesion and who are candidates to rRT. The present findings, taking into account the radiobiology of PCa (which benefits of hypofractionation and higher prescription dose), suggest to increase the dose inside the primary tumor. Further work has to be done to assess a risk-adapted prescription protocol for patients with multifocal lesions and high values of TLCKA, who could benefit of an increased dose to the Intraprostatic Dominant Lesion.

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SALVAGE HYPOFRACTIONATED RADIOTHERAPY FOR PROSTATE CANCER: ACUTE TOXICITY

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Aims: To evaluate acute toxicity and the preliminary outcome of hypofractionated salvage radiotherapy (Hypo-SRT) with helical tomotherapy after radical prostatectomy (RP).

Methods: From March 2013 to December 2016, 71 patients underwent Hypo-SRT for biochemical (BR) or local recurrence (LR) after radical prostatectomy (PR). Median age was 63 years (range 45-84). The surgical Gleason score was : <7 in 25 patients, (41%), 7 in 25 (38%), >7 in 17 (21%); median PSA pre-SRT was 0.73 ng/ml (range: 0-8.65). RT schedule: 28/71 (41%) patients with BR received 2.25 Gy in 32 fractions (Total dose:72 Gy); 43/71 (59%) patients with LR received 2.1 Gy in 33 fractions (Total dose: 69.3 Gy) to the prostate/seminal vesicle bed and 2.25 Gy in 33 fractions to the LR site (total dose:74.25 Gy) using a simultaneous integrated boost (SIB) technique; 8/71 (10%) patients received 1.6 Gy to the pelvic lymph nodes (total dose 52.8 Gy), using a SIB technique. Hormone therapy (LHRH analogue and/or anti-androgen) was administered to 21 patients (29%) with high risk features. Toxicity was graded according to the Common Terminology Criteria for Adverse Events version v4.0. Biochemical failure was defined by ASTRO criteria. The Mann-Whitney test compared clinical and dosimetric variables in groups with and without acute toxicity.

Results: The median follow-up was 17 months (range:3-46).The median duration of HT was 88,5 months (range 2-168). Only G1-G2 acute genitourinary (GU) and intestinal (GI) toxicities occurred. Acute grade 1 GU toxicity occurred in 33 patients (46.5%), with 25 (35%) developing cystitis, 7(10%) urinary incontinence and 1(1.5%) hematuria. Acute grade 2 GU toxicity (cystitis) developed in 3/71 (4%) patients, with 1(1.5%) also affected by urinary retension and 1(1.5%) by urinary incontinence. Acute grade 1 GI toxicity

(proctitis) occurred in 25/71 patients (28.5%), which was associated with rectal bleeding in 4 (5.5%). Acute grade 2 GI toxicity (proctitis) developed in 4/71 (5.5%) patients, which was associated with rectal bleeding in 2 (3%); moreover 1(1.5%) patient developed diarrhea G2. Post Hypo-SRT the median PSA was 0.02 ng/ml (range:0-7.01) and the nadir was 0.003 ng/ml (range: 0-5.67). Biochemical recurrence and /or loco-regional relapse occurred in 11/71 (15.5%) patients at a median of 18.5 months after treatment (range: 8-46). Dmax to the prostate/seminal vesicle bed was greater in patients who developed acute GI toxicity.

Conclusions: Low grade acute GU and GI toxicity and early biochemical response demonstrated that moderate Hypo-SRT was safe and effective. A longer follow-up is required to confirm these outcomes.

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HYPOFRACTIONATION AND ABIRATONE ACETATE IN THE TREATMENT OF BONE METASTASES IN PATIENTS WITH HORMONE REFRACTORY PROSTATE CANCER

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Aims: The hypofractionated radiotherapy plays a fundamental role in the treatment of bone metastases. At our center, we evaluated the feasibility and effectiveness of two schemes hypofractionation: 8 Gy single dose and 8 Gy in two fractions to be made within a week of each other. The two irradiation techniques have been associated with the new molecules used in medical therapy.

Methods: From July 2014 to March 2017 they were treated 31 patients with bone metastases from hormone refractory prostate cancer . The median age of patients studied was 72 years with bone metastasis respectively localized in the dorsal and lumbar spine in 50% of cases, 30% at the level of bilateral lower limbs and the remaining 20% at the level of the pelvis. Radiation therapy was by hand in a single dose in 60% of cases in patients with worse P.S. while in the remaining 40% it was backed bifractionation treatment. All patients were administered simultaneously, the abiraterone acetate 1 g / day in combination with LHRH analogue every three months.

Results: All patients were reassessed after 30-40 days of therapy. In no case were registered signs of toxicity. In 85% of cases there has been a reduction in their analgesic therapy administered dose.

Conclusions: In our experience, the radiotherapy hypofractionated 8 Gy in a single session or, alternatively, 8 Gy in two weekly sessions in conjunction with the abiraterone acetate was well tolerated and had a good impact both as regards the control of the pain is the improvement of quality of life.

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MODERATE HYPOFRACTIONATED HELICAL TOMOTHERAPY POSTPROSTATECTOMY: ACUTE, LATE TOXICITY AND BIOCHEMICAL CONTROL IN ADJUVANT AND SALVAGE SETTING

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Aims: to evaluate safety and efficacy of adjuvant (AR) and salvage (SR) Hypofractionated Radiotherapy (RT) in patients (pts) with prostate cancer and adverse pathologic features and to compare outcome between adjuvant vs early salvage radiotherapy (eSR).

Methods: A total of 76 consecutive prostate cancer pts, median age 68, with adverse pathologic features were treated with a moderate Hypofractionated postoperative RT (Helical Tomotherapy) from April 2013 to January 2017. We retrospectively identified 33 men receiving AR (treatment given within 6 months from surgery with PSA ≤0.2 ng/mL) and 43 receiving SR (RT delivered after 6 months from surgery or with PSA≥0.2 ng/mL). Among SR pts 15 received RT at a PSA level ≤0.5 ng/mL and we defined as eSR. In AR and SR group the median doses were 63,8 Gy (60.9-66Gy) to the prostatic bed, 49,3 Gy (48-55,1 Gy) to the pelvic lymph nodes and 63,8 Gy (61.6-70 Gy) to the prostatic bed or macroscopic disease, 49,3 Gy (48-55,1 Gy) to the pelvic lymph nodes respectively, in 28 or 30 fractions with simultaneous integrated boost (SIB). The acute and late Genitourinary (GU) and Gastrointestinal (GI) toxicities were scored according to the Common Terminology Criteria for Adverse Events, v4. Biochemical progression was defined as PSA level rise of ≥0.2 ng/mL or more above the post radiotherapy nadir.

Results: All 76 pts completed the planned treatment, with good tolerance. After a median follow-up of 15 months (6-40), acute GU toxicities were recorded, G1 8/33(24%), G2 1/33(3%) and G1 12/43 (28%), G2 2/43(4%) in AR and SR settings respectively. For GI toxicities, G1 6/33(18%), G2 1/33(3%) and G1 10/43(23%), G3 1/43(2%) in AR and SR respectively. Regarding late toxicity, no ≥G2 events were found. We observed, a Biochemical Control (BC) in 84% and 88% of the AR and SR pts, respectively. 1 pt died for systemic progression disease. We furthermore observed no relevant difference, in terms of BC, between AR and eSR (84% vs 80%)

Conclusions: Moderate Hypofractionated (SIB) postoperative RT with Helical Tomotherapy produces low rates of Toxicity, and demonstrates encouraging efficacy. Longer follow-up is needed to assess late toxicity and clinical outcomes.

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PROSTATE STEREOTACTIC ABLATIVE RADIATION THERAPY USING VMAT AND SIMULTANEOUS INTEGRATED BOOST TO DOMINANT INTRAPROSTATIC LESION: IS THERE A ROLE FOR NERVE-SPARING?

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Aims: We explored the potential of volumetric modulated arc therapy (VMAT) to spare the critical erectile structures in complex SABR treatments of prostate cancer with a simultaneous integrated boost (SIB) to the dominant intraprostatic lesion (DIL).

Methods: Five patients were selected for replanning. DILs were defined using T2-weighted, dynamic contrast-enhanced and diffusion-weighted MRI. Nerve structures were contoured and expanded by a uniform 2 mm margin. The prostate (or the prostate plus 1 cm of seminal vesicles for intermediate-risk patients) and the DIL were expanded uniformly by 3 mm to create the planning target volumes (PTVprost and PTVdil, respectively). Gold seeds were implanted in the prostate for image-guided purposes. PTVprost and PTVdil dose prescription was 35 Gy an 40 Gy, respectively, in 5 fractions. The doses were prescribed to cover >95% of PTVs. Steep dose fallout outside PTVs will be prioritized. Dose constraints present in current literature, corrected for EQD2 late effects, were used for rectum, bladder and other OARs. All VMAT plans were generated in a dual-arc modality. Original clinical plans were optimized with a standard 10mm width MLC (ST-VMAT). Plans aiming to nerve-sparing were generated using 10mm width MLC (NS10-VMAT) and 5mm width MLC (NS5-VMAT). Dose-volume histograms for PTVs and OARs were compared between the plans using a 2-tailed paired t-test.

Results: Planning with two strategies (with and without nerve sparing) demonstrated comparable planning target coverage for ST-VMAT, NS10-VMAT and NS5-VMAT (PTVprost D95%: 98.6%, 98.0% and 98.3%; PTVdil D95%: 98.6%, 98.0% and 98.3%). Dmean for both PTVs were found not statistically different. D98% was found >90% for all patients and techniques. No significant differences were found in sparing rectum, bladder, penile bulb, urethra and femoral heads between the three plans. With regard to vessel-sparing, VMAT plans aiming to nerve sparing provided a significant reduction of dose irradiation. NS10-VMAT and NS5-VMAT provided a mean dose reduction by 20.2% and 30.8%, respectively. Vessel V30 decreased from 91.6% to 34.7% and 20.2% for NS10-VMAT and NS5-VMAT plans, respectively.

Conclusions: We showed that nerve-sparing SABR using VMAT-SIB strategy is dosimetrically feasible, allowing nerve-sparing and highly conformal plans, benefits of hypo-fractionation, dose escalation to DIL and fast treatment delivery. The use of narrower leaf-width MLC increased the quality of plans.

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SHORT-TERM RADIOTHERAPY (RT) FOR EARLY PROSTATE CANCER WITH CONCOMITANT BOOST TO THE DOMINANT LESION (AIRC-IG-13218): PRELIMINARY INVESTIGATIONS OF QUALITY OF LIFE AFTER THE END OF THE ACCRUAL

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Aims: The focus on toxicity outcomes and Quality of Life (QoL) when evaluating contemporary methods of treating prostate cancer has been increasing, especially for extreme hypofractionated RT. The aim of this first report is to examine the preliminary data and focus the attention on the acute effects of the treatment on urinary toxicity, sexual function and their impact on QoL.

Methods: We examined patient-reported outcomes among 65 pts in the AIRC-IG-13218 trial who completed questionnaires before diagnosis, at the end of RT and 1 month after treatment. Patients fulfilled validated measures that assessed urinary, sexual function and specific effects on quality of life, anxiety and depression, and general health with International Prostate Symptom Score (IPSS), International Index of Erectile Function – 5 (IIEF-5) and QLQ-C30.

Results: We completed the accrual of the planned 65 patients affected with early localized prostate cancer and treated with extreme hypofractionated RT at Our Institution between June 2015 to May 2017. The whole prostate is treated to a dose of 36.25 Gy in 5 fractions

(7.25 Gy/fraction) whereas the dominant lesion (DIL) receives a simultaneous integrated boost of 37.5 Gy in 5 fractions (7.5 Gy/fraction). Median age, iPSA, and GS were as follow: 74 yrs (range 52.2-82.5 yrs), 6.39 ng/ml (range 1.1-25), 6 (range 6-7), respectively. NCCN risk categories were represented as follows: low 13 (20%) of pts, intermediate 52 (80%). At the time of this analysis the available data concern the 60 pts who completed the RT course. Median IPSS score was 5.5, 7 and 8 at baseline, at the end of RT and after 1 months, respectively. Median IIEF was 14.5, 6 and 7.5 at baseline, at the end of RT and after 1 months, respectively. Quality of life was 83.7%, 78.3% and 80.3% at baseline, at the end of RT and after 1 months, respectively (Figure 1).

Conclusions: The analysis of data is still ongoing. This preliminary assessment showed that despite the moderate worsening of urinary and sexual function quality of life remain substantially stable during the first month follow-p with a trend in improving one month after RT. The observed acute toxicities are predictable and in line with reported effects of short course RT. Further analysis will be warranted to evaluate persistence or improvement in terms of symptoms and quality of life scores.

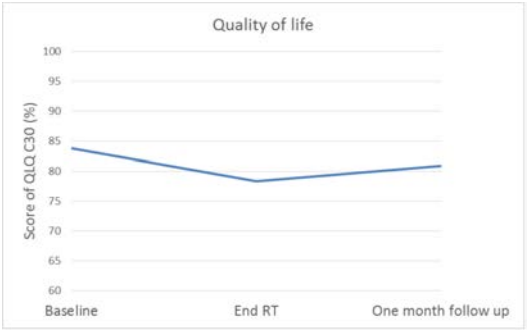

Figure 1.

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HYPOFRACTIONATED RADIOTHERAPY AND ABIRATERONE IN PATIENTS WITH METASTATIC CASTRATE RESISTANT PROSTATE CANCER

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Aims: Palliative radiotherapy (pRT) is primarily employed for palliation of bone pain in patients with castrate-resistant prostate cancer (CRPC).We describe a series of patients treated with abiraterone acetate and undergoing palliative radiotherapy for bones metastasis with a moderately hypofractionated scheme.

Methods: We retrospectively analyzed 29 patients with CRPC that received abiraterone and concomitant pRT in two Radiotherapy Department (ASL Bi and ASL TO4) between January 2012 and November 2015. Eleven patients underwent surgery and subsequently adjuvant or salvage radiotherapy, nine were subjected to radiotherapy alone and nine had initially metastatic disease. All patients developed CRPC which previously progressed on luteinizing hormone-releasing hormone (LHRH) analogue therapy and maximal androgen blockade. All patients were treated with Zoledronic acid, to prevent skeletal-related complications. Twenty eight patients were treated with docetaxel and one was treated with Radium-223. The average time between the onset of the disease and the appearance of metastases was six years. All patients were treated with abiraterone and concomitant hypofractionated RT of at least one and up to 5 bony lesions. The lesions of spine and pelvis predominated (48% and 29% correspondingly). Total radiation dose varied between 8 Gy to 30 Gy (median dose 20 Gy in 4 fractions, generally 30 Gy in 10 fractions). Pain palliation was assessed in patients who had clinically significant baseline pain. All patients were also receiving synchronous prednisone and LHRH analogue therapy.

Results: The average follow-up was 16 months. All patients demonstrated an excellent biochemical response. Median PSA level was significantly reduced from 30 ng/ml (range 7-190) to 2 ng/ml (range 0,5-138) after pRT. pRT resulted in pain palliation in 80% of symptomatic patients and side effects were mild. At December 2016 twenty two patients were death. The average survival from the administration of abiraterone is about 14 months.

Conclusions: Hypofractionated radiotherapy is an effective tool for palliation of symptoms commonly caused by metastatic prostate cancer, concomitant use of abiraterone is feasible and effective in the treatment of bone metastasis from prostate cancer.

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THE EFFECTS OF ENZALUTAMIDE IN COMBINATION WITH RADIOTHERAPY: IN VITRO STUDY

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Aims: Radiotherapy combined with hormone therapy is the standard treatment for patients with locally advanced/high risk prostate cancer (PC). To date, Androgen Deprivation Therapy (ADT) with LH-RH agonist or antagonist is the standard first line treatment in metastatic PC, but progression to castration resistant disease (mCRPC) remain inevitable. Androgen receptor (AR)

plays a crucial role in the development and progression of metastatic PC. Here we investigated the potential radiosensitizing effect of Enzalutamide, a second-generation anti-androgen which inhibits AR at multiple levels, on human PC cell lines.

Methods: Androgen-dependent LNCaP cells and androgen-independent PC3 cells were treated for 48 h with 10 μM Enzalutamide and then exposed to different single doses of ionizing radiation (IR) (0, 2, 4 and 6 Gy). The radiosensitizing effect of Enzalutamide was assessed by clonogenic cell survival assay and analysis of the DNA damage by immunofluorescence staining of γ-H2AX foci.

Results: In LNCaP cells, Enzalutamide treatment resulted in the decrease of cell survival at all IR doses tested. Already after 2 Gy irradiation the surviving fraction was reduced from 0.44 in controls to 0.34 in presence of the drug. An increased (and sustained over time) number of γ-H2AX positive nuclei in Enzalutamide treated LNCaP cells was observed, suggesting a possible impairment of the DNA repair machinery. Enzalutamide did not exhibit a significant radiosensitizing effect on PC3 cells at 2 Gy and the number of γ-H2AX positive nuclei decreased with time, indicating that Enzalutamide does not alter the DNA repair ability of PC3 cells. At higher IR dose levels the radiosensitizing effect of Enzalutamide increases.

Conclusions: The combination of Enzalutamide with IR significantly increases the radiosensivity of the hormone-dependent LNCaP cell line. Molecular mechanism underlying the radiosensitization may reside in the impairment of DNA repair machinery. These preclinical data are of a key importance in order to design future prospective clinical trials.

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CHOLINE (CH)-PET/TC FOR EARLY DETECTION AND PROMPT THERAPY IN OLIGOMETASTATIC PROSTATIC CANCER PATIENTS

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Aims: We present our experience in oligometastatic prostatic cancer patients(pts) underwent to salvage stereotactic body radiotherapy (SBRT) after early diagnosis with (Ch)-PET/TC of lymph node or bone lesions.

Methods: Between September 2010 and September 2016, 42 prostate cancer pts with 44 recurrent isolated oligometastases, were treated with SBRT, 38 (90%) with lymph node and 6 (10%) with bone lesions, respectively. Median age was 68 years (yrs) (range, 52-77), median Gleason score at the primary diagnosis was 7 (range, 5-9). Median time from primary treatment to SBRT was 60 months (m) (range 9–194). Diagnosis of disease relapse was made with Ch-PET/CT. Median PSA values before SBRT was 2.25ng/ml (range, 0.52-9.58). Sixteen (38%) of 42 pts received adjuvant hormonal therapy (HT) before the diagnosis of relapse and stopped HT before SBRT. Fourteen (33.5%) of 42 pts underwent only SBRT, remaining 12 (28.5%) received concomitant HT, 11 of these pts discontinued HT after SBRT. Two (5%) pts underwent SBRT for two synchronous lymph node lesions. Gross tumor volume (GTV) was delineated using Ch-uptake and planning target volume was defined as the GTV plus a 5 mm isotropic margin. Mostly, two different fractionation schemes were used: 5 × 8Gy in 26 (59%) lesions and 3 × 10Gy in others 6 (13.5%). Response was assessed with PSA evaluation scheduled every 3 m during the first year and then every 6 m. Pts with a reduction or a stability of PSA level were considered responders, Ch-PET-CT was done in case of a PSA level increase.

Results: Median follow-up was 30 m (range 6-76). Mean time of biochemical progression from the end of SBRT was 8 m (range 4-50). We registered a complete concordance between PSA increase and progression of disease at Ch-PET/CT control. After SBRT, 14 responders (33.5%) remained biochemical relapse free, the others 28 (66.5) pts had a PSA increase due to an outfield progression. Of these last pts, 10 were treated with SBRT, 7 for lymph node recurrence and 3 for bone lesions. After SBRT, no acute o late toxicity were registered.

Conclusions: In prostate pts with biochemical progression Ch-PET/CT can be useful for an early diagnosis of oligometastasis. In this setting SBRT resulted effective and well tolerated. After SBRT, Ch-PET-TC should be considered only in case of PSA level increase.

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STEREOTACTIC RADIOTHERAPY IN OLIGOMETASTATIC PATIENTS WITH RENAL CELL CARCINOMA

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Aims: The aim of this study was to evaluate the performance of stereotactic radiotherapy (SRT) with either CyberKnife (Accuray, Sunnyvale, CA) or Vero™ (BrainLab Mitsubishi Feldkirchen, Germany) in terms of toxicity and local control (LC) of cranial or extracranial metastasis in oligometastatic renal cell carcinoma (RCC) patients (pts).

Materials and Methods: Between January 2012 and September 2015, 29 patients and 33 lesions were treated. SRT was during a systemic therapy. The total

radiotherapy doses ranged from 10 to 54 Gray (Gy), given in 1 to 3 fractions. The biological equivalent doses (BED) and 2 Gy-per-fraction equivalent dose (EQD2) were calculated using the / =10 Gy for tumors.

Results: After a median follow-up of 14 months (range 1-36), we achieved the best result in gr 3 (complete remission (CR) and stable disease (SD) in 77.7% and 22.3 % of pts) versus 60 % and 40 % in Gr 2 and 50 and 50 % in Gr 1. Eleven pts had more than 12 months follow-up: 11/11 had complete response in the site of treatment and two had progression disease (PD) in other site (both pts are of Gr 1).

Conclusions: SRT is a feasible and safe approach in oligometastatic RCC patients with an excellent LC and no toxicity in our series. SRT might play a role in the management of selected RCC patients allowing for a delay in the start of a systemic therapy and its toxicity or a drug holiday after a long treatment period.

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TARGET DEFINITION IN SALVAGE RADIOTHERAPY (RT) FOR RECURRENT PROSTATE CANCER (PCA) AFTER PROSTATECTOMY: FROM THE INVISIBLE TO THE VISIBLE CONCEPT

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Aims: Salvage Radiotherapy (sRT) for biochemical post-prostatectomy recurrence includes prostatic bed. Thanks to advances in imaging (choline PET MRI, etc.) it is possible to identify the macroscopic local recurrence. This has led to greater interest in short course RT schedule in highly selected pts. The aim of this study is to report the feasibility of extremely hypofractionated RT for isolated relapse in the prostatic bed. Secondary endpoints will be progression free survival (PFS) and overall survival (OS).

Methods: Inclusions criteria are as follows: RT-naïve pts (no previous adjuvant pelvic RT); biochemical recurrence according to EAU guidelines and followed by clinically evident local recurrence assessed with MRI or/and [11C] choline PET; N0, M0, informed consent. Biochemical response will be evaluated with PSA level variation (PSA) every 3 months after treatment: biochemical response (BCR) as PSA lower than -20%, progression (BCP) as PSA>+20% and stability (BCS) as -20%< PSA<+20%. Clinical follow-up will be performed at 6 and 12 months after treatment and every 12 months afterward in order to assess genito-urinary (GU) and gastrointestinal (GI) toxicity (RTOG-EORTC).

Results: We retrospectively analyzed 14 pts treated between 6/2016 and 5/2017 for clinically visible Pca recurrence in the prostatic bed. Median age, initial PSA (iPSA) and Gleason score (GS) were 65 (range 53-78), 6.1 ng/ml (range 4.3-18) and 7 (range 5-9), respectively. Median clinical progression after surgery was 131 months (range 3-158). Median PSA at clinical progression was 1.2 ng/ml (range 0.17-3.29). Median sRT dose was 32.5 Gy (range 30-35) in 5 fractions (alternating days) was given with image guided IMRT. 4 patients received concomitant hormonal therapy (HT) and sRT. No GI or GU acute toxicity > G2 was reported, only 1 G1 GI and in 1 G1 GU events were registered. The analysis of clinical outcomes is still ongoing. In 5 pts PSA evaluation and clinical follow-up at 6 months were available; BCR was observed in 4 pts and BCP was observed in 1 pt. PFS in these pts was of 80%. No late GI or GU toxicity > G2 was reported.

Conclusions: On the basis of the available data, extremely hypofractionated salvage IMRT is a feasible and safe for isolated macroscopic recurrence in the prostatic bed, with a low acute toxicity profile. Our preliminary results should be confirmed in a larger court of patients with longer follow-up.

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VOLUMETRIC MODULATED ARC THERAPY IN THE EXCLUSIVE AND ADJUVANT TREATMENTS OF GENITOURINARY CANCER: DATA FROM A SYSTEMATIC REVIEW

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Aims: The shape of nodal target represents a condition particularly suitable to benefit from volumetric modulated arc therapy (VMAT) in high risk prostate (PC) and endometrial cancer (EC). Results relative to VMAT toxicity and clinical outcome are emerging, but still sparse. Aim of this analysis was to review the available data from clinical outcome studies in PC and EC.Methods: A systematic review based on PRISMA

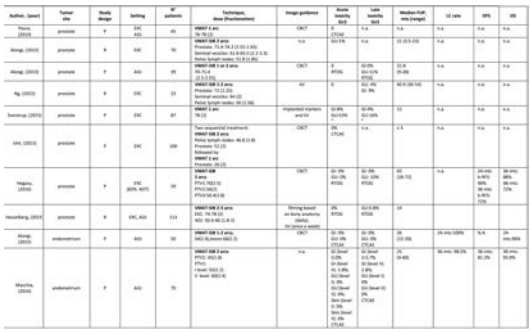
methodology of papers reporting clinical studies on VMAT was carried out using the National Library of Medicine. The following words were searched: "volumetric arc therapy" OR "vmat" OR "rapidarc" AND "radiotherapy"AND Clinical Trial. Only in English articles were considered. Data on PC and EC were extrapolated and represent the object of this analysis.

Results: PC: 8 studies (5 prospective and 3 retrospective) have been enclosed. 5 studies addressed only exclusive setting, while the remaining investigated adjuvant setting or both. Most of patients were treated by VMAT-SIB 2-3 arc techniques, almost all using image guidance (IG). In 2 papers only prostate was treated, using one arc technique up to 78 Gy/2Gy fraction. Both authors reported that IG-VMAT is a safe treatment for PC with mild changes in urinary (GU) and gastrointestinal (GI) symptoms after 1 year from VMAT end. PSA decreased to undetectable values at end of treatment, thus leading to consider clinical outcome as encouraging. Pelvic nodes, prostate and seminal vesicles were treated by 5 authors by a 1-3 arcs technique, with doses ranging from 46.8 Gy for nodal coverage to 78 Gy for prostate irradiation. Almost all used IG, and 335 patients were treated from 2012 to 2016. VMAT SIB resulted technically feasible and safe providing high target coverage and acceptable GI and GU toxicity. All but one studies failed to report data on local control or overall survival (Table).

EC: 2 Phase I-II studies enrolling patients treated on pelvic lymph nodes and boosted on the vaginal cuff by a VMAT-SIB 2 arcs techniques have been enclosed. The 2-y local control rates were 98.5% and 100% respectively, with overall survival rates ranging from 94% and 96% (Table). Both authors judged VMAT-SIB feasible and well tolerated, notwithstanding prolonged follow-up is needed.

Conclusions: The present analysis suggests that VMAT, especially when large volumes need to be irradiated, and 2-arc SIB strategy is used, or high sensitive structure sparing is required could be considered an effective safe modality.

Table 1. VMAT-SIB in genitourinary cancer



Legend: P: prospective study; R: retrospective study; EXC: exclusive; ADJ: Adjuvant; VMAT: Volumetric Modulated Arc Therapy; SIB: Simultaneus Integrated Boost; kV: kilovoltage X-ray imaging; CBCT: Cone Beam Computed Tomography; GI: Gastrointestinal; GU: Genitourinary; FUP: follow-up; mts: months; n.a.: not available; LC: local control; DFS: Disease Free Survival; OS: Overall Survival; b-RFS: biochemical relapse-free survival; RTOG: Radiation Therapy Oncology Group scale; CTCAE: Common Terminology Criteria for Adverse Events scale; a PCSS: Prostate Cancer Symptom Scale questionnaire .

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PRELIMINARY RESULTS OF MODERATE HYPOFRACTIONATED IMAGE-GUIDED RADIOTHERAPY DELIVERED WITH TOMOTHERAPY FOR LOW-INTERMEDIATE RISK PROSTATE CANCER

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Aims: Based on radiobiology evidence, hypofractionated radiotherapy has the potential of improving treatment outcomes in prostate cancer patients. We report preliminary results of our single center prospective phase I/II trial of CT-MR based moderate image-guided radiotherapy delivered with helical tomotherapy (HHT) for low-intermediate risk (LR and IR) prostate cancer.

Methods: From September 2013 to March 2017, 29 patients were enrolled: 72% LR, 28% IR according to NCCN definition. Inclusion criteria were: histological diagnosis of prostate adenocarcinoma, IPSS<19, age<85, KPS>60. Median age and pre-treatment PSA were respectively 76 years (range 55-80) and 9.73 ng/ml (2.1-16). Short term androgen deprivation therapy was allowed and administered in 34% of cases. CT and MR simulation scans were performed with a reproducible rectal emptying and a comfortable bladder filling. Target volumes were delineated basing on CT-MR image fusion: a single CTV, consisting of prostate plus seminal vesicles base, for LR patients and a CTV1 (prostate plus seminal vesicles base) and CTV2 (upper remaining of seminal vesicles) for IR patients. IMRT plans were created using an isotropic 5mm CTV margin to PTV expansion, with a prescription dose of 60 Gy for LR, 60 Gy and 54 Gy for IR in 20 fractions. Daily Megavoltage CT was performed prior to each fraction to verify setup accuracy.

Results: After a median follow-up of 16 months (range 2-41) toxicity profiles, according to CTCAE V4.0, were: acute G1 and G2 gastrointestinal (GI) events in 35% and 14%; acute G1 and G2 genitourinary (GU) events in 69% and 7%, no ≥G3 occurred. Late GI and GU toxicity were G1 in 17%, no ≥G2, G1 in 39% and G2 in 5% respectively. Quality of life evaluation through EPIC questionnaire reported mild decline of urinary function after 3 months, with a trend to resolution within 1 year; GI discomfort was generally limited to the treatment time, resolving within 6 months. No biochemical failure occurred during follow-up.

Conclusions: Our data support moderate hypofractionation for LR-IR prostate cancer, as the use of Tomotherapy results in favorable toxicity profiles, that can be ascribed both to careful patient selection and to the combination of CT-MR based planning with daily IGRT.

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ADJUVANT HYPOFRACTIONATED RADIOTHERAPY FOR PROSTATE CANCER: ACUTE TOXICITY

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Purpose: To evaluate acute toxicity and preliminary outcome of hypofractionated adjuvant radiotherapy (Hypo-ART) with helical tomotherapy after radical prostatectomy (RP).

Methods and Materials: From February 2014 to Genuary 2017, 40 prostate cancer patients received Hypo-ART for pT2-3 N0-1 and/or R1disease. Median age was 65 years (range 53-78). The surgical Gleason score was: <7 in 3 patients (7,5%),7 in 23 (57,5%) and >7 in 14 (35%). Before RP the median PSA was 6,71 (range: 1.13-44. 48) which dropped to 0.035 ng/ml (range: 0 -1,97) before Hypo-ART. RT schedule: all 40 patients received 2.25 Gy in 29 fractions (total dose: 65.25 Gy) to the prostate/seminal vesicle bed; 16(40%) patients also received 1.8Gy in 29 fractions to the pelvic lymph nodes (total dose: 52.2 Gy). A simultaneous integrated boost (SIB) technique was used. Hormone therapy (LHRH analogue and/or anti-androgen) was administered to 18 (45%) patients with high risk features. Toxicity was graded according to the Common Terminology Criteria for Adverse Events version v4.0. Biochemical failure was defined by ASTRO criteria. The Kaplan-Meier method determined time-to- acute toxicity events. The Mann-Whitney tested compared clinical and dosimetric variables in groups with and without acute toxicity.

Results: Median follow-up was 16,5 months (range: 3-32).The median duration of HT was 14 months (range 6-36). Only G1-G2 acute genitourinary (GU) and intestinal (GI) toxicities occurred. Acute grade 1 GU toxicity occurred in 16/40 patients (40%), with 15(37,5%) developing cystitis and 1(2.5%) urinary incontinence. Acute grade 2 GU toxicity occurred in 3/40 (7.5%) patients with 1 (2.5%) patient developing hematuria, 1(2.5%) urinary incontinence and 1(2.5%) urinary retension. Acute grade 1 GI toxicity (proctitis) occurred in 14/40 patients (35%), which was associated with rectal bleeding in 5 (12.5%) and diarrhoea in 7 (17,5%). Acute grade 2 GI toxicity (proctitis) developed in 3/40(7,5%) patients, which was associated with rectal bleeding in 1(2.5%) and diarrhoea in 1 (2.5%). Post Hypo-ART the median PSA was 0.02 ng/ml (range:0-0.22) and the nadir was 0.01 ng/ml (range: 0-0.11). At the last follow-up no patient presented evidence of biochemical or loco-regional recurrence. No differences emerged in clinical and dosimetric variables in group with or without acute toxicity.

Conclusions: These results suggest that moderate Hypo -ART is safe, effective and well-tolerated . A longer follow-up is needed to assess late toxicity and disease-free survival.

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HYPOFRATIONATED ADJUVANT RADIOTHERAPY AFTER RADICAL PROSTATECTOMY

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Purpose: Few data are available about hypofractionated in post-prostatectomy. The aim of the study was to investigate retrospectively outcome, acute and late complications in prostate cancer treated with postoperative and salvage intent using moderate hypofractionated 3D conformal radiotherapy (Hypo).

Materials and Methods: 69 Consecutive patients (pts) were treated. The mean age was 66 years, median 69 (range 51-77). According to 2.2017 NCCN prognostic classification 29% pts was intermediate risk, 42% high risk, 23% very high risk, and 4% metastatic. The pts were treated with total dose 62.5 Gy in 2.5 fraction (25 fractions) on prostatic fossa and one pts with 62 Gy 3 Gy fraction; 5 fractions/weeks with LINAC 6-15 MV, 7 fields. The mean prostate specific antigen (PSA) at the diagnosis was 18.7 ng/ml; median 10.4 (range 0.59-188). Surgical pathological specimens showed pT2 31% (R1 81%), pT3a 41% (R1 57%, Close 7%), pT3b 26% (R1 72%). Androgen deprivation therapy (ADT) was administrated in 20%. Mean follow-up was 54 months (m), median 53 m, (range 34-72 m). All the pts were clinically evaluated for urinary and rectal late complications according to CTC.AE 4.0 and RTOG/EORTC scale.

Results: Five-year biochemical disease-free survival (bDFS) was 68% and overall survival (OS) was 95%, 2 pts dead for other cause and 1 pts dead for prostate disease. 26% alive with disease (AWD). Mean PSA at last follow-up was 0.8, median 0.08 (range 0-13). Acute toxicity: genitourinary (GU) ≥ G2 in 12% of pts and gastrointestinal (GI) ≥ G2 in 5% of pts. Late toxicity: GU ≥ G2 in 12% (1 pts with G4 rectal-urinary fistula and 3 pts with urethral strictures). GI ≥ G2 5 %. No pts developed grade 4 GI complication. Urinary incontinence ≥ G2 was 19%

Conclusions: Same studies reported an increased severe GU late toxicity compared to GU toxicity in standard fractionated (SF) regimens. In our data moderate hypofractionated regimen appears a feasible option with similar toxicity to SF. Hypo is well tolerated if only prostate fossa is treated without the use anticoagulants.

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SBRT RE-IRRADIATION THERAPY FOR LOCALLY RECURRENT PROSTATE CANCER AFTER EXTERNAL-BEAM RADIATION THERAPY

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Purpose: Optimal management of locally recurrent prostate cancer after definitive radiation therapy is still problematic: it is necessary to ensure sufficient dose to tumor without giving too much toxicity. The development of highly accurate radiotherapy devices could offer precise irradiation while sparing healthy tissues. The aim of this study is to evaluate the toxicity, the efficiency and dose responses of re-irradiation with stereotactic body radiotherapy (SBRT) in patients with recurrent of prostate cancer after external- beam radiation therapy.

Materials and Methods: From April 2011 to March 2017, SBRT was administrated to 11 patients for isolated local recurrence of prostate cancer. 10 patients were a high risk while a patient was an intermediate risk. The pts was previously treated with external-beam radiation therapy to a median dose of 76,6Gy (range 68-78Gy). After a median time of 40 moths (range 13-84 month), the patients had a recurrences confirmed by multiparametric MRI and total body 18F-fluorocholine PET-CT. The prescribed dose was 30 Gy in 3fx to 80% isodose (total dose to isocenter was 37,5Gy, BED100=84,4)in 9 pts and 30Gy in 6fx to 80% isodose in two patients. The target delineation was performed on plan CT-MRI fusion to limit the normal tissue toxicity especially for rectum wall and bladder. The VMAT treatment was delivered by 6MV beam modulator Linac with 4mm MLC. Patient set-up and isocenter position were controlled before each fraction by CBCT. Toxicity was evaluated according to CTCAE v. 4.0 and the treatment response was evaluated by PSA.

Results: Median follow-up was 8 months (range 1-18). Local control was achieved in all treated lesions regardless of dose/fx prescription. Two patients (18%) had a biochemical failure due to metastatic progression without evidence of local recurrence. Treatment was well tolerated, no grade >2 acute gastrointestinal or late toxicities were reported.

Conclusions: SBRT re-irradiation of intraprostatic recurrences after external beam RT showed favorable results in terms of in-field local and biochemical control. In our experience the only two relapses occours outside of prostate gland. The SBRT re-irradiation can be considered for intraprostatic recurrence instead of brachitherapy or surgical approach. Toxicity was low and acceptable. The results needed to be confirmed with a greater number of case.

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THE ROLE OF MAGNETIC RESONANCE IMAGING IN TREATMENT PLANNING FOR EXCLUSIVE EXTERNAL BEAM RADIOTHERAPY IN PROSTATE CANCER: VOLUMETRIC AND DOSIMETRIC ANALYSIS

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Aims: The purpose of this study is to evaluate the role of magnetic resonance imaging (MRI) in the delineation of clinical volumes during treatment planning for prostate cancer exclusive external beam radiotherapy (RT).

Methods: Fifty-nine patients (pts) with prostate cancer treated in our University Hospital underwent MRI of the pelvis. MRI was used as diagnostic exam to better define staging according with TNM, 7th edition. Moreover, T2-MRI images were fused on CT simulation images. Gross Tumor Volume (GTV, prostate +/- seminal vesicles), and organ at risks (bulb of penis, bladder, rectum) were contoured both on CT and T2-MRI images. For each patient, we created two image sets: CT images (GTV CT) and MRI images (GTV MRI). The treatment planning was elaborated on fused images and contours (CT+MRI). Pts were treated with VMAT (volumetric arc therapy), or with IMRT (intensity modulated radiotherapy) technique. All cases were treated with image guided radiotherapy. The prescribed dose to PTV (CT+MRI) was 76 Gy for low risk patients and 78 Gy for intermediate and high risk patients. The planned dose to seminal vesicles was 60 Gy in cT1-cT2 and 66 Gy in cT3 tumors. For each patient GTV CT was compared with GTV MRI and with CTV MRI+CT. We also compared treatment planning with CT or MRI images.

Results: To date, we have analysed data from 35 out of 59 pts: 2 pts with low risk cancer, 17 with intermediate risk and 16 with high risk prostate cancer according with NCCN 2017 classification. GTV CT was 56.51cc (range: 29.57-96.06), GTV MRI was 44.43 cc (range: 20.94-76.70). CT and MRI volumes differed by 22.90% (12.88 cc) $p<0.05$ with t-Student test. We compared bulb of penis, bladder and rectal dosimetric parameters according with QUANTEC. Organs at risk volumes and preliminary results were reported on Table 1.

Conclusions: The comparison between GTV CT and GTV MRI emphasized a volumetric reduction in favour of MRI contours in particular better definition in bulb of penis contours. Consequently, the comparison between treatment planning showed a clear reduction in V50 and D50 bulb of penis and in V70, V60 and V40 of rectum. There was also observed a reduction in bladder parameters (average dose, V50 and V65). From this preliminary data, it emerges a central role of MRI ima-

ging during radiotherapy treatment planning with reduction in GTV volumes and reduction of delivered dose at organs at risk.

Table 1. Volumetric and dosimetry parameters.

	MRI	CT	p-value
Bulb of penis cc	16.2	18.4	<0.05
- V_{50} (%)	4.37	29.54	<0.05
- D_{50} (Gy)	13.65	35.69	<0.05
Rectum cc	125.6	113.0	n.v.
Rectum V_{70} (%)	3.43	4.61	0.06
Rectum V_{60} (%)	9.64	11.72	<0.05
Rectum V_{40} (%)	29.58	33.78	<0.05
Bladder cc	155.6	158.4	n.v.
- Average dose (Gy)	22.89	20.22	0.066
- V_{50} (%)	18.82	15.20	0.058
- V_{65} (%)	14.59	12.04	0.062

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RADIOINDUCED MODIFICATIONS OF THE OBTURATOR MUSCLES AS DERIVED FROM TEXTURAL ANALYSIS OF T2W-MRI ACQUISITIONS AFTER PROSTATE CANCER RADIOTHERAPY

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Aims: Main purpose of this study was to investigate the radio-induced modifications of the pelvic muscles through a quantitative analysis of MRI acquisitions and dose distributions, in patients treated with external beam radiotherapy (RT) for prostate cancer. We concentrated on the internal obturator muscles that might influence continence due to the relation of their fascia to the superior and inferior layers of the diaphragmatic part of the pelvic fascia [1].

Methods: T2-weighted-MR images were acquired with a 1.5T scan in thirteen patients before radiotherapy (MRI1) and at 12 months after the end of RT (MRI2). Internal obturator muscles were manually delineated upon MRI1 and automatically propagated on MRI2 by elastic registration. Planning CT were co-registered and 3D-dose distributions deformed accordingly. 13 textural features were extracted in each sub-volume from the histogram/co-occurrence matrix. Percentage variation of each feature with respect to the lowest iso-dose region were calculated. Differences between each normalized iso-dose parameter extracted before and after radiotherapy were computed and dose-response curves were built.

Results: Iso-dose regions between 30 and 75 Gy were identified within the obturator muscles. 6 textural features exhibited a dose-dependent behavior (see Table). In particular, the mean T2w intensity showed an exponential growth with dose that can be described by the relationship intensity=0.4*exp(0.06*dose) (see Figure). Skewness and kurtosis, calculated from the histogram, and contrast and dissimilarity, calculated from the co-occurrence matrix, presented a non-linear decrease.

Conclusions: MRI acquisitions allowed to derive a dose-response curve for structural modifications of obturator muscles after irradiation. A significant increase in signal intensity, exponentially associated to the dose received by the internal obturator muscles was observed. The more enhanced decrease in skewness, kurtosis and contrast in the high dose regions can be interpreted as a loss of the structured tissue organization, in favour of a more homogeneous pattern. These variations are more evident where the absorbed dose is higher and can be compatible with an inflammatory status that normally follows RT, and which is still evident one year after RT completion. With an increased number of available patients, possible associations with toxicity will be investigated.

Reference

1. Tienza et al. Int Urol Nephrol 2015

	Δ pre - post RT	mean T2 [%]
Histogram	*Δ Mean*	58,6± 20,9 **
	Δ Variance	212± 84,3 **
	Δ 95th percentile	77,7± 23,5 **
	Δ Entropy S_1	5,60± 5,68 **
	Δ Skewness	-8,68± 23,6 *
	Δ Kurtosis	40,8± 319 *
GLCM	*Δ Energy*	15,4± 8,96 **
	Δ Correlation	17,8± 6,70 **
	Δ Homogeneity	30,5± 10,6 **
	Δ Entropy S_2	-3,52± 2,18 **
	Δ Contrast	-35,8± 13,9 **
	Δ Dissimilarity	-23,4± 7,91 **
NGTDM	*Δ Coarseness*	45,5± 27,2 **
	Δ Contrast	-23,5± 21,3 **
	Δ Busyness	-27,0± 22,8 **
	Δ Complexity	-29,3± 9,23 **
	Δ Strength	82,8± 33,2 **
	Δ Fractal Dimension	-2,60± 1,10 **

* p<0.05
**p<0.001

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IMPACT OF ORAL HYALURONIC ACID AND CHONDROITIN SULFATE IN REDUCING URINARY TOXICITY DURING RADICAL RADIOTHERAPY IN PROSTATE CANCER: A PRELIMINARY EXPERIENCE.

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Aims: Acute urinary toxicity is a common adverse event affecting patients undergoing radiotherapy for prostate cancer. IALURIL ® SOFT GELS is a dietary supplement containing curcumin, quercetin, hyaluronic acid and chondroitin sulfate. The aim of this prospective study was to determine the efficacy and safety of IALURIL®SOFT GELS in reducing acute genito-urinary toxicity in patients affected by prostate cancer treated radiotherapy in the radical or in the adjuvant/salvage setting.

Materials and Methods: Forty-two patients affected by localized prostate cancer were prospectively enrolled. 22 patients (52%) received radical treatment (9 with conventional and 12 with hypofractionated treatment); eight (19%) and 12 (29%) patients received adjuvant and salvage treatment, respectively.

The Interstitial Cystitis Symptoms Index (ICSI) and the Interstitial Cystitis Problem Index (ICPI) questionnaires were administered in all patients on day 1 of treatment (T0), at the half (T1) and at the end (T2) of the treatment. Furthermore, acute urinary toxicity was reported according to CTCAE v 4.03 for all patients. A matched control series of 42 patients, treated with radiotherapy at our institute, was evaluated reporting acute urinary toxicity according to CTCAE v 4.03. None of the patients from the control series underwent IALURIL®SOFT GELS supplementation during RT.

Results: Acute urinary toxicity reported according to ICSI and ICPI has showed statistically significant variations during treatment; Wilcoxon signed rank-test showed increase in terms of cystitis and urinary urgency during treatment (T1 vs T2, T1 vs T3, $p<0.001$ and T1 vs T3, p 0.015, respectively). Reported acute urinary toxicity, according to CTCAE, was G0, G1 and G2 in 16 (38%), 18 (43%) and 8 (19%) vs 8 (19%), 12 (29%) and 13 (31%), in the Ialuril vs control group, respectively. Furthermore, no cases of >G3 acute toxicity was reported in the Ialuril® sof gels group, while 8 (19%) and 1 (2%) patients in the control group had G3 and G4 toxicity. The chi-squared (2) test showed a statistically significant differences in terms of > G3 acute urinary toxicity between the two groups (p 0.007).

Conclusions: In the current analysis, supplementation with IALURIL ® SOFT GELS showed significant benefit in terms of acute urinary toxicity in patients undergoing RT for prostate cancer.

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RETROSPECTIVE ANALISYS OF PATIENTS UNDERGOIN STEREOTACTIC BODY RADIOTHERAPY (SBRT) IN SECONDARY NON-BONE LESIONS OF METASTATIC RENAL CELL CARCINOMA (MRCC) IN TREATMENT WITH VASCULAR ENDOTHELIAL GROWTH FACTOR (VEGF) TYROSINE KINASE INHIBITORS

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Aims: A traditionally radioresist tumor such as mRCC nowadays showed in several studies good response rates to radiotherapy treatment of metastatic lesions. While most of these studies include patients with secondary bone lesions, today there is no prospective or retrospective study on the use of radiotherapy in patients with non-bone mRCC metastases in order to consolidate the response to medical therapy (TKI or mTOR inhibitors) or to treat the individual oligoprogression sites. Primary outcome of the study was to evaluate the response rate of non-bone lesions treated with SBRT according to RECIST 1.1 criteria in patients with renal carcinoma who were previously subjected to oncological treatment with medical therapy (Sunitinib or Sorafenib), at Azienda Ospedaliero-Universitaria in Parma.

Methods: From April 2016 to February 2017 retrospective data were collected from 9 patients treated at Azienda Ospedaliero-Universitaria in Parma, all living, 2 females and 7 males, avarage 65.3 years of age (57-80 years) with SBRT-treated non-skeletal metastases on one site. Range doses were 15 Gy – 45 Gy (average 33 Gy) in 1 to 5 fractions (average 4 fractions). All patients were treated with antiangiogenetic medications. The SBRT treated metastases were located at brainstem (1 case), lung (2 cases), chest thoracic lymph node (1 paratracheal, 1 peripheral and 1 parasternal), paraortic lymph node (1 case), ileo-psoas region (1 case), supraclavicular region (1 case). All patients were followed up with CT every 3-4 months. The answer was evaluated using the Recist 1.1 criteria.

Results: After SBRT treatment, 77,8% of patients showed metastasis volumetric reduction, while 22,2% of patients reported dimensional stability of the lesion, without toxicity due to the treatment, and also having a periodical suspension of terapy with mTOR inhibitors or TKI.

Conclusions: This study showed that the combination of SBRT on metastatic lesions of renal cell carcinoma and TKI or mTOR inhibitors allows good local and systemic control of desease in a significant percentage of patients. Because of the limited number of patients in the analyzed sample the statistical study is not significant, but this trend is very interesting and important for new set of treatment of this patients. For this reason we are planning a multicentre retrospective study to con-

firm this trend, obtain more informations on this kind of approach and start to evaluate other new indications for SBRT.

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ADJUVANT RADIOTHERAPY FOR RENAL CELL CARCINOMA

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Aims: Despite the high incidence of loco regional failure after nephrectomy in patients with renal cell carcinoma, the role of adjuvant radiotherapy has not yet well investigated and the literature is limited to clinical studies carried out more than 30 years ago with 2D radiotherapy techniques and an unacceptable toxicity. In order to evaluate the safety and the feasibility of VMAT technique in a postoperative setting, we performed a dosimetric study in 15 patients who underwent nephrectomy.

Methods: We considered the postoperative Computer Tomography Scan (CT) of 15 patients after nephrectomy for renal cell carcinoma. On the CT scan of every single patient we performed two radiotherapy plans delivering 50 Gy in 25 fractions: 1) using 2D technique (2 opposite fields) 2) Using VMAT technique. We compared the toxicities of the 2 treatments, with particolar regard to the small bowel toxicity.

Results: All plans performed with VMAT technique reached the abdominal constraints, whereas not any performed using 2D technique did so.

Conclusions: Considering the DVH of each plan delivered with VMAT technique, it can be noted that state-of-art RT technique could be associated with a lower complication rate compared to the older techniques. So postoperative radiotherapy, delivered via that state-of-art technique, could be safely used in the treatment of RCC pts with the purpose of improving local control and survival. Nevertheless, further clinical studies are warranted in order to confirm our Results:

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SALVAGE IMAGE-GUIDED STEREOTACTIC MULTIPLE RE-IRRADIATION FOR LOCALLY RECURRENT PROSTATE CANCER: SOMETHING VENTURED, SOMETHING GAINED. UPDATED RESULTS

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Aims: Local prostate cancer (PCa) recurrence is treated routinely by systemic therapy. This scenario is unusual in oncology, as focal approaches are usually preferred for isolated recurrences. Recently, the availability of high precision radiotherapy (RT) has allowed for re-RT in carefully chosen clinical settings. The aim of our study is to present the technical feasibility and efficacy of multiple re-RT for locally recurrent PCa in selected patients (pts).

Methods: Retrospective analysis of an updated series of pts who received multiple (>2) re-RT with stereotactic image-guided technique and hypofractionated RT. Six pts received a third RT, of those two received a forth RT course. One pt underwent surgery as primary treatment. All pts were discussed in the multidisciplinary tumor board. Local relapse was assessed by multiparametric magnetic resonance and/or choline positron emission tomography. Histological confirmation of recurrence was required in three cases. All pts had been evaluated for toxicity from previous RT according to RTOG/EORTC. Biochemical control was assessed according to Phoenix definition. Dosimetric constraints were based on previous institutional experience on PCa re-RT. Gross tumor volumes (GTVs) were limited to the site of relapse; planning target volume margins were achieved expanding the GTVs of 3 mm posteriorly, and of 5 mm in any other direction.

Table 1. Summary of radiation treatments by patient.

	Treated Volume	Technique	Total Dose; Dose/fraction	BED (α/β=1.5 Gy)
Patient 1- NCCN 2017 Initial Risk Group: Intermediate				
Sept-Nov 2005 (67 ys)	Prostate+ 1/3 Seminal Vesicles	3D-CRT	76 Gy; 2 Gy/fract.	177.3 Gy
Feb 2010 (72 ys)	Prostate (GTV 48.81 cm^3)	SBRT CyberKnife®	30 Gy, 6 Gy/fract.	150.0 Gy
Sept-Oct 2013 (75 ys)	Intraprostatic lesion (apex) (GTV 25.18 cm^3)	SBRT CyberKnife®	25 Gy, 5 Gy/fract.	108.3 Gy
May 2016 (78 ys)	Intraprostatic lesion, apex (GTV 1.0 cm^3)	SBRT CyberKnife®	25 Gy, 5 Gy/fract.	108.3 Gy
Patient 2- NCCN 2017 Initial Risk Group: Low				
Jan-March 2005 (65 ys)	Prostate+ 1/3 Seminal Vesicles	3D-CRT	76 Gy; 2 Gy/fract.	177.3 Gy
March 2012 (72 ys)	Prostate (GTV 25.06 cm^3)	SBRT CyberKnife®	25 Gy, 5 Gy/fract.	108.3 Gy
Sept 2015 (76 ys)	Intraprostatic lesion, left lobe (GTV 3.1 cm^3)	SBRT CyberKnife®	30 Gy, 6 Gy/fract.	150.0 Gy

Patient 3- NCCN 2017 Initial Risk Group: Intermediate				
Feb-March 2003 (52 ys)	Prostate	3D-CRT + Brachytherapy	50 Gy; 2 Gy/fract. + 100 Gy I-125 seeds	N.E.
Apr-May 2010 (59 ys)	Prostate (GTV 24.19 cm^3)	3D-CRT	30 Gy, 6 Gy/fract.	150.0 Gy
May 2013 (62 ys)	Peri-prostatic node (GTV 12.98 cm^3)	IMRT VERO®	32 Gy, 4 Gy/fract.	117.33 Gy
Feb 2017 (66 ys)	Seminal vesicles, proximal portion (GTV 9.98 cm^3)	IMRT VERO®	25 Gy, 5 Gy/fract.	108.3 Gy
Patient 4- NCCN 2017 Initial Risk Group: High				
Jan-March 2007 (55 ys)	True pelvis, prostate and seminal vesicles boost	3D-CRT	76 Gy, 2 Gy/fract.	177.3 Gy
Apr 2014 (62 ys)	Left apex and right peripheral zone (GTV1 + GTV2 6.415 cm^3)	IMRT VERO®	30 Gy, 10 Gy/fract.	90.0 Gy
June 2016 (64 ys)	Right prostate lobe (20.0 cm^3)	IMRT VERO®	25 Gy, 5 Gy/fract.	108.3 Gy
Patient 5- NCCN 2017 Initial Risk Group: High				
Oct 2003 (56 ys)	True pelvis, prostate and seminal vesicles boost	3D-CRT	78.4 Gy 2 Gy/fract.	182.93 Gy
Jun-Jul 2015 (68 ys)	Prostate (GTV 30.65 cm^3)	IMRT VERO®	30 Gy, 6 Gy/fract	150.0 Gy
May 2017 (70 ys)	Intraprostatic lesion, left lobe (GT 4.27 cm^3)	IMRT VERO®	25 Gy, 5 Gy/fract	108.3 Gy
Patient 6- NCCN 2017 Initial Risk Group: Intermediate				
May-Jun 2009 (56 ys)	Prostate bed	3D-CRT	70 Gy, 2 Gy/fract.	163.33 Gy
Jun 2014 (61 ys)	Left-posterior para-uretheral region (GTV 7.31 cm^3)	IMRT VERO®	25 Gy, 5 Gy/fract.	108.3 Gy
February 2017 (63 ys)	Ureterovesical junction, antero-lateral portion, left (GTV 3.71 cm^3)	IMRT VERO®	25 Gy, 5 Gy/fract.	108.3 Gy

Legend: BED: Biologically Effective Dose; 3D-CRT: Three Dimensional-Conformal Radiation Therapy; GTV: Gross Tumor Volume; IMRT: Intensity Modulated Radiotherapy; NCCN: National Comprehensive Cancer Network, SBRT: Stereotactic Body Radiation Therapy; fract: fraction; ys: years; NE: Not Evaluable.

Results: Mean age at third RT course was 65.6 years; all pts had good performance status per Karnofsky and ECOG scoring systems. At diagnosis, three cases were classified as intermediate risk PCa, two as high and one as low per NCCN 2017. Mean prostate specific antigen (PSA) at the time of first and second relapse was 3.4 and 5.4 ng/mL, respectively. Mean interval between the first and second RT was 74.8 months, mean interval between the second and third RT was 33.5 months. Mean ADT-free interval after the second RT course was 24.6 months. No acute or late moderate to severe GU or GI events were recorded; chronic mild GU toxicity was reported in one pt after the second RT course.

Conclusions: Biochemical and radiological response was registered in all pts, overall toxicity profile was good. Some room for further dose escalation is suggested. Additionally, re-RT may be regarded as an option for avoiding/deferring ADT in carefully selected pts. Larger series and longer follow-up are warranted to assess the potential of multiple re-RT in the setting of local salvage therapies for PCa.

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STEP-AND-SHOOT IMRT VS DWA: A DOSIMETRICAL COMPARISON OF PROSTATE CANCER TREATMENTS

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Aims: To compare Step-and-Shoot Intensity Modulated Radiation Therapy (IMRT) and Dynamic Wave Arc (DWA) radiotherapy for radical prostate cancer treatments, performed with the VERO system.Each plan was evaluated with regards to PTVs, rectum and bladder DVHs and to the pre-treatment Quality Assurance (QA) results.

Methods:Since 2012 prostatic patients with organ confined disease were treated at European Institute of Oncology (IEO) with GiveMeFive protocol applied to the NCCN risk categories low (T1-T2a,PSA<10 ng/mL, Gleason score <7) or intermediate (T2b or T2c,PSA between 10 and 20 ng/ml, Gleason score of 7); personalized indication for high risk pts (PSA>20 ng/mL, Gleason score>7);an extreme hypo-IGRT schedule (32.5-35 Gy/5 fractions on alternate days) was prescribed.On April 2017 DWA upgrade was performed: this is an extended form of Volumetric Modulated Arc Therapy (VMAT) with a continuous varying ring position.The RayStation TPS v.6.0 was clinically integrated on the VERO system and plans were calculated on a 2x2x2 mm3 resolution dose grid (Collapsed Cone algorithm v.3.3) and delivered using 2 arcs. 15 patients were treated with DWA until now. All plans were also calculated on a same dose grid (pencil beam algorithm) with iPlanNet v.4.5.4 using 7IMRT fields.DVHs evaluation was performed comparing D95%, D2% and D50% for PTVs, V50%,V80%,V90% and V100% for rectum, V100% and V50% for bladder.Pre-treatment QA were performed using ArcCHECK®phantom(Sun Nuclear Corporation,Melbourne,FL) with the plug inserted for absolute point dose measurements(0.053 cm3 Exradin ion chamber) and SNC Patient software(v. 6.6.2,Sun Nuclear Corporation,Melbourne,FL), applying 2D gamma evaluation (γ) (absolute dose, 2%-2mm criteria and 10% dose threshold).

Results: Mean DVHs values for IMRT versus DWA treatments are reported in Table 1. Pre-treatment QA

presented an average γ of 96.5±2.5% for DWA (91%÷99.2%), with a mean percentage variation of the absolute dose value between measurements and calculations of -1.16±0.01% (-1.87%÷0.02%). The time delivery is reduced from about 15 minutes for IMRT treatments to about 5 minutes for DWA.

Conclusions: From the preliminary results, the dosimetric goals of the two techniques are successfully achieved, with a good accuracy in terms of γ analysis for DWA. Even if non-coplanar arcs do not represent a main advantage in prostate treatments, DWA permits a lower time delivery, which can be extremely convenient to prevent intra-fraction organ motion.

Table 1. PTV, rectum and urinary bladder DVH values obtained with IMRT and DWA plans.

	IMRT	DWA		IMRT	DWA		IMRT
PTV			Rectum			Bladder	
$D_{95\%}$	94.9%	95.9%	$V_{100\%}$	0.1%	0.1%	$V_{100\%}$	1.1%
$D_{50\%}$	100.1%	100.5%	$V_{90\%}$	1.5%	1.6%		3.3 cm^3
$D_{2\%}$	103.0%	103.5%	$V_{80\%}$	3.9%	4.0%	$V_{50\%}$	11.6%
			$V_{50\%}$	13.0%	11.5%		

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EARLY SALVAGE RADIOTHERAPY AFTER RADICAL PROSTATECTOMY IN RECURRENT PROSTATE CANCER PATIENTS

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Aims: Early salvage radiotherapy (ESRT) following radical prostatectomy (RP) for prostate cancer is a potentially curative treatment for some men with a detectable prostate -specific antigen (PSA). The aim of this retrospective study is to evaluate the clinical outcome of 37 patients (pts) submitted to SRT between 2012 and 2016 at our institution.

Outcomes included biochemical relapse-free (bRFS) distant metastases free (DMFS)and prostate cancer specific survival (PCSS).

Methods: From 2012 to 2016 60 pts underwent adjuvant radiotherapy after RP while salvage RT was administered in 37 pts. The characteristics of this second group of patients were analyzed. SRT was due to delayed rise in PSA in 24 pts (65%), in 13 (35%) also with clinical evidence. Median age was 70 years. 72% of pts had pT3a disease or greater, 45% of pts had Gleason score >/= 8 while 51% of pts had positive surgical margins. 56% of pts had undetectable postoperative PSA and median time from RP to SRT was 30 months (6-96). The median RT dose was 70 Gy (range 64-76 Gy) using intensity modulated radiation therapy with Volumetric Modulated Arc Therapy (VMAT). Men with high risk clinicophathological features were treated selectively to the pelvic lymph nodes at treating physician discretion. Adjuvant androgen ablation was associated in 29 pts (78%).

Results: Median follow up was 27 months (12-48). Biochemical recurrence was defined as posttreatment PSA 0.2 ng/mL or greater and occurred in 4 pts (16%). bRFS was 83% and stratified by PSA was 97 %, 82 % and 76 % for PSA < 0.3 ng/mL, 0.3-0.7 ng/mL and > 0.7 ng/ml. All patients treated with early SRT are alive. Only 4 pts (30%) treated for clinical relapse are ned, metastasis-free survival was 92.5%, prostate cancer-specific survival 97%, and overall survival 94.9%

Conclusions: Immediate Post operative RT is associated with an increased risk of acute and late side effects.

Salvage radiotherapy administered at the first sign of biochemical recurrence might be associated with durable cancer control in selected patient. According to recent trials there is an increasing hazard for biochemical failure , salvage androgen deprivation therapy, distant mts and prostate cancer mortality with increasing pre SRT values.

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TWO-PHASE 3D-CONFORMAL RADIOTHERAPY WITH 5 FIELDS FOR PROSTATE CANCER: IS IMRT ALWAYS NECESSARY?

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Aims: Three-Dimensional Conformal Radiotherapy (3DCRT) and Intensity Modulated Radiation Therapy (IMRT) play a vital role in the care of patients (pts) with prostate cancer. This study aims to develop and evaluate a 5-field technique (5F-3DCRT), to determine if doses to organs at risk (OARs) are lower than the traditional box technique (BOX-3DCRT) and to quantify pts who benefit from IMRT since tolerance doses are overcome even with 5F-3DCRT.

Methods: We elaborated and optimized a two-phase 3DCRT with 5 fields of photons ≥ 10 MV (5F-3DCRT) to minimize doses to OARs. From January to December 2016, 54 treatments for low and intermediate prostate cancer pts were planned with Oncentra EB TPS, using different 5-field geometries and a box technique. Phases of treatment, energy of beams, coverage of volumes were kept the same with all modalities. Prescribed doses were 55 and 15Gy (2.5Gy/fraction). Rectal D(V15%), D(V25%), D(V35%), D(V50%), D(V80%) and D(V90%), vesical D(V15%), D(V25%), D(V30%) and D(V50%), femoral D(V5%) and median penile bulb doses were calculated. Doses to OARs were compared by R statistical program.

Results: Considering all pts and all the rival plans, a two-phase 5-field technique proved to be the best combination of beams. Compared to BOX-3DCRT, the posterior beam at 180° was replaced by two oblique beams: two posterior oblique fields (130 and 230°) in the first phase to prostate and seminal vesicles and two

anterior oblique fields (50 and 310°) in the second phase to prostate only. Pts were in the supine position. The different configuration between phases was justified by the different relative positions of target volumes, since vesicles make the first volume slightly more posterior than the second one. Kruskal-Wallis and post-hoc Dunn's tests identified significant differences regarding rectum. Contrasts regarding other OARs were not significant. Only 2 pts (4%) exceeded dose constraints and were treated with IMRT.

Conclusions: The proposed 5F-3DCRT technique gave the lowest rectal irradiation, revealing to be the best radiation beam geometry. In light of our data, IMRT, which is complex and not widespread in all radiotherapy departments, is not justified in all pts. Further discussion will concern the identification of that small subset of pts who might benefit from IMRT, not being irradiated with conformal techniques in compliance with all constraints.

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IMRT WITH SIB IN HIGH RISK PROSTATE CANCER

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Aims: To describe our experience in high-risk PC patients submitted to hypofractionated Intensity-Modulate radiation Therapy (IMRT) on prostate bed and pelvic nodes with an additional simultaneous integrated boost (SIB).

Methods: We reviewed patients who have been admitted at our Department for both definitive and adjuvant radiotherapy. We have considered clinical and irradiation data, evaluating gastrointestinal (GI) and genitourinary (GU) toxicities on the basis of National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.0.

Results: From February 2013 to May 2017 we treated 38 patients. The mean age was 70.1 years. Mean PSA at enrollment was 15.13 ng/ml. Median follow up was 27 (range, 8–70) months. Treatment was delivered at the dose of 60.2 to 70.5 Gy (mean 64.8) in 28 – 29 fractions both on the prostate and prostate bed; on pelvic nodes a total dose of 47.6Gy (1.7/per day/28 fractions) was delivered. Androgen deprivation therapy (ADT) was administered in 17/34 patients. All patients completed the therapy. Mean PSA at last follow-up was 0.77 ng/ml ($P<0.01$ vs initial evaluation). Acute genitourinary (GU) Grade 1-2 toxicities were observed in 4/38 (10.5%) patients; chronic genitourinary (GU) Grade 1 toxicity was observed in 2/38 (5%). Acute gastrointestinal (GI) Grade 1-2 toxicities were observed in 6/38 (15.8%) patients; chronic GI Grade 1-2 toxicity was observed in 9/38 (23.7%) patients.

Conclusions: SIB-IMRT is a safe and effective treatment in the set of high risk prostate cancer patients, resulting in low rates of acute/late toxicities. A longer follow-up is necessary to confirm the low profile of toxicities.

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EVALUATION OF EFFICIENCY OF THE SET-UP CORRECTION STRATEGY DURING TREATMENT OF PROSTATE CANCER BY AVERAGE GEOMETRIC SHIFTS IN RADIOTHERAPY DEPARTMENT OF BIELLA HOSPITAL

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Aims: To evaluate the efficiency of our image-guided radiotherapy protocol in the intensity modulated treatment of prostate cancer. Efficiency was evaluated through RayStation 6® (RaySearch Laboratories, Stockholm, Sweden) special tool which allows to recalculated RT plans simulating an isocenter shift.

Methods: A total of 14 consecutively patients with high-risk prostate cancer, were treated at our center (6 salvage and 8 radical radiotherapy) since May 2016. All patients received definitive VMAT with prophylactic nodal RT. Dose prescription was 52 Gy in 26 fractions to pelvic nodes and subsequent boost to prostate bed (70-72 Gy), or seminal vesicle (68 Gy) and prostate gland (80 Gy) with 2Gy/die fractionation. The planning target volume margins for all clinical target volumes (CTVs) were 8 mm except a posterior margin of 5 mm. The plan was delivered after online Cone Beam CT imaging and position correction for the first 5 fractions and weekly. Systematic set-up errors in the three dimensions were calculated and corrected with a threshold of 5 mm. Per patient a new plan was generated simulating the isocenter shift according to average geometric shifts, and the dose-volume histograms (DVHs) from the planned and perturbed dose distributions were compared on RayStation 6®.

Results: After the isocenter shift simulation in all pelvis treatment CTVs coverage by 95% isodose (D95) was maintained. Planned mean CTV D95 was 51,4 Gy and perturbed was 51,1 Gy (0,5% variation). D95 variation exceeding 2% was observed in only one patient. Prostate bed CTVs coverage was kept within limits of 95%. Planned and perturbed mean D95 were respectively 18,2 Gy and 18,0 Gy (0,7% variation). In seminal vesicle and prostate treatment one patient showed marginally compromised CTVs coverage: respectively 15,1-9,4 Gy instead of 15,2 -11,4 Gy prescription (5-26 % variation to 15,9-11,9 Gy planned). Another one patient showed D95 variation exceeding 2% but dose was kept within limits. The perturbed plan DVH was significantly outside the range of the planned in 5 patients for rectum and 4 patients for bladder (2 both rectum and bladder).

Conclusions: Our analysis of perturbed dose distributions showed a good coverage of CTVs in all pelvis treatment. We observed that dose distributions in small CTVs (seminal vesicle, prostate gland or prostate bed) are more affected by set-up errors. Our set-up correction strategy has allowed us to reduce the positioning error and our CTVs-PTVs margins showed to be relevant.

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EVALUATION OF PATIENT SETUP ERROR IN SIB-IMRT PROSTATE TREATMENTS AND PTV MARGIN ASSESSMENT

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Aims: To evaluate the patient set-up error and to assess the optimal planning target volume (PTV) margin to the clinical tumour volume (CTV) in patients with prostate cancer treated with hypo-fractionated SIB IMRT.

Methods: From December 2015 to March 2017, 56 patients with histologically confirmed low-(LR), intermediate (IR) and high risk (HR) adenocarcinoma of the prostate cancer were treated with SIB-IMRT with a dose of 75.24Gy/33f. Our retrospective study was conducted to evaluate patient set-up errors along the 3 translational directions (vrt, long, lat). All patients were positioned supine and scanned in head-first position with combi-fix immobilitation device. For each patient, SIB-IMRT plans were generated using Eclipse TPS Varian. CTV was the only prostate for low risk and prostate and vesicles seminals for IR and HR. CBCT of all patients was performed during first 3 days, then once a week. On the CT images, all structures were contoured by the same radiation oncologist in accordance with the ICRU reports 62. PTV margin of 7mm all around except 5mm in the posterior was given to the CTV. The patient set-up error (the shift between actual and expected patient position with respect to simulation CT) was registered along the 3 translational directions and was used to calculate the systematic (Σ) and random (σ) set-up errors for each individual patient and the patient group. Set-up error measurements were used to calculate the CTV-to-PTV margins using Van Herk's formula, where the PTV margin is given by $2.5\Sigma+0.7\sigma$.

Results: About 400 image dataset was analysed: the frequency of patient set-up error less than 5mm was 72%, 81% and 96% in lateral, longitudinal and vertical directions, respectively. Rarely, the results showed more than 7mm error in the lateral and longitudinal directions. The analysis reported that the set-up error was lesser in vertical direction compared to the lateral and longitudinal directions. The CTV-PTV margin was calculated using Van Herk's formula and was about 5mm in the 3 directions.

Conclusions: The set-up error in the vertical direction was found to be less than the other two directions. The optimal CTV-PTV margins were determined using the systematic and random set-up errors. With the use of IGRT for patient set-up, we were confident to reduce margin from 7 to 5mm all around. With the knowledge of patient setup errors, the optimal CTV-PTV margin can be determined to ensure adequate dose to CTV, specific to our centre.

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HYPOFRACTIONATED RADIATION FOR THE TREATMENT OF LOCALIZED PROSTATE CANCER.

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Aims: It is now accepted that prostate cancer has a low alpha/beta ratio, establishing a strong bases for hypofractionation (HRT) of prostate radiotherapy. Patients (pts) with localized prostate cancer are treated with conventional radiotherapy (RT) over 8 to 9 weeks instead HRT is given over a shorter time with larger doses per treatment. We hypothesized that HRT and RT are similar in toxicity and efficacy.

Materials and Methods: Between January 2016 and April 2017 in our Department 34 pts were treated with moderate HRT for localized prostate cancer, the median age was 76 years old (range 66-83). All pts were staged with ultrasound-guided biopsy and pelvic magnetic resonance imaging; only pts with intermediate and high risk disease also underwent bone scan. As for their risk prognostic group (according to the definition of NCCN), men were classified: 1 pts (3%) very low (T1c, Gleason Score (GS) $\leq$ 6, PSA< 10 ng/ml), 1 pts (3%) low (T1-T2a, GS $\leq$ 6; PSA < 10 ng/ml), 15 pts (44%) intermediate (T2b-T2c or GS 7 or PSA 10-20 ng/ml), 12 pts (35%) high (T3a or GS 8-10 or PSA > 20 ng/ml), 5 pts (15%) very high (T3b-T4, Primary Gleason pattern 5). Androgen deprivation therapy (ADT) was administered to 25 pts (74%) before and after radiotherapy. The prescription dose was 64 Gy (320cGy/fx) for prostate and 54 Gy (270cGy/fx) for seminal vescicles in 20 fractions erogated with Helical Tomotherapy to 7 pts (20%) and VMAT to 27 pts(80%).

Results: Dose Volume Histogram (DVH) goals for the rectum were such that the V57 < 10.2%, V44<32%, V35<43% and for bladder V53 < 14%, V49<27%, V35<47%. Acute and late toxicity were assessed using the RTOG; toxicity was defined to be acute or late if occurred within 3 months or more following the treatment respectively. With a median follow up of 6 months (range 1-13) , 7 pts were lost and 1 pts died for preexi-

sting hematologic disease. All pts were evaluable for acute genitourinary (GU) and gastrointestinal (GI) toxicity. 4 pts (15%) had a grade 1 (G1), 4 pts (15%) grade 2 (G2) and no pts experiencing any grade 3 (G3) and grade 4 (G4) GU toxicity. Equally for GI toxicity 3 pts (12%) had a G1, 3 pts (12%) G2 and no one G3 and G4. Only 10 pts (29%) were evaluable for late toxicity. GU toxicity: 1 pts (10%) had G1, 1 pts (10%) G2 and no pts G3 and G4. Instead no GI problem was reported in our experienced.

Conclusions: The treatment was well tolerated with 70% of pts with no GU acute toxicity, 76% no GI, 80% no late GU toxicity and 100% no GI. In our experience moderate HRT is safe.

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MOVEMENT SET-UP ERRORS AND ORGAN MOTION EVALUATION IN IMRT TREATMENT OF PROSTATE CANCER: OUR EXPERIENCE

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Aims: In the Radiotherapy Center of Rieti, prostate cancer is treated with IMRT. We started a study to evaluate the prostate gland movements and set-up errors to define appropriate margins to CTV, based on our technologies.

Methods: We enrolled 50 patients from January 2015 to March 2017 with hystologic diagnosis of prostate adenocarcinoma. Patients were treated with External radiotherapy, using IMRT tecnique. Patients were positioned both in supine and prone positioning depending on the type of treatment and body patient structure. The treatment was delivered with the Clinac 2100-CD (Varian) equipped with MLC Millenium. The planning CT was used as reference for organ motion and set-up errors evaluation. During the course of the treatment, 4 CTs were performed for all 50 patients. Before each CT and the radiotherapy session, patients had full bladder and empty rectum, via a standard procedure used in our centre. On each CT, the CTV (prostate gland and seminal vesicles) and the OAR (rectum and bladder) were contoured by the same physician to avoid any inter observer variability. The organ movement was evaluated off-line using Eclipse CT registration module. We measured for each patient the displacement of the CTV centroid, the CTV extension in the CC direction and the variations of the distances between CTV and bone marks. Set-up errors are characterized by a systematic component (Σsetup), due to the preparation of the treatment, and a random component (σsetup), due to the execution of the treatment. These errors were evaluated for each patient acquiring 20 portal images using an EPR (Electron Portal Image Device, Varian) device, and comparing them with the reference DRR images generated by TPS Eclipse. (Σsetup)and (σsetup) were computed analyzing patients setup three axes (x,z,y) variations.

Results: Average CTV centroid variations in x,z,y axes were <3.6 mm, average CTV – Bone Markers distances in AP and LL directions was <2.6 mm. In CC direction the maximum variation was 3.2 mm.

Conclusions: Finally, we combined data from Organ Motion CT and SET-UP errors using Van Herk formula, and we observed that a 5 mm set-up margin in CC and LL axes, and a 7 mm set-up margin in AP axys are sufficient to allow a adequate target coverage.

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ACUTE TOXICITY IN PROSTATE CANCER PATIENTS UNDERGOING PELVIC RADIOTHERAPY, WITH VMAT TECHNIQUE AND IGRT

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Aims: To evaluate acute toxicity in prostate cancer patients, undergoing pelvic radiotherapy, with VMAT technique and IGRT.

Methods: A total of 16 consecutively patients with high-risk prostate cancer, were treated ad our center (8 salvage radiotherapy and 8 radical radiotherapy) from May 2016 to May 2017. All received definitive IMRT-VMAT with prophylactic nodal RT. After radical prostatectomy, patients were treated on pelvic nodes (52 Gy/26 fr.) and prostate bed (70-72 Gy/35-36 fr.). Radical Radiotherapy was performed on pelvic nodes (52 Gy/26 fr.), seminal vesicle (68 Gy/34 fr.) and prostate gland (80 Gy/40 fr.). The planning target volume margins for all clinical target volumes (CTVs) were 8 mm with uniform expansion except a posterior margin of 5 mm. The plan was delivered after online Cone Beam CT imaging and position correction for the first 5 fr. and subsequently weekly. Systemic set-up error were corrected with a treshold of 5 mm. Acute toxicity was evaluated using RTOG (Radiation Therapy Oncology Group) Acute Radiation Morbidity Scoring Criteria.

Results: We analyzed acute toxicity during treatment and three months after radiotherapy. In patients treated with radical radiotherapy we detected grade zero GU (Genito Urinary) toxicity in 2 patients (25%), 4 patients with grade 1 GU toxicity (50%) and two patients with grade 2 acute, (25%) GU toxicity, we have not found grade 3/4 acute toxicity. Grade zero GI (Gastro intestinal toxicity) in 6 patients (75%) and grade 1 in 2 patients (25%), no grade 2/3 or 4 toxicity. In patients treated with adjuvant or salvage radiotherapy we detected six patients with grade zero GU toxicity (75%) and 2 with grade 1 (25%) toxicity, no grade 2, 3 or 4 GU toxicity. 3 patients with grade zero GI toxicity (37,5%), 2 grade 1 (25%) and 3 with grade 2 (37,5%) GI toxicity, any patients with grade 3 or 4 toxicity. No interruptions for treatment-related toxicity were recorded. All patients treated with radical radiotherapy were simultaneously subjected to hormone therapy, LH – RH analogous.

Conclusions: With a mean pelvis volume of 310,18 cm^3 and a pelvic dose of 52 Gy, we have observed a low

gastrointestinal an genitourinary toxicity. Radiotherapy with VMAT on the whole pelvis in unfavourable prostate cancer patients is well tolerate with a mild pattern of toxicity.

P200

FEASIBILITY STUDY: EVALUATION OF A CUSTOMIZED WORKFLOW TO ASSESS DAILY RECTUM AND BLADDER VOLUME CHANGES AND DOSE CONSTRAINTS COMPLIANCE DURING VMAT PROSTATE CANCER RADIOTHERAPY

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Aims: Volumetric Modulated Arc Therapy (VMAT) for the treatment of prostate cancer enables a better conformity to the target while sparing the surrounding normal tissues and potentially allows to increase the dose to the target. The scope of this work is to evaluate the feasibility of using a customized workflow in a commercial software to determine volume changes and dose distribution modification to rectum and bladder in every fraction radiation treatment.

Methods: Five patients were selected in this retrospective feasibility study. Patients (median age 73 years) were affected by GS 6 (3+3) low risk prostatic adenocarcinoma and were treated through IGRT (image-guided radiation therapy) using Varian Clinac 2100C/D equipped with kV imaging system with CBCT option. The total prescribed dose for each patient was 70 Gy, in 28 fractions. VMAT treatment plans were created in Eclipse Varian TPS. Daily CBCT (cone-beam CT) were carried out before delivery for on-line match anatomy position verification. After treatment, rectum and bladder volumes were manually delineated on every single CBCT (transferred to MIM 6.6 Software) and then compared with the volume outlined in the planning CT by means of a customized workflow to take into account online image registration and get statistical values of volumes. Furthermore, for each daily CBCT, DVH (Dose-Volume Histogram) for those organs were also evaluated and compared with the planned DVH.

Results: Total CBCT analyzed were 140. Anatomy changes from planning volumes reach differences of 270 cc for bladder and 123 cc for rectum. Mean variation in the position of center of mass along the 3 directions is up to 1,1 cm for bladder and up to 1,4 cm for rectum. Overall compliance with OAR dose constraints is assessed by frequency values of deviation from those based on 2.5 Gy equivalent QUANTEC: V55Gy, V60Gy for rectum and V60Gy for bladder.

Conclusions: The impact of interfractional anatomical changes on daily dosimetric OAR constraints can be take into account for replanning strategies by means of MIM software through a customized workflow allow an in-depth quantitative evaluation of daily CBCT. Further investigations are needed to improve statistics and clinical correlations among daily anatomical changes to OAR dose, in order to assess the robustness of the course of RT and get quantitative parameters to guide decision-making replanning evaluation strategies.

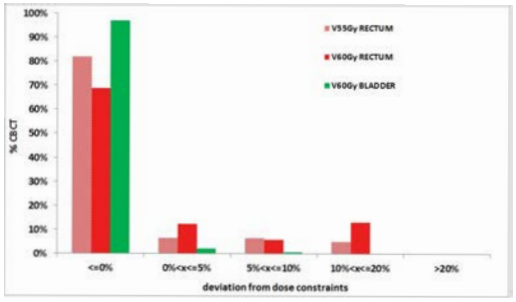

Figure 1.

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QUALITY OF LIFE IN PROSTATE CANCER RADIOTHERAPY: AN ELECTRONIC PATIENT REPORTED OUTCOME (PRO)

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Purpose/Objective: The gap between physicians rates reporting adverse events and PROs among prostate cancer(PCa) patients has already known. Furthermore, among existing Quality of Life(QoL) questionnaires, there isn't a unique scale used to assess patients' answers, making it difficult to compare them. Our aim was to develop an electronic PRO tool to systematically assess and, possibly, reduce the impact of radiotherapy adverse events on PCa patients' QoL, both during treatment and follow-up.

Materials and Methods: This tool creation implicated a four-step process. In the first, we collected items from dedicated QoL questionnaires already validated in literature. Then, we identified a reliable scale to report side effects. A series of questions and answers was elaborated in the third step. The last phase was to implement a friendly interface for patients, including the items previously organized.

Results: Our efforts are part of a broader project called VALEO meant to provide patients and their caregivers with several applications, to help them copy the therapeutic process. In the three main domains for PCa, that is to say urinary, bowel and sexual, we organized a comprehensive list of all the most relevant items extracted by the existing questionnaires, choosing, in the second phase, the CTCAE v4.03 scale. For the third step, a team of physicians, dedicated in PCa management, were supported by experienced psyco-oncologi-

sts, especially involved in the phrasing process. A set of questions, that recalled CTC scale, was created.

In the last phase, "interface implementation", a central role was played by web-designer and communication experts team; the final version, intended to run as a mobile devices application, was reviewed and approved both by physicians and psyco-oncologists. An innovative and comprehensive list of items for PCa patients receiving radiotherapy was elaborated. Physicians examining the patients linked the PROs to a well-established scale of toxicity. Such correspondence will be established by the physicians examining the patients who may confirm, from a medical point of view, the effective correlation of the PROs with the toxicity scale.

Conclusions: This innovative tool should provide both patients and physicians with an useful tool to reduce, and possibly prevent, adverse events during and after radiotherapy with a consequent in improvement in terms of QoL, overcoming the discrepancies reported in literature.

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STEREOTACTIC BODY RADIATION THERAPY (SBRT)-VMAT: DATA FROM A SYSTEMATIC REVIEW

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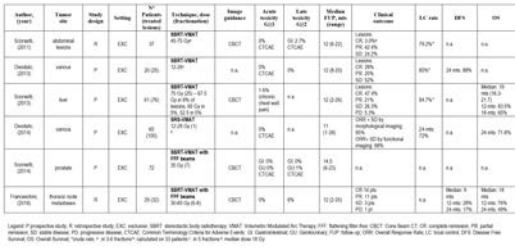
Aims: In the "oligo-metastatic" setting, local approach may improve outcome by keeping the burden of disease below the lethal threshold. For these patients, a broad variety of alternative local therapeutic approaches are available. Stereotactic body radiation therapy (SBRT) is a high- precision technique providing improved volume targeting and smaller irradiated volumes of normal tissue. Volumetric arc radiotherapy (VMAT) increase delivery efficiency and reduce risk of intra-fraction deviations both in terms of set-up errors and organ motion; therefore, VMAT may represent a valuable technique for SBRT treatment. Aim of our analysis was to systematically review the available literature to better define toxicity and clinical results of SBRT-VMAT in patients with oligometastases.

Methods: A systematic review based on PRISMA methodology of papers reporting clinical studies on VMAT was carried out in December 2016 using the National Library of Medicine (Pubmed/MEDLINE). The following words were searched: ""volumetric arc therapy""[All Fields] OR ""vmat""[All Fields] OR ""rapidarc""[All Fields]) AND ""radiotherapy""[All Fields] AND Clinical Trial [All Fields]. Only article published in English were considered. Data on SBRT - VMAT were extrapolated from the review and represent the object of this analysis.

Results: Six clinical studies (2 retrospective and 4 prospective phase I-II trials) were analyzed. These studies reported results on 284 patients accounting for 342 lesions and in the majority of these, cone beam computed tomography was used for daily treatment verification. All but one reported clinical outcomes in term of response to treatment, as reported in the Table. Notwithstanding the large variability of total dose and dose per fraction arising from the studies analysis, the local control rate was high (range: 72%-94.7%) and recorded toxicities (CTCAE scale) were low. In particular, severe chronic chest wall pain reported in one study (1.6%) and acute myocardial infarction occurred in 1 patient with a positive cardiac history.

Conclusions: The possibility to integrate SBRT-VMAT in the context of a systemic treatment due to intrinsic low toxicity and fast administration makes this approach very attractive. The introduction of VMAT for SBRT has resulted in marked reduction of treatment time (especially by FFF beams technology), intra-fraction uncertainties, costs related to highly complex treatment, and higher patient acceptance and compliance to treatment.

Table 1. Stereotactic body radiation therapy (SBRT)-VMAT.



P203

ROLE OF NEOADJUVANT OR DEFINITIVE RADIOTHERAPY WITH CONCURRENT CHEMIOTHERAPY IN LOCALLY ADVANCED VULVAR CARCINOMA: A SYSTEMATIC REVIEW

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Aims: Vulvar carcinoma (VC) is a relatively rare type of malignancy and constitutes 3% of gynecological cancers. Due to rarity, age of onset and anatomic site, vulvar cancer is disregarded or underestimated up to a locally advanced stage. Chemoradiation treatments (CRT) before or after a more conservative surgery represents a promising option to reduce the volume of the tumor, allowing the radical resection and reducing the genital mutilation. Therefore, a systematic review of the literature in order to evaluate the efficacy and safety of chemoradiation treatments was performed, aimed to understand what is the best treatment regimen according to clinical setting in locally advanced VC.

Methods: From Pubmed (2000-2016) database, a literature search was performed including published prospective and retrospective English-language articles on CRT in locally advanced VC with more than 25 patients treated. The following data were recorded: number of patients, enrolment period, median follow up, treatment characteristics, chemotherapy regimen, and results in terms of toxicity and outcome.

Results: Based on inclusion criteria, 7 studies were selected accounting for 291 patients (median number of patients per study: 42 (range: 28-58)). All but one studies were retrospective, with only one phase II trial. Studies were heterogeneous in terms of RT (dose, fractionation, techniques, use of brachytherapy [BRT] boost) and schedules of chemotherapy. 2D and 3D conformal RT were the most used techniques, while IMRT was used in two trials alone as well as BRT boost if surgery was not performed. Various concurrent chemotherapy schedules were administered: weekly Cisplatin (3/7), 5-Fluorouracil (1/7), 5-Fluorouracil + Cisplatin (3/7) or 5-Fluorouracil + Mytomicin C (2/7). Acute grade ≥ 3 toxicities were mostly cutaneous (range:14%-54%) and intestinal (range: 0%-29.3%) ones, with a less frequency of bladder severe toxicity (range: 0%-7%). Data about the complete clinical response rate were reported in 5/7 studies (range: 28%-72%), while the length of follow-up was very variable. An overview of clinical outcomes among studies is reported in the Table 1.

Conclusions: Only few mostly retrospective studies have been published in the last decade on CRT in locally advanced VC, probably due to the rarity of this tumor. Because of the long time span, there was a large heterogeneity in terms of treatment characteristics and evaluation criteria. Clinical results were strongly influenced by technical features. Prospective randomized studies are needed to better evaluate patients outcome, especially with modern high-precision RT techniques.

Table 1.

Authors [publication year]	Setting	Duration of follow up	Local Control	Progression-Free Survival	Overall Survival
Beriwal [2013]	Preoperative	3-11 mo	3 y: 65.9%	3 y: 65.9%	3 y: 61.2%
Tans [2011]	Exclusive	6-144 mo	4 y: 75%	4 y: 71%	4 y: 65%
Rogers [2009]	Exclusive	median 37.14	5 y: 60%	5 y: 30%	5 y: 30%
Moore [2012]	Exclusive	median 24.8 mo	53.4%*	53.4%*	60%*
Mak [2011]	Exclusive, Preoperative	median 31.5 mo	2 y: 67.8%	2y: 58.1%	2y: 71.3%
Landrum [2008]	Exclusive	3-161 mo	85%*	85%*	75%*
Montana [2000]	Preoperative	56-89 mo	31.6%*	31.6%*	82% *

*Crude value

P204

THE ROLE OF RADIOTHERAPY IN EXTRAMAMMARY PAGET'S DISEASE (EMPD): A LARGE SYSTEMATIC REVIEW

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Objective/purpose: Extramammary Paget's disease (EMPD) is an uncommon neoplasm. Surgery is considered as the gold standard, but, in selected cases radiotherapy (RT) can be an effective alternative or an useful completion to ensure local and lymph nodal control. Aim of this review was to define the role of RT therapy in EMPD.

Materials and Methods: A systematic search of the bibliographic databases PubMed and Scopus from January 1986 through January 2017 was performed including studies published in English, Italian, Spanish, French and German language.

Results: 19 articles fulfilled the selection criteria and were included in our review. No randomized controlled trials or case control studies were founded. RT was well tolerated with acceptable toxicity.

Conclusions: To date, RT can play a central role in patients unfit for surgery, for patients who underwent multiple surgery for relapse or in adjuvant setting for patients with high risk of recurrence.

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HELICAL TOMOTHERAPY VAGINAL-CUFF SIMULTANEOUS INTEGRATED BOOST (SIB) AND SEQUENTIAL BOOST (BS) IN ADJUVANT IRRADIATION OF GYNAECOLOGICAL TUMORS

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Aims: To evaluate preliminary results of the use of Helical Tomotherapy (HT) for vaginal cuff simultaneous integrated boost (SIB) and sequential boost (SB) in adjuvant treatment of gynaecological malignancies

Methods: We retrospectively enrolled 26 patients (pts) with uterine neoplasm. Median age was 68 (range 43-83), 8 (30.8%) pts with cervical cancer (CC), 18 (69.2%) with endometrial cancer (EC). According to FIGO 2009, CC were IB1 in 2, IB2 in 4 and II in 2 patient; EC were IA in 2 patient, IB in 4 pts, II in 6 pts, IIIA in 2 and IIIC in 4 pts. Chemotherapy was administered in 14 (53.8%) pts. We prescribed a median dose to the pelvis of 50.4 Gy (range 45-50.4), median dose/fraction 1.8 Gy (range 1.8-2) delivered with 3dcrt in 12 (46.2%) pts, and with HT in 14 (53.8%) pts who underwent HT-SIB performed with a median prescription dose to the vaginal cuff of 60.2 Gy (range 59.36-60.2) and a median dose per fraction of 2.15 Gy (range 2.12-2.3). SB was performed after 3DCRT whole pelvis irradiation in 12 pts using a 1.5 cm cylinder applicator in order to identify vaginal cuff with a prescription dose of 9 Gy (3 Gy/fx). Daily megavoltage CT scan was performed prior to each fraction to verify setup accuracy. Toxicity evaluation was conducted following CTCAE V4.0 criteria. Clinical Outcomes were analyzed.

Results: With a median follow-up of 6 months (range 4-35), all pts are alive. Actuarial 1-year Local Control rates were respectively 100% for EC and 75% for CC, detecting 2 central recurrences in pts with CC treated with SIB to vaginal cuff with a prescription dose of 59.36 Gy. Acute toxicity profiles were as follows: for genitourinary we detected G1 in 8 (30.8%) pts, G2 in 4 (15.4%) pts, with no ≥G3 observed; gastrointestinal adverse events were G1 in 16 (61.5%)pts, G2 in 8 (30.8%) pts, no ≥G3. Only one patient with CC experienced acute G2 haematological toxicity due to concurrent chemoradiation. No late ≥G2 GI and GU toxicities detected.

Conclusions: Our preliminary results support the use of HT for the administration of SIB and SB for adjuvant treatment of uterine neoplasms as a safe and feasible technique, with promising clinical outcomes. A larger sample size and a longer follow-up are required.

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EXCLUSIVE RADIOTHERAPY AND BRACHITHERAPY FOR SURGICALLY INOPERABLE ENDOMETRIAL CANCER: EVALUATION OF THE FEASIBILITY AND THE IMPACT ON LOCAL CONTROL IN ONE CENTER'S EXPERIENCE

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Aims: To analyze feasibility, tolerance and impact on local control in endometrial cancer in patients ineligible for surgical management.

Methods and Materials: Patients affected by endometrial cancer stage I NOS-IV were treated with radiotherapy (ERT) +/- endocavitary brachytherapy (BRT) boost in our center from August 2015 to April 2017.

Results: A total of 8 patients were analyzed. Median age at diagnosis was 75 years (range 68-81 years). All the cases were discussed in a multidisciplinary meeting. Surgery was excluded due to patients comorbidities: severe obesity (3 cases), cardiovascular pathology (5 cases), respiratory insufficiency (1); in particular 4 patients had more than one comorbidity. No patient was eligible for chemotherapy treatment. Seven patients had endometrioid adenocarcinoma with most being well differentiated (4 cases), and 1 patient had malignant mixed mullerian tumor (TMMM). FIGO stage was: I NOS in 3 cases; IB in 2 cases; IIIB in 1 case; IIIC2 in 1 case; IV in 1 case. All patients received ERT and 7 patients also received a BRT boost. ERT doses and volumes were: in 5 patients whole pelvis with a total dose of 50.4 Gy/1.8 Gy fraction, 5 fractions a week; in 3 patients whole uterus with macroscopic disease (adenopathies) with a total dose of 36.75-42 Gy/5.25 Gy fraction, 1 fraction a week. This hypo-fractionated schedule was chosen for the subset of very compromised patients. Radiotherapy treatment planning was performed using the VMAT technique. BRT doses and volumes were: 26-28 Gy/6.5-7 Gy per fraction, twice a week, using the endocavitary Fletcher applicator to cover uterus, cervix, and the upper third of the vagina. The single patient who didn't receive the BRT boost was stage IV and was treated with the hypo-fractionated schedule. Total time of the whole treatment was 57 days (range 47-70). The median follow up was 7 months (range 21-1). No genitourinary toxicity was recorded; gastrointestinal toxicity G2 was recorded in 1 patient of the group of hypo-fractionated schedule.

Conclusions: Our data, regarding exclusive ERT+BRT treatment in the subset of patients with inoperable endometrial cancer, suggests the feasibility of the treatment, because it results in a non-aggressive management. Disease local control was 100% considering however the limitations of a short follow up and

the number of cases in the study. Given the rarity of the situation, more data is needed to evaluate the impact on local control Results

P207

THE ROLE OF PET-CT IN THE IMRT OF CERVICAL CANCER: THE EXPERIENCE OF THE INSTITUTE OF CANDIOLO

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Aims: This paper evaluates the impact of of FDG CT-PET in the treatment of cervical cancer by volumetric radiation and chemotherapy.

Methods: From June 2010 to October 2015, 38 patients (pts) with cervical cancer were treated by radiotherapy, 21 with curatively (4 recurrences) and 17 with postoperatively (5 with positive margins). The mean age was 58 years (range 32-88). The FIGO stage was: IB1 in 7 pts, IB2 in 3 pts, IIA1 in 5 pts, IIA2 in 2 pts, IIB in 13 pts, IIIA in 2 pts, IIIB in 2 pts, IIIB2 in 1 pt, IIIC2 in 1 pt and IVA in 2 pts. 24 pts received concurrent chemotherapy (CHT), 3 neoadjuvant CHT and 1 neoadjuvant and concomitant CHT. 3 pts were treated with IMRT by LINAC, 34 pts with image-guided IMRT-SB-IGRT using Helical Tomotherapy; 1 patient received exclusive High Dose Rate (HDR) brachytherapy. Tumor doses were ranged from 54 to 70.4 Gy in 30-32 fractions (fr); dose to the pelvis were from 50.4 to 54 Gy / 25-30 fr. In 5 pts was treated lumbar-aortic chain (51 Gy/30 fr); 14 pts received a boost on PET positive lymph nodes with dose range from 54 to 66 Gy/30 fr). 24 pts were treated with HDR boost with dose/fraction of 6-15 Gy in 1-3 frs.

Results: 37 pts received a PET-CT to staging and planning, 33 of these had a PET-CT evaluation post RT. PET –CT changed the previous stage of disease in 6/37 cases (16%). 33 pts received also Magnetic Resonance (MRI) to staging, of these 10 showed positive lymph-nodes (30%), conversely PET CT showed positive nodes in 20 pts (54%). 26 pts underwent a PET CT after RT: 18 pts showed a complete response (CR), 7 a partial response (PR), 1 pt a local persistence of lesion and a distance progression disease (PD). The time from end of treatment to PET evaluation was variable from 1 to 15 months (mean 4.3 months). About 6 pts with PR, 3 showed CR at the following PET-CT (8,12 and 14 months), 1 local stable disease (SD) and distance metastases and 2 showed local and distance PD. The mean time for response detection by PET-CT was 5,7 months.

Conclusions: FDG-PET changed tumor stage in 6/37 cases (16%) allowing a dose escalation on lymph-nodes detected and finally showed to be a sensitive and reliable method in the evaluation of radio-chemotherapy treatment response. The optimal timing of execution remains to be defined by further studies.

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18FDG-PET/CT BASED SIMULTANEOUS INTEGRATED BOOST (SIB) FOR DEFINITIVE INTENSITY MODULATED RADIOTHERAPY (IMRT) AND CHEMOTHERAPY IN LOCALLY ADVANCE CERVICAL CANCER

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Aims: To evaluate toxicity and outcome of IMRT with 18FDG-PET/CT based SIB and chemotherapy for locally advance cervical cancer (LACC).

Methods: From August 2014 to December 2016, 13 patients (pts) with LACC were prospectively assessed at two radiotherapy centres: 12 pts evaluable for the analysis, underwent chemo-radiation with IMRT and SIB, another 1 with metastatic disease, refused treatment. Staging and follow-up were performed with clinical and instrumental evaluation, (*i.e.*, CT, MRI, 18FDG-PET/CT). Particularly, pelvis was treated with IMRT and SIB was done on positive nodes with 18FDG-PET/CT based planning. Using the Fletcher applicator, a CT-based planning high dose-rate brachytherapy (HDR-BT) was delivered as subsequent boost on primary tumor. Cisplatin concomitant chemotherapy was administered each week for all duration of IMRT. PET response and toxicity were graded according to CTCAE v 4.03 and PERCIST, respectively.

Results: Patients characteristics were: median age 64 years (range, 32-82), median KPS 100% (range, 90-100%), histology squamous cell carcinoma. FIGO clinical stage was shown in Table 1. In 8 (61%) pts 18FDG-PET/CT showed more extensive nodal or metastatic disease with respect to CT and MRI. Both IMRT and SIB were defined on the basis of 18FDG-PET/CT. SIB was delivered on 20 positive nodes. IMRT median dose on to the pelvis and draining lymph nodes was 48,6 Gy in 27 fractions (frs) (range, 45-50,4 Gy). SIB median dose was 54 Gy in 27 frs (range, 53,7-60 Gy). HDR-BT boost of 26/24 Gy in 4 frs was administer to the primary tumor. Median number of irradiated positive nodes per case was 2 (range, 1-4) with median nodal SIB volume of 18,6 cc (range, 5-114 cc). After a median follow-up of 21 months (range, 6-32), 11 (94%) pts have clinical and radiological complete local response, and 1 (8%) stable disease. Between 11 responders, one had a distant relapse after 27 months. Acute toxicity was: nausea G1-2 in 3 pts, dysuria G2 in 2, proctitis G2 in 3, diarrhoea G1-2 in 3, neutropenia G3 in 2 pts. Late toxicity was: vaginal stenosis G1 in 1, dyspareunia in 1, hematuria G1 in 1 and rectal bleeding G3 in 1 case, respectively.

Conclusions: IMRT and SIB in the region of 18FDG-PET/CT positive nodes seem to be an effective therapy with acceptable toxicity and can be useful in the treatment of LACC. Moreover, 18FDG-PET/CT can

influence treatment plan because it has a high specificity in nodal involvement detection.

Table 1. Stage of disease after 18FDG-PET/CT.

FIGO stage	N° of patients
IIA 1	
IIB 8	
IIIB	2
IVA	1
Nodal involvement +	10
Nodal involvement -	2

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THE USE OF IALURIL SOFT GELS IN WOMEN TREATED WITH PELVIC RT: PRELIMINARY EVALUATION OF GENITO-URINARY TOXICITY

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Aims: Radiation cystitis represents a frequent complication of radiation therapy of pelvic tumors. Symptoms include dysuria, pollachiuria, nocturia, urgency, abdominal pain and hematuria, and can lead to bacterical cystitis requiring antibiotic medication. The aim of this study is evaluate whether the use of Ialuril soft gels (Hyaluronic acid-chondroitin sulfate-curcumin and quercetin) during radiation treatment, in this setting, can lead to a benefit in terms of genito-urinary acute toxicity and in the prevention of postradiation cystistis. In fact Hyaluronic acid and chondroitin sulfate may restore the glicosaminoglycan (GAG) layer and take a beneficial effect in protecting the bladder and urinary tract.

Methods: Twenty women (median age 59,3 years old) undergoing pelvic RT for vulvar, vaginal, anal, endometrial or cervical cancers were recruited prospectively. Two cps/day were administrate during the week before the beginning of RT, followed by 1 cp/day during the RT course and following week, to ten patients (experimental arm). The other ten patients (controls) did not receive this kind of treatment. The patients have been stratified according to dose/volume constraints for urinary bladder irradiation. All patients were screened for urine test and cultures (with antibiogram if necessary) before the start (T0), in the middle (T 1/2) and at the end of the treatment (T1). Acute genito-urinary toxicity was evaluated according to the CTCAE 4.02 scale and their difference was tested with Chi-Square Test.

Results: In the experimental arm the following GU toxicities were reported: G0: 7 (70%), G1: 2 (20%), G2 1 (10%), G3 0 (0%). In the control patients: G0: 2 (20%), G1: 6 (60%), G2 2 (20%), G3 0 (0%). This trend did not reach the statistical significance (p:0.078); three patients had urinary infection before the treatment, but none at the subsequent controls (T1/2 and T1) had urinary infections. In the controls arm all patients had negative exams before the treatment, but 2 women showed an E.Coli infection during the treatment (T 1/2) treated with antibiotics.

Conclusions: Although the number of patients enrolled in this preliminary study is very small, we can conclude that the oral use of Ialuril may represent a non invasive and efficacy remedy for women undergoing pelvic radiotherapy.

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OVERALL TREATMENT DAYS (OTD) IN GYNAECOLOGICAL CANCER, THE TOTAL TREATMENT TIMING EFFECTIVENESS ON SURVIVAL

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Aims: To evaluate the impact of Overall Treatment Days (OTD) (including no treatment days) on survival in gynaecological cancers.

Methods: By November 2008 to April 2012 95 endometrial cancer pts. (no recurrences) treated in adjuvant according this treatment schedule: 18 Gy in 3 fractions as Boost after EBRT (50 Gy/5 weeks) or Reverse boost before the same EBRT. Same technique for each patient as for EBRT as for BRT. The survival comparison resulted slightly favourable to Reverse group: median 5,83 vs 4,81 years (P=0,70). As we noted that the total treatment time was longer in Boost group we evaluated the gap after external beam in this group. The gap resulted a median delay of 35 days (range 7-134). So the OTD were different in considered schedules. We evaluated this factor in comparison of survival curves with the Kaplan Meier method of entire population of the study.

Results: Median follow-up 5,35 years (range 1,13-7,33). Performing survival evaluation according OTD the cut-off resulted ≥70 days. So we recorded two groups Median-55 (range 40-68) of 70 pts. vs Median-96 (range 72-159) of 25 pts. In Median-55: age 66 (range 36-84); stage distribution was pT1b 13 pts., pT1c 35, pT2 9, other stages 4; grading distribution G1 19 pts., G2 43, G3 8; lymph node status performed in 58 pts. (N0=53, N1=5) in other 12 NX. In Median-96: age 58 (range 31-79); stage distribution was pT1b 6 pts., pT1c 15, pT2 3, other stages 1; grading distribution G1 10 pts., G2 13, G3 2; lymph node status performed in 23 pts. (N0=21, N1=1) in other 2 NX. The late toxicity as G3- G4 was 4 pts. (5%) in Median-55 group and 2 (8%) in Median-96 population. Only relapse recorded in 1 (alive) of group Median-55. Survival comparison that considered Median-55 vs Median-96 resulted favourable to first group and more significant, median 5,67 vs. 4,79 years (P=0,21).

Conclusions: Reduce to the maximum the entire treatment is mandatory. Probably Reverse boost as method for a better management of the scheduling of

entire treatment (avoiding treatment suspension) is more effective in gynaecological cancers with acceptable toxicity compared to other schedule. To avoid acute toxicity and minimize OTD we now prefer the Reverse schedule.

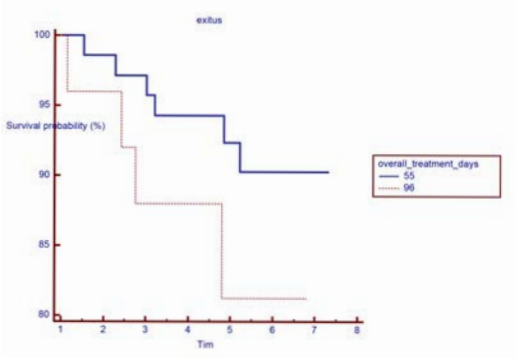

Figure 1.

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AN UNEXPECTED RESPONSE OUT OF THE IRRADIATED FIELD: A CASE REPORT

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Aims: The abscopal effect refers to the ability of localized radiation to trigger systemic antitumor effects. Only one case of the abscopal effect in local advanced cervical cancer (LACC) was yet described.

Methods: The case of a woman with LACC with bone metastases (BM) that showed an abscopal effect of radiation therapy (RT) is reported.

Results: A 56-year-old woman was referred to our Department for LACC. We requested a staging by PET/CT that showed 18F-FDG uptake in pelvic lymph nodes (LNM) and in soma of D11- D12 suggestive for metastases. The MRI of the spine confirmed the BM involving of the half left soma and the ipsilateral pedicle of D11. No histological bone confirmation was performed. Whole-pelvis irradiation was applied with Volumetric Modulated Arc Therapy (total dose: 50.4 Gy, fraction size: 1.8 Gy) with a SIB (single dose of 2 Gy) to the LNM and a concurrent CDDP (40 mg/mq weekly). BM was outside the irradiated field and irradiation of the para-aortic lymph nodes was not performed. The RT treatment was followed by HDR brachytherapy BT (28 Gy, two weekly fractions of 7 Gy each) and the BT dose was delivered to HR-CTV delineated on MRI images. The total treatment time was < 50 days. After one month of treatment, PET/CT did not show metabolic activity in the pelvic nodes and in uterine area and, surprisingly, the pathological 18F-FDG uptake in BM spontaneously disappeared. MRI showed a substantial decrease of BM. Patient underwent sequential chemotherapy with CBDCA AUC 5 and Paclitaxel 175 mg/mq (1q21,total courses: 4). She is still alive with no evidence of disease.

Conclusions: The abscopal effect is believed to create from local RT's capacity to arouse systemic immune effects to control unirradiated tumor. To date, there is no established consensus on the optimal dose, fraction, timing of RT to combine with immunomodulation to generate an abscopal response. The abscopal effect with RT alone was a relatively rare event but it's usually described during the combination with immunotherapy. CDDP during RT plays cytotoxic effects as radiosensitizer, hypoxic cell sensitizer, cell-cycle perturbator and DNA adducts producer but recent studies have shown that CDDP does not induce immunogenic cell death. The uncommon occurrence of abscopal effects maybe reflects existing barriers to successful immunization by RT. This data needs to be further investigated

P212

11C-CHOLINE PET/CT GUIDED SALVAGE TOMOTHERAPY FOR LYMPH NODAL RELAPSE IN PROSTATE CANCER

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Aims: To report clinical outcomes in prostate cancer pts with lymph nodal relapses, treated with salvage tomotherapy and Simultaneous integrated boost (SIB) dose escalation on 11 C-Choline PET/CT positive lymph nodes.

Methods and Materials: From April 2005 to October 2016, 145 prostate cancer patients presenting lymph nodal relapse at 11 C-Choline PET/CT were treated with salvage tomotherapy. Some patients were treated several times, so the total number of treatment sessions was 160. Median age at initial diagnosis was 62.5 (45.6-78.5) years, initial PSA was 13.85 (2.5-541.0) ng/ml, GS=8 (5-10), 137 patients were treated with initial surgery (12 prostatectomy only, 125 prostatectomy+ pelvic lympadenectomy) and 8 with radical radiotherapy. Ninety-two patients were treated with radiotherapy before the salvage treatment and 103 with hormonal therapy. Forty-six patients were already hormonal resistant. Median age at relapse was 69 (50-87) years, median PSA at relapse was 2.34 (0.18-187)

ng/ml and median number of lymph nodes diagnosed with choline PET/CT was 2(from 1 to >20). Nine patients were treated only on the positive lymph node, while 136 patients were treated with prophylactic radiotherapy on the lymph nodal chains to a median dose of 51.8 Gy/ 28 fr with simultaneous integrated boost dose escalation at a median dose of 65.5 Gy. Androgen deprivation therapy for a median of 12 months was prescribed in all except 30 pts.

Results: With a median follow up of 34(0-139) months 23 patients were died, 13 with progressive disease. Crude relapse rate was 54.4% and median time to relapse was 16 (0-123.5 months). Three months after the end of salvage radiotherapy a PSA response was registered in 88.8% of therapies. Twenty-one pts presented only biochemical relapse, 14 pts lymph nodal relapse, 35 pts bone +/- lymph-nodal or visceral relapses and 5 pts diffuse relapses. Only two G3 genito-urinary acute toxicities were registered, with no G3 bowel or rectal toxicity. Late G3 toxicities were 7, 6 genito-urinary and 1 rectal.

Conclusions: Salvage radiotherapy, 11C-Choline PET/CT guided, in lymph nodal relapses of prostate cancer allows to obtain a median time to relapse longer than with systemic therapies, even in already castration resistant patients with more than three positive lymph nodes. With a low toxicity almost half of patients were free of relapse almost three years after the treatment.

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PROSTATE CANCER WITH SYNCHRONOUS OLIGOMETASTASES: A SINGLE CENTER ANALYSIS OF TOXICITY AND CLINICAL OUTCOME IN 22 PATIENTS (UPDATED REPORT)

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Aims: The current standard of care for patients with metastatic prostate cancer (mPCa) at diagnosis is androgen deprivation therapy (ADT) with or without anti-androgen and chemotherapy. The recent large case series showed that local therapy (radiotherapy RT, surgery etc) may improve tumor outcome, Aim of this study was to define the role of a local RT treatment in the mPCa setting.

Methods: We retrospectively reviewed data of patients with PCa and bone oligometastases at diagnosis treated in our Institution with ADT followed by cytoreductive prostate-RT with or without RT on metastases. Biochemical and clinical failure (BF, CF), overall survival (OS) and RT-toxicity were assessed.

Results: We identified 22 patients treated with ADT and external-beam RT on primary between June 2008 and March 2016. Median age, Gleason score and initial PSA were 64.9, 8 and 14.7, respectively. The median number of bone metastases at the time of diagnosis was 1 (range, 1- 4). All cases were discussed on the multidisciplinary tumor board. All patients but four were treated also on bone metastases. RT on primary with moderately and extremely hypofractionated regimes started after 10.3 months (3.9-51.7) from ADT initiation After a median follow-up of 26.4 months (range, 10.3-55.5) 20 patients are alive. 12 patients showed BF after a median time of 23 months (range, 14.5-104) and CF after a median of 23.6 months (range, 15.3-106.1) from the start of ADT. The most common site of recurrence was bone. Three patients became castration resistant starting a new therapy, median time to castration resistance was 31.03 months (range, 29.9-31.5 months). According to RTOG/EORTC, only one patient developed acute Grade 3 genitourinary toxicity. No late Grade > 2 adverse events were observed.

Conclusions: Prostate RT in oligometastatic patients is safe and offers long-lasting local control. When compared to ADT alone, RT on primary seems to improve biochemical control and long-term survival, however this hypothesis should be investigated in prospective studies. Further research is warranted in order to evaluate RT on primary and oligometastases and to define the optimal dose, timing and combination with systemic therapy.

P214

RADICAL RADIATION THERAPY FOR OLIGOMETASTATIC BREAST CANCER: RESULTS OF A PROSPECTIVE PHASE II TRIAL

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Aims: We conducted a prospective phase II multicentric trial to determine if radical radiation therapy to all metastatic sites might improve the progression-free survival (PFS) in oligometastatic breast cancer patients. Secondary endpoints were local control (LC), overall survival (OS) and toxicity.

Methods: Inclusion criteria were the following: oligometastatic breast cancer with ≤ 5 metastatic sites, FDG-PET/CT staging, no brain metastases, primary tumor controlled. Radiotherapy could be delivered using both stereotactic body radiotherapy (SBRT) technique or fractionated intensity modulated radiotherapy (IMRT). SBRT consisted in 30-45 Gy in 3 fractions, while IMRT was delivered to a total dose of 60 Gy in 25 fractions. We hypothesized that radical radiation therapy could increase the PFS from 30% to 50% at two years.

Results: 54 patients with 92 metastatic lesions were enrolled. Forty-four were treated with SBRT, and 10 with IMRT. Sites of metastatic disease were the following: bones 60 lesions, lymph nodes 23 lesions, lung 4 lesions, liver 5 lesions. After a median follow-up of 30 months (range, 6-55 months), 1- and 2-year PFS was 75% and 53%, respectively. The 2-year PFS obtained was higher than the hypothesized value. Two-year LC and OS were 97% and 95%, respectively. Radiation therapy was well tolerated, and no Grade ≥3 toxicity was documented. Grade 2 toxicity were pain and fatigue in 2 cases.

Conclusions: Radical radiotherapy achieves excellent results in terms of progression-free survival in oligometastatic breast cancer patients. While waiting for data from randomized trials, the use of radical radiation therapy to all metastatic sites in patients with oligometastatic breast cancer should be considered a valuable option, and its recommendation should be individualized.

P215

MAGNETIC RESONANCE IMAGING (MRI) - BASED RADIOMIC ANALYSIS FOR PREDICTING RESPONSE TO RADIOTHERAPY OF SPINAL BONE MARROW METASTASES: A FEASIBILITY STUDY

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Aims: Malignant spinal lesions are a major cause of morbidity and reduction in quality of life in oncological patients. Magnetic resonance imaging (MRI) plays a crucial role in differentiation of response to therapy. However, morphological T1 and T2 imaging analysis provides only qualitative variation in lesion appearances. Purpose of this study is to test textural features of pre-treatment T1 and T2 images by dedicated software of image analysis, for predicting quantitatively response to therapy.

Methods: Four patients (2 lung cancer; 1 prostatic cancer; 1 breast cancer) for a total of 10 vertebral lesions with pre- and post-radiotherapy MR imaging were included. Each lesion was analysed on pre- and post-treatment T1 and T2 fat saturated images for signal intensity and dimensional criteria. Each lesion in pre- and post-treatment images was contoured at a radiotherapy treatment planning console. The obtained data were transferred to an automated data extraction system for morphological, statistical and textural analysis. Overall features for each lesion were computed as the median of by-slice values. The morphological imaging and radiomic features data from pre-treatment MRI were compared with the post-treatment ones.

Results: Eight lesions responded to radiotherapy on MR morphological imaging. Two metastatic vertebral bodies showed progression (increase of dimensions and new metastatic spine lesions). In the 8 stable lesions, the analysis disclosed a reduced variance for some textural features: maximum joint entropy, inverse moment normalized and correlation in T1 images, and inverse different moment normalised and correlation in T2 images. However, these two features had similar variance in the two lesions with disease progression. Interestingly, the variance of the mentioned features was different if the stable lesions were compared with the whole population. For maximum joint entropy in T1 images the variance ratio between the two populations was 0.9, whereas the correlation was 1.13. For inverse moment normalized in T2 images the variance ratio between the two populations was 1.1.

Conclusions: The paucity of lesions analysed does not allow the construction of a predictive model. However, this feasibility study provides a methodology for conducting comparative textural analysis and suggests the possibility to apply textural analysis in predicting response to radiotherapy in oncological patients with spine metastases.

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RADIOTHERAPY FOR OLIGOMETASTATIC CANCER: A SURVEY AMONG RADIATION ONCOLOGISTS OF LOMBARDY (AIRO-LOMBARDY), ITALY

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Aims: Local approach including radiotherapy (RT) is frequently proposed in oligometastatic cancer (OMC) and provides high local control and, in some cases, long lasting progression-free and treatment-free survival. Our aim was to evaluate the use of RT for OMC among the radiation oncologists of the Lombardy, Italy.

Methods and Study Design: A survey with 12 items regarding data of 2016 was sent to all 34 Lombardy RT centers using emailing list of the Lombardy Section of the Italian Society of Oncological Radiotherapy (Associazione Italiana di Radioterapia Oncologica-Lombardia, AIRO-L). The survey included 6 general items regarding institutional policy on OMC and 6 specific items regarding patients (pts) numbers and disease/treatment characteristics.

Results: 14 centers answered the survey (41%). All 14 centers responded to the general items and 13 centers submitted patient/disease/treatment characteristics. General items: The majority of centers (8/14) consider OMC if number of metastases is less than 5 metastases localized in one or more organs (7/14). Radical therapy for OMC is proposed in all 14 centers. The most commonly prescribed dose/fraction is 5-10 Gy (8/14) using schedules of 3-5 fractions (11/14). All responders declared their interest in the Lombardy OMC multicenter collaboration including prospective and/or observational studies. Patient data items: A total of 15.681 pts were treated in 2016 with external beam RT in the 13 responding centers and 1087 pts were treated for OMC (7%). Primary tumor included lung, prostate, breast, colo-rectal, kidney and other malignancies in 33%, 21%, 12%, 10%, 6% and 18% of all OMC pts, respectively. Brain, lymph node, lung, bone, liver and others were the most common treated sites (24%, 24%, 22%, 17%, 8% and 5% of all sites, respectively). The majority of pts (75%) were treated for one metastasis, while 14%, 4% and 7% pts received RT to 2, 3 and more than 3 lesions, respectively. The vast majority of pts (95%) were treated with image-guided intensity modulated RT or stereotactic RT and 5% were treated with 3-dimensional conformal RT technique.

Conclusions: Our survey showed that OMC is frequently treated with RT in Lombardy. Extreme hypofractionation and high precision RT modalities are commonly employed. The initiative of multicenter and multidisciplinary collaboration has been undertaken in order to prepare the platform for prospective and/or observational studies in OMC.

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DOSE ESCALATION IN EXTRACRANIAL STEREOTACTIC RADIOTHERAPY: AN INTERIM ANALYSIS OF A FASE I CLINICAL TRIAL

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Aims: To present the interim results in terms of safety and efficacy of a multi-arm phase I study on stereotactic body radiotherapy (SBRT) delivered by means fixed non-coplanar fields or volumetric arc therapy in patients with primary or metastatic tumours in various extra-cranial body sites. The trial was aimed to determine the maximum tolerated dose (MTD) of 5 fractions SBRT treatment.

Methods: The clinical trial design was very articulated including seven arms (Table 1). Each patient was sequentially enrolled in a given study arm, according to tumour site and clinical stage. The total dose, prescribed to the target isocenter (ICRU 62), ranged from 20 to 50 Gy (biologic effective dose=28-100 Gy, / =10) according to different arms of the protocol; the doses per fraction ranged from 4 to 10 Gy along 5 days. Dose escalation was based primarily on acute and subacute toxicity because late toxicity can occur months or years later. Dose limiting toxicities (DLT) were defined as any treatment-related non haematological adverse effects rated as Grade > 3 or any haematological toxicity rated as > 4 by Radiation Therapy Oncology Group (RTOG) criteria. The maximum tolerable dose has been reached if one third of patients experience a dose-limiting toxicity. Preliminary data about acute toxicity and late toxicity, tumour response and early local control were investigated and reported.

Results: 282 consecutive patients (M/F: 166/116; median age: 69, range 35-90) with 376 lesions were treated. Of these, 119 were primary or metastatic lung tumors, 13 were metastatic liver tumours and 188 were

nodal metastases. Median follow-up was 19 months (2-157). Maximum tolerated dose was defined in 4 (a, b, c and f) of the 7 arms of the study, while recruitment of other arms (d, e, g) is still ongoing (Table 1). Grade 2 acute toxicity rate was 5.6%. Overall response rate was 82.2 % (CI 95%: 77.2-86.3) with a complete response rate of 58.8% (CI 95%: 52.8-64.4). 12-and 24-months actuarial local control (freedom from progression in the irradiated site) were 84.3% and 73.7%, respectively. Four patients (all previously irradiated in the same site) had severe (>grade 3) late toxicity.

Conclusions: SBRT delivered in 5 consecutive fractions up to the doses evaluated in the first part of this trial is well tolerated. The maximum tolerable dose has reached in four of seven study arm.

Table 1. Study arms and dose levels (Gy) planned and reached (underlined) in the different arms of the study.

				retreatment		boost	
Dose levels (Gy)	primary and metastatic lung intraparenchymal tumours (a)	paramediastinal or near chest wall primary and metastatic lung parenchymal tumours (b)	primary or metastatic cancers except lung tumours # (c)	previous RT > 60 Gy ## (d)	previous RT ≤ 60 Gy (e)	after RT ≤ 50 Gy (f)	after RT > 50 Gy (g)
I	25	25	25	20	25	25	20
II	37 5	30	30	25	30	30	25
III	45	35	35	30	35	35	30
IV	50	40	40	35	40		
V		45	45	40	45		
VI		50	50	45			

lymph nodal disease (H&N, thorax, abdomen, pelvic), liver and adrenal metastases, prostate and pancreatic cancer
or previous small bowel irradiation

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LINAC-BASED SBRT FOR OLIGOMETASTATIC LYMPH NODES IN HORMONE-SENSITIVE AND CASTRATION RESISTANT PROSTATE CANCER PATIENTS WITH VMAT AND FLATTENING FILTER FREE BEAMS: PRELIMINARY RESULTS

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Aims: To evaluate the feasibility and the early side effects of Stereotactic Body Radiotherapy (SBRT) for oligometastatic lymph nodes in hormone-sensitive and castration resistant prostate cancer (PC) patients.

Methods: Between April 2014 and January 2017, 65 nodal lesions in 26 oligometastatic hormone-sensitive and castration resistant PC patients, were treated with SBRT using VMAT and flattening filter free beams. Prescribed doses and schedules of fractionation varied, ranging from 30 Gy in 5 fractions to 40 Gy in 4 fractions. Most commonly used schedules were 35 Gy in 5 fractions and 36 in Gy in 6 fractions. Biochemical response, acute and late toxicity were analyzed. In 45/65 (69 %) lesions were treated in castration-resistant PC patients, 20/65 (31%) in metastatic hormone sensitive PC patients. PET/CT was performed with Choline in 40/65 (62%) and 68-Ga PSMA in 25/65 (38%). Toxicity were evaluated using CTCAE v.4.0. Local control was assessed by means of PET/CT scan and PSA reduction.

Results: At a median follow-up of 12 months (range 3-26), a biochemical response was observed in 75% of treated cases. In all cases, imaging evaluation at 3 months after treatment was available: complete response was found in 56/65 (86%) cases and stable disease in 9/65 (14%) cases. No in-field recurrence was detected. Thus, overall response rate was 100%. In 11/65 (17%) cases out of field recurrence was reported. Median time to progression out of field (14%) was 3 months (range 3-27 months). At the time of analysis, one patient died for non-oncological causes. Twenty-two patients, among the 26 patients treated (85%), were still free of disease. SBRT was well tolerated: Only two patients experienced G1 acute gastrointestinal toxicity. Late toxicity was evaluated in patients with more than 6 months of follow-up. We did not observe any acute or late G2-G3 toxicity.

Conclusions: SBRT for oligometastatic lymph nodes in hormone-sensitive and castration resistant PC patients is feasible and well tolerated. Longer follow-up is needed to assess late toxicity and the impact of this impressive local control rate on clinical outcomes.

P219

RADIOSURGERY DELIVERED BY VOLUMETRIC INTENSITY MODULATED ARC THERAPY IN PRIMARY OR OLIGOMETASTATIC PATIENTS: ONGOING RESULTS OF A CLINICAL PHASE I TRIAL

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Aims: To report the ongoing results of a Phase I trial testing extracranial stereotactic body radiosurgery

(SBRS) delivered by volumetric intensity modulated arc therapy in primary or metastatic cancer patients.

Methods: Each enrolled patient was included in a different phase I study arm, according to tumour site and disease stage (lung, liver, bone, advanced), and sequentially assigned to a dose level established by the protocol. Acute and late toxicity, tumour response and early local control were investigated and reported.

Results: 185 lesions in 121 consecutive patients (M/F: 72/49 median age: 69; range 40-93) were treated. Of these, 40 were primary or metastatic lung tumours, 36 were liver metastases, 66 were bone metastases, 41 lymph nodal metastases, 1 was a primary pancreatic tumours and 1 was a primary vaginal tumour. Dose prescription ranged from 12 to 30 Gy in single fraction to the Planning Target Volume. Median follow-up was 15 months (1-68). Only 1 patient had a dose limiting toxicity (grade >3). The grade 1 and 2 toxicity rate was 16.7% e 2.7% respectively (CTCAE 4.03). Overall response rate based on CT/MRI was 75.7 % (CI0.95: 68.2%-83%) with a complete response rate of 52.4% (CI0.95: 44.5%-61.7%). Actuarial local control (defined as irradiated site progression freedom) was 77.7% and 63.4% at 2 and 4 years.

Conclusions: To date, only one patient experienced dose limiting toxicity and tumour response, local control rate and toxicity profile appear encouraging. The maximum tolerable dose has not yet been reached in any study arm.

Table 1. Dose levels (Gy) planned and reached (underlined) in the different arms of the study

Dose level	Lung	Liver	Bone	Advanced
1	26	26	12	16
2	28	28	14	18
3	<u>30</u>	<u>30</u>	16	20
4	32	32	18	22
5	34		20	<u>24</u>
6			22	
7			<u>24</u>	

P220

18FDG-PET/CT AS A POTENTIAL PREDICTOR OF RESPONSE IN LIVER OLIGOMETASTASES SBRT: A PRELIMINARY EXPERIENCE

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Aims: to investigate metabolic parameters as predictive of local response after Stereotactic Body Radiation Therapy (SBRT) for liver-oligometastases

Methods: Inclusion criteria of the present retrospective study were: a) metachronous liver oligometastases; b) absence of progressive disease≥6months (mo); c) metastases≤3; d) BED > 100Gy; e) evaluation of SBRT-response by means of 18-FDG-PET/CT for at least two subsequent evaluations; f) Karnofsky performance status >80; g) life-expectancy>6 mo. The following metabolic parameters were defined semi-quantitatively for each metastases: 1) SUV-max; 2) SUV-mean; 3) Metabolic Tumor Volume (MTV)-total tumor volume with a SUV ≥ 2.5; 4) Total Lesional Glycolysis (TLG)-SUV mean MTV. Local control was defined as absence of recurrence in the field of irradiation.

Results: Between October 2014 and February 2017, twenty-two patients for a total of forty-one liver metastatic lesions met the inclusion criteria of the study. At the time of the analysis, the median follow up was 16.3 mo (range, 6-32 mo). The most frequent primary tumor sites were colorectal (31%) and lung (24%). Pre-SBRT, median SUV-max was 8.74 (range, 4.49 – 23.59), median SUV-mean was 4.6 (range, 3 – 7.46), median MTV was 5.74 cc (range, 0.9-80.64) and median TLG was 24.1 (range, 3.6 - 601.5). High values of SUV-mean and SUV-max pre-SBRT related to local failure. In detail, at the time of the analysis, the rate of in-field failure was 66.7% in case of pre-SBRT SUV-mean>5 and 61.1% for pre-SBRT SUV-max>10. At statistical analysis, metastases with SUV-mean>5 (p 0.04; OR 4.75, Sensitivity = 50%, Specificity = 82.6%, AUC 0.66) and SUV-max>10 (p 0.02; OR 5.03, Sensitivity = 69%, Specificity = 70%, AUC = 0.69) showed higher rates of in field-failure compared to the remaining lesions.

Conclusions: According to current findings, pre-SBRT SUV max and SUV mean could predict response in liver oligometastases. To date, biological equivalent dose represents a predictive parameter of local control for liver metastases submitted to SBRT. The present results could be integrated in SBRT strategy in order to customize dose prescription taking into account the single-metastases metabolic profile.

P221

STEREOTACTIC FRACTIONATED RADIOTHERAPY IN CHOROIDAL METASTASES

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Aims: Preliminary assessment about feasability and toxicity of stereotactic fractionated radiotherapy in choroidal metastases with the integration of photodynamic and systemic therapies.

Material and Methods: From 2009 to 2016, 34 patients were treated (11 males; 23 females) with clinical and radiological diagnosis of choroidal metastases.

Middle age: 58 years. Primary tumor: 47% breast cancer, 29% lung cancer e 24% others. 29 patients had extraocular metastases. 52,8 % of patients received photodynamic treatment before radiotherapy, just one case received photodynamic treatment after radiotherapy. We performed an image fusion between MR images and CT images in four cases. The CTV covered all choroid and macroscopical lesions; a 3 mm isotropic expansion of CTV defined the PTV. Omolateral lacrymal gland was partially excluded from PTV. 6 MV X rays of CLINAC 600, DBX, Varian with micromultileaf BRAINLAB M3® with leaves 3mm far from the isocenter were used. Radiation doses: from 20 to 36 Gy with 2-4 Gy per fraction. In 27,8% of cases we gave a supplementary dose due to the presence of macroscopical lesion at CT images.We calculated a total dose to allow re-treatment on small volumes. Techniques: static-fields, IMRT, Dynamic arc-therapy.

Results: Regarding ocular structures we had low toxicity in acute phase: G1 in 83,3 % and G2 in 16,7 % of patients. One case of choroidal bleeding and glaucoma due to pharmacological treatment with NSAIDs was reported.

Conclusions: Stereotactic fractionated radiotherapy in choroidal metastases with oncological systemic therapies is feasible, characterized by low toxicity and well tolerated. Moreover, the exclusion of most of optical nerve and the total exclusion of brain, permit the feasability of this treatment before or after a whole brain irradiation. One patient had disease progression and needed a re-treatment, well tolerated. We are going to evaluate the long term remission.

P222

DIFFUSION-WEIGHTED MAGNETIC RESONANCE IMAGING IN PAINFUL BONE METASTASES: USING QUANTITATIVE APPARENT DIFFUSION COEFFICIENT AS AN INDICATOR OF EFFECTIVENESS OF SINGLE FRACTION VERSUS MULTIPLE FRACTION RADIOTHERAPY

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Aims: The aim of this study is to determine the optimal single-dose radiotherapy schedule for the treatment of painful bone metastases and to verify if different dose and fractionation could cause different biological effects on affected bone. This has been achieved using functional Magnetic Resonance Imaging (MRI) with diffusion-weighted imaging (DWI).

Methods: Fifteen patients received Multiple Fractions Radiation Therapy (MFRT) with a total dose of 30 Gy in 10 daily fractions of 3 Gy and 15 patients received a Single Fraction Radiation Therapy (SFRT) with a dose of 8 Gy, delivered with 3D conformal multiple field technique. Quantitative Apparent Diffusion Coefficient (ADC) values after SFRT or MFRT were compared with response to treatment (pain relief), assessed by Visual Analogue Scale (VAS) before radiotherapy and at 1 and 3 months after the completion of treatment.

Results: The two schedules resulted both in good efficacy in terms of pain control (median VAS of 8 at baseline and median VAS of 0 at 3 months), without evidence of significant difference of MFRT and SFRT at 1 and 3 months post radiotherapy. In both treatments pain reduction was associated with an increase in the ADC, most likely corresponding to increased cancer cell death. However, the median ADC value increase between the baseline and 3 months was 575 points (from 1010 to 1585, p=0.02) in the MFRT group, and only 178 points (from 1417 to 1595) in the SFRT group.

Conclusions: MFRT and SFRT resulted similarly in good pain control at 1 and 3 months, but the higher increase in the ADC values after MFRT could explain the greater duration of pain relief and the lower frequency of retreatments reported by some Authors with longer fractionation, both especially valuable in this subset of patients. To confirm these data longer follow-up at 6 months and 1 year in surviving patients would be necessary.

P223

CRITICAL APPRAISAL TO OLIGOMETASTIC BRAIN PATIENTS TREATED WITH RADIOSURGERY DELIVERED WITH VOLUMETRIC MODULATED ARC THERAPY

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Aims: To evaluate single fraction brain radiosurgery (SRS) performed with volumetric modulated arc therapy (VMAT) as alternative to whole brain radiotherapy (WBRT) in carefully selected brain metastatic patients (pts).

Methods: Since October 2014 till April 2017, 36 pts were treated with SRS for metastatic brain cancer (number of lesions ranging from 1 to 3). 32 out of 36 were evaluable for follow up. Pts underwent SRS on 58 brain lesions; 3 pts were treated twice, after developing new brain lesions; 2 pts had previous WBRT. Median age was 68 years (range 42–86), female/male ratio :15/17; prescription dose ranged between 20- 24 Gy for lesions with a diameter of 2 cm or less, 18-21 Gy if diameter between 2 and 3 cm, and 15-21 Gy in case of previous radiation treatments. Histologically, the primary was non small cell lung cancer (NSCLC) in most of pts, then breast cancer. The RPA prognostic class was 1-2. Pts were immobilized with specific thermoplastic mask, treatment planning was carried out using contrast enhanced CT images after matching with diagnostic

contrast enhanced MRI images. Therapy was delivered by LINAC Trilogy (Varian), equipped with a 120 leaves MLC, using a 6 MV SRS photon beam and 1000 MU/minute dose-rate, after planning with RapidArc (RA) technique. On-line CBCT were performed for verifying set-up. Steroids were administered before and after the procedure. Follow up was performed with a contrast enhanced MRI imaging, every three months.

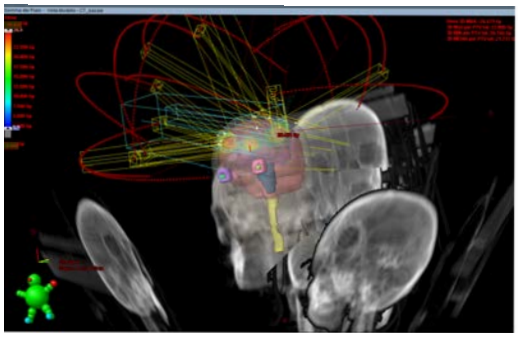

Figure 1.

Results: Quality of target coverage, measured through Paddick Conformity Index, found an average of 0.65±0.07. The treatment resulted well tolerated, only a patient developed a symptomatic thalamic brain radionecrosis, as late effect, successfully managed. Through a mean follow up of 6 months (range 3-18), 14 pts are not still alive, 10 of whom for extracranial progression. Twelve cerebral PD (most of them out of treated metastases), 17 SD and 3 RC were achieved. Among pts with PD, 3 were re-treated with SRS, obtaining SD for all, while the other 3 pts underwent WBRT.

Conclusions: SRS is a valid alternative to whole brain radiotherapy in carefully selected pts with limited number of brain metastases, resulting in a high probability of local control and good tolerance, however carrying a risk of failure in not-treated brain regions. Quality of target coverage using RA is also competitive with other radiosurgical tecniques, avoiding invasive immobilization devices and fastening overall treatment time.

P224

SAFETY OF NIVOLUMAB IN ASSOCIATION WITH RADIATION THERAPY TREATMENT IN PATIENTS WITH METASTATIC SOLID CANCERS.

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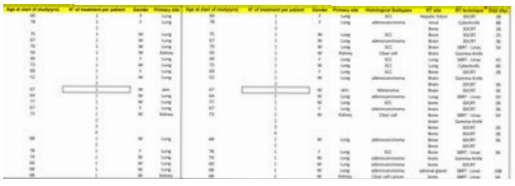
Background and purpose: Role of immunotherapy for the treatment of various neoplastic disease is constantly increasing. Radiation therapy (RT) often plays an essential role in the management of these diseases.Data from literature about the concomitant administration of these two treatment are sparse. Here we present the results from a prospective analysis, evaluating safety and feasibility of Nivolumab and RT concomitant association in the metastatic setting.

Materials and Methods: Data from 21 patients with stage IV melanoma (5%), renal cell (14%) and lung cancer (81%) treated since august 2015 were prospectively collected. Treatments were considered concomitant when interval between systemic therapy and RT did not exceed 2 months, Nivolumab interruption was allowed only during RT course. RT was performed either in the palliative or oligometastatic setting. Patients could receive RT on multiple sites during the course of their systemic therapy. Measured endpoints were Progression free survival (PFS) and Best objective response rate (ORR) to nivolumab therapy, classified as Partial response (PR), Stable disease (SD) or Progressive disease (PD).

Results: Baseline population features are summarized in Table 1. Median duration of exposure to Nivolumab was 5.6 months (range 1-21), with a median of 14 delivered cycles (range 4-42). After a median follow up time of 6 months (range 1-21), results showed a median PFS of 4 months (range 1-21). Best ORR to Nivolumab was PR in 3 cases(14%), SD in 7 (34%) and PD in the remaining 11 cases (52%). Median Biological Equivalent Dose (BED) of 41 Gy (range 17.6 – 108) was administered in RT schedules excluding 4 cases treated with intracranial Radiosurgery. Most frequent adverse events were increase in transaminase levels, nausea and dyspnea, reported in 19%, 19% and 14% of patients, respectively. Breakthrough pain occurred in 3 cases (14%). Reported toxicities were mainly G2 (48%) and G3(33%), no G4 adverse event occurred. Four patients are currently undergoing Nivolumab treatment.

Conclusions: Combined RT- Nivolumab therapy appears to be a safe and an feasible choice for patients in the metastatic setting. Despite variable doses and fractionations applied, we have not encountered any unexpected toxicities. Our analysis confirm that no additional toxicity could be addressed to concomitant administration of RT and Nivolumab.

Table 1. Study arms and dose levels (Gy) planned and reached (underlined) in the different arms of the study.



P225

DESCRIPTION AND FIRST CLINICAL APPLICATION OF A NEW AND UNIQUE TECHNIQUE FOR THE INTENTIONAL INDUCTION OF THE ABSCOPAL AND BYSTANDER EFFECTS: PARTIAL HIGH-SINGLE-DOSE IRRADIATION OF THE HYPOXIC TUMOUR SEGMENT IN OLIGOMETASTATIC PATIENTS AS A RESULT OF TRANSLATION OF THE PREVIOUS PRE-CLINICAL EXPERIMENTAL RESULTS TO A CLINICAL SETTING

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Aims: The results of our previous pre-clinical *in vitro* study, focusing on targeting tumor hypoxia to induce a strong abscopal/bystander effects, were recently translated to a clinical setting to test whether our pre-clinical results could be translated in a safe and effective way to a clinical setting. Aim of the following study is to describe our unique technique and to report on initial results in a series of consecutive oligometastatic patients whose dominant bulky masses were irradiated partially (targeting exclusively hypoxic segment) with high-single dose radiotherapy focusing on intentional induction of abscopal/bystander effect. We provide data that support the contention that high-dose radiation to the part of a large tumor volume has the potential to induce a robust bystander and abscopal effects.

Material and Methods: 14 consecutive oligometastatic patients with hypoxic bulky tumors were included in this preliminary clinical study. By considering the tumor proprieties through functional (PET) and structural (contrast-enhanced CT) imaging we defined for each lesion individually our target to be irradiated: the hypoxic tumor segment, a so-called "bystander tumor volume" (BTV), which corresponded in average to only 30% of total GTV (mean GTV volume 198 cc, mean diameter 7,4 cm) (Figure 1A). Thus, all bulky masses were treated partially by irradiating their centrally located BTV (without creating CTV and PTV: no additional margins were added to the BTV) with 10 or 12Gy in single fraction prescribed to the 70% isodose line (Dmax: 14 or 18 Gy, respectively). Treatment was delivered by 6MV FFF (flattening filter free) photon beams with dose rate up to 1400 MU/min. A stereotactic radiotherapy plan was calculated on PINNACLE3 with multiple coplanar static beams. Before every treatment was performed, a kilovoltage cone-beam CT was carried out. No patient received chemotherapy or immunotherapy. Results: In all treated patients, a significant bystander and abscopal effects after mean time of 3 weeks were observed (Figure 1B). Overall response rates for symptom relief and mass response were 100%. No patient experienced acute or late toxicity of any grade. Conclusion: By using our method it was possible to induce intentionally important abscopal and bystander effects in all cases without immunotherapy and with no toxicity. Described technique represents a simple 1-day treatment showing a high potential for induction of regional and distant non-targeted effects.

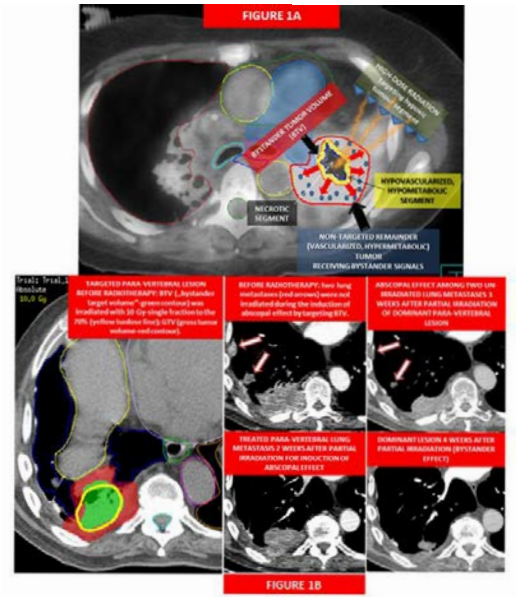

Figure 1A and B.

P226

ASSOCIATION OF RADIOTHERAPY AND NEW ANDROGEN PATHWAY INHIBITORS (ABIRATERONE AND ENZALUTAMIDE) IN OLIGOMETASTATIC PATIENTS: A PRELIMINARY EXPERIENCE

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Purpose: Radiotherapy(RT) has a consolidate role in palliating bone metastasis and increasing biochemical and local control rate in oligometastatic cancer patients. Recently,the introduction of the newer androgen receptor (AR) pathway inhibitors,Abiraterone Acetate (AA) and Enzalutamide (ENZA),has shown a direct impact in reducing bone metastases skeletal events and prolonging overall survival in patients with metastatic castration-resistant prostate cancer (mCRPC). Aim of this study is to describe our experience with the association of RT and AA/ENZA in mCRPC patients.

Materials and Methods:Between February 2016 to April 2017 8 mCRPC patients were treated with AA or ENZA (5 ->AA;3->ENZA).During hormonal therapy 6 patients underwent to RT: 2 for bone progression and 4 for nodal recurrences. All patients underwent [(11)C] choline-positron emission tomography/computed tomography before RT. The median PSA pre-RT was 3.3

ng/ml (1.8-4.7). 5/6 patients were treated with stereotactic body radiotherapy and prescribed dose was 30 Gy in 5 fractions (1 patient was treated to two isolated nodal sites in different time). One patient was treated with 36 Gy in 12 fractions because of local bone extension of disease. Response to treatment was assessed with periodical PSA evaluation.Toxicity was evaluated according to CTCAE vers.4.02.

Results:The median follow-up was of 7 months (range 2-15). The median age was 69 years. A significant reduction of PSA was observed in 5 patients and a progression disease was observed in a patient who underwent to chemotherapy. No toxicity was recorded in the combination of radiotherapy and AA or ENZA.

Conclusions:This preliminary experience shows that RT can be administered safely with new drugs and this association represents an emerging treatment option in order to continue the drug somministration in mCRPC with progression disease.

P227

MOLECULAR IMAGING GUIDED SABR FOR ISOLATED OR LIMITED LYMPH NODES WITH VMAT AND FLATTENING FILTER FREE BEAMS: PRELIMINARY RESULTS IN OLIGOMETASTATIC PATIENTS

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Aims: To evaluate the feasibility and the early side effects of Stereotactic Ablative Radiotherapy (SABR) for isolated or limited lymph nodes in oligometastatic (OM) cancer patients

Methods: Between March 2014 and January 2017, 95 lesions, in 45 OM patients with isolated or limited lymph nodes involvement, staged on PET/CT, were treated with SABR, delivered using Volumetric Modulated Arc Therapy (VMAT) and flattening filter free (FFF) beams. Prescribed doses and schedules of fractionation varied, ranging from 35 Gy in 10 fractions to 45 Gy in six fractions. Most commonly used schedules were 36 Gy in 6 fractions and 35 Gy in five fractions. The median age was 66 years (38–91 years) and 35 out of 50 were male. Median follow-up was 12 months (4–32 months). Major primary tumor sites included prostate (55%) and colorectal (13%). The node sites included 49% abdominal, 41 % pelvic, 5% thoracic, 3 % cervical, and 2 % axillary and internal mammary. PET/CT was performed with 18F-FDG in 32/95 lesions (34%), Choline in 40/95 (42%), Ga68-PSMA in 23/95 (24%).Toxicity were evaluated using CTCAE v.4.0. Local control was scored by means of PET/CT scan.

Results: All patients completed the treatment without interruptions. Acute toxicity was minimal: 3/45 (7%) patients reported diarrhea grade 1, 1/45 (2%) showed fatigue grade 1 and 1/45 (2%) showed erythema G1. No acute Grade 2 or higher and no late toxicity were recorded. Median follow-up was 12 months. Metabolic response on PET/CT was evaluated as follows: complete response in 85/95 (90%) of treated lesions, partial response in 1/95 (1%),stable disease in 4/95 (4%), progression in field in 5/95 (5%).Thus, overall response rate was 95%. During follow up, failure were reported as follows: in a single case we observed in field failure only, after 7 months. In other 15 patients we recorded out of field failure. In 3 patients synchronous in field/ out of field failures were found.

Conclusions: PET/CT guided SABR is a feasible approach for isolated or limited lymph node recurrence in OM patients, offering excellent in-field tumor control with low toxicity profile. Longer follow-up is needed to assess late toxicity and the influence of local control on clinical outcomes.

P228

FEASIBILITY OF A HIGHLY HYPOFRACTIONATED RADIOTHERAPY TREATMENT FOR NON SPINAL BONE METASTASES

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Aims: To evaluate the feasibility, toxicity and preliminary results of highly hypofractionated radiotherapy for non-spine bone metastases.

Methods: Subjects with non-spine bone metastases from different primary sites were treated at our institution. The prescribed dose was 21 Gy with 7 Gy per fraction for all patients delivered using 3D conformal radiotherapy or intensity modulated radiotherapy with almost 5 coplanar fields. Patients were treated in supine position using vacuum-locked or other customized devices. Local control was evaluated at least after three months after treatment completion by means of radiological exams, while pain responses assessed at the end of treatment and every three months thereafter. Acute toxicity (defined as toxicity <90 days) were reported and graded as per standardized Common Toxicity Criteria for Adverse Events 4.0 criteria.

Results: Between May 2016 and May 2017, 15 subjects (for 15 treated lesions) with non-spine bone metastases were treated. The median age of patients at the time of RT was 64.0 years. The most common primary sites were breast cancer, lung cancer and prostate cancer (28,6% respectively). The most common treated site was the acetabulum (26.7%). All patients with pain before RT, experienced a complete pain response. Among them, only 5 patients (33.3%) have been evaluated at follow up (median follow up 4.83 months)

while the others are currently on treatment. Three patients (60%) experienced a partial response at the first imaging (MRI or CT), 1 a complete metabolic response at PET-CT and 1 a stable disease. No patient had local progression. None patient developed acute toxicity in terms of pain flare up and nobody developed pathologic fractures.

Conclusions: Highly hypofractionated radiation therapy is a feasible and tolerable treatment for non-spine bony metastases. Longer follow-up will be needed to accurately determine response and late effects.

P229

STEREOTACTIC BODY RADIOTHERAPY FOR ISOLATED LYMPH NODE RECURRENCE IN PATIENTS WITH PROSTATE CANCER

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Aims: To investigate the role of stereotactic body radiation therapy (SBRT) in the treatment of patients affected with nodal recurrence of prostate cancer within the pelvis.

Methods: Between November 2012 and January 2017, 21 patients, for a total of 36 lesions, were treated with SBRT delivered with IGRT technique. Median age was 73.5 years (range 64-88); 19 patients underwent surgery as primary treatment, while 2 underwent radical radiotherapy. Adjuvant and salvage radiotherapy were administered in 6 and 12 patients, respectively. All patients were free from androgen deprivation therapy (ADT) at the time of nodal recurrence detection and all, except one, underwent choline-PET before SBRT. Most patients (67%) received 40 Gy in 5 fractions, while 33% received 45 in 6 fractions. In 2 patients ADT was associated with SBRT. Acute and late toxicity (assessed at 3 and 6 months), biochemical response, local control and pattern of disease progression were analyzed.

Results: A major biochemical response (>70% in PSA reduction) was achieved in 12 patients (57%), a partial response (30-69% PSA reduction) in 4 patients (19%), a stability in 2 (10%) and a biochemical progression in 3 patients (14%). During follow-up period 9 patients (43%) underwent biochemical progression, 6 (29%) of whom after an initial response to treatment. All patients who experienced biochemical progression underwent diagnostic imaging (TC+Bone Scan or Choline-PET), with no evidence of in-field recurrence. At a median of 14.5 months after SBRT, 5 patients (24%) underwent imaging-documented progression with bone metastasis. With a median follow-up of 20 months (range 2-48), 11 patients (52%) are currently free from progression/recurrence. SBRT was well tolerated: we did not observe any acute or late event.

Conclusions: Our experience shows that SBRT, associated with IGRT in the planning and delivery phases, is a safe, effective and minimally invasive treatment for limited nodal recurrence in oligometastatic prostate cancer. Because of its low toxicity and excellent local control, this treatment represent a feasible option not only to improve the outcome, but also to delay further systemic treatments (and related toxicity) in this subset of patients.

P230

COMBINED TREATMENT WITH ABIRATERONE ACETATE AND RADIOTHERAPY IN PATIENTS AFFECTED BY METASTATIC PROSTATE CANCER: OUR EXPERIENCE

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Aims: Abiraterone Acetate in combination with prednisone has been approved by the European Commission for the treatment of castration-resistant metastatic prostate cancer in patients with progression of the disease. With this work we wanted to evaluate the possible side effects and benefits that a combined treatment with Abiraterone Acetate and Radiotherapy had on the pain reduction and the radiological stability compared to the group of patients who are treated with bisphosphonates.

Methods: From December 2015 to January 2017, 93 patients aged between 65 and 74 were treated with palliative radiotherapy. All patients had a mCRPC in progression. 27 patients of these ones were initiated to a Abiraterone Acetate; while the other 66 patients were treated with the bisphosphonate therapy in combination with analogue LH-RH and bicalutamide. Each patient was given a questionnaire to record daily any side effects and the possible pain reduction or increase during the radiotherapy treatment. The 80% of patients receiving biphosphonates used opioids, the remaining 20% assumed NSAIDs and occasionally paracetamol. Among patients receiving Abiraterone Acetate, the 30% used opioids, the 37% needed only paracetamol and the rest did not take any medication. The skeletal segment most frequently affected was the rachis and the pelvis.

Results: No one has interrupted the radiant treatment; In the group of patients treated with Abiraterone Acetate, the liver and kidney function index remained standard throughout the duration of the treatment. The 18% of these patients had only a bearable thrombocytopenia and no other side effects. All patients have proved a significant pain reduction since the first radiotherapy treatment sessions. In the group receiving bisphosphonates, the 35% have mild leucopenia with associated anaemia. The remaining patients had no other side effects. The 68% of patients showed the reduction of the pain after the first 5 sessions of Radiotherapy; the 18% of them had a reduction of the pain since after 1 week after radiotherapy treatment, and the remaining 14% proved no improvement of symptomatology.

Conclusions: In mCRPC, the use of Abiraterone is indicated for the treatment of patients with asymptomatic or paucisymptomatic metastatic disease. Specifically, in patients treated with Abiraterone it has been observed an increased degree of the pain palliation, associated with a short time to obtain the analgesic effect with a significant benefit on the pain response.

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STEREOTACTIC BODY RADIOTHERAPY (SBRT) FOR BONE OLIGOMETASTATIC NON SMALL CELL LUNG CANCER (NSCLC): RESULTS IN 17 CONSECUTIVE PATIENTS TREATED AT EUROPEAN INSTITUTE OF ONCOLOGY

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Aims: To evaluate outcome, local control and toxicities in pts treated with SBRT on bone oligometastases from NSCLC.

Methods: We retrospectively collected data of pts treated on bone oligometastases from NSCLC with SBRT at our Institution between 05/2012 and 12/2016. In this analysis pts with less than five lesions at time of SBRT detected with positron emission tomography/computer tomography (PET/CT), Magnetic Resonance Imaging (MRI) and CT were enrolled. All concomitant treatment and previous treatment were allowed. All patients expressed written informed consent for research purpose. Clinical evaluation and Imaging were performed every three mos after SBRT to update oncologic outcome and toxicities. Progression free survival (PFS) as well as Overall Survival curves were elaborated with Log-Rank Test.

Results: Seventeen pts were treated on 20 bone lesions. Thirteen pts were male. Median age and Karnofsky Performance Status (KPS) score were 69 years and 90, respectively. Initial treatment included surgey and definitive chemo-radiotherapy in seven (41%) and one (7%) pts, respectively. Ten (59%) pts were found in stage IV at the diagnosis. Median total dose, dose per fraction and number of fractions delivered were 20 Gy, 8 Gy and 3, respectively. All pts received Image Guided RT. In 4 (29%) pts, concomitant treatment (chemotherapy and target therapy in 1 and 3 pts, respectively) was added to SBRT. In 11 (65%) pts evident disease was found on the primary tumor (T) and/or locoregional lymph nodes (N). Median follow-up was 16 mos. No acute or late toxicity were reported. Clinical progression was evaluated in 13 pts (76%) after a median time of 3 mos (range 1.6-23 mos). In-field progression occurred in 5 pts (29%). One-year PFS and OS (fig.) rates were 26% and 79%, respectively. At the time of analysis 10 (59%) alive with disease and 7 (41%) pts dead of disease.

Conclusions: SBRT is safe and allows good local control rate (~70%). In our series 41% of pts showed progressive disease later than 6 mos: further investigation with larger cohorts is warranted to identify pts that could benefit most from this treatment modality alone to postpone systemic therapies as well as their optimal combination.

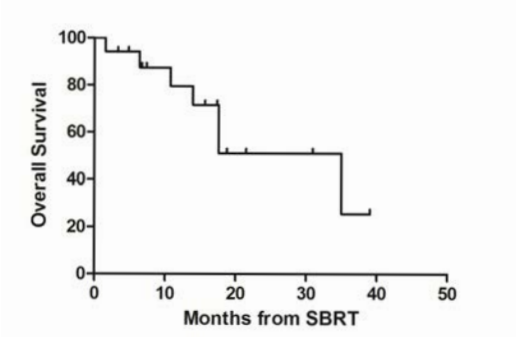

Fig. Overall Survival for bone oligometastatic NSCLC patients after SBRT on bone metastases.

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STEREOTACTIC BODY RE-IRRADIATION FOR SPINAL AND BONE METASTASES

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Aims: To evaluate pain relief and imaging-based local control of bone metastases in patients previously treated with conventional external beam radiation therapy (EBRT) and then re-treated with stereotactic body radiotherapy (SBRT).

Material and Methods: We retrospectively analyzed patients re-irradiated for painful or complicated (risk of fracture or cord compression) spinal and non-spinal bone metastases performed with SBRT in European Institute of Oncology between March 2012 to October 2016. The spinal lesions were treated with the Cyberknife system and the non-spine lesions were treated with the BrainLab–Vero system. The inclusion criteria were: previous irradiation of the same bone seat and a Karnofsky performance status (KPS) greater than 70. Pain relief was evaluated with the unidimensional subjective scale NRS (Numerical Rating Scale) in all

patient. The radiological response and local complication (bone fracture, myelopathy) was evaluated by medical examination and diagnostic examinations (MRI, CT and PET-CT). Local response was defined as dimensional radiological stability or reduction for the re-irradiated lesions evaluated with MRI or CT. For the lesions evaluated with PET-CT we considered local response as reduction or stability of FDG uptake by the re-irradiated lesion.

Results: 30 patients were re-treated on 31 bone lesions (13 was spine lesion, 18 was non spine lesion). The median age and KPS was 63 years and 90, respectively. The median total dose and number of fractions of the initial EBRT was 20 Gy and 10 fractions, respectively . The median SBRT total dose and number of fractions were 18 Gy (dose range 6-30 Gy) and 3 (fraction range 1-20), respectively. The median time interval from EBRT to re-irradiation SBRT was 13.6 months, and the median duration of patient follow-up was 11.6 months. In 31 treated lesions, 16 were symptomatic before re-irradiation. After re-treatment we observed complete pain resolution in 10 lesions (62.5%), partial remission in 5 lesions (31.25 %) and pain stability in 1 lesion. The 15 remaining lesions were asymptomatic and remained asymptomatic after re-treatment. In 1 case we observed worsening of the pain. After a median time of 90 days (first follow-up), we observed radiological response in 27 lesions(with MRI for 7 lesions, with PET/CT for 11 lesions and with CT for 9 lesions). We observed 1 (3%) radiological complete response, 7 (26%) partial response and 16 (59 %) radiological stability. In 3 (11%) lesions we observed a radiological progression. We have evaluated local control and pain after a median time of 11.6 months: for 8 (27%) lesion we observed progression of disease in field, for 19 (60%) lesions we haven't observed any in field progression (stable disease) and 4 (13%) lesions were non evaluable. 13 of the 16 symptomatic treated lesions were asymptomatic at the last follow-up. There were no cases of radiation myelopathy, and bone fracture rate was 3%.

Conclusions: Re-irradiation SBRT of bone metastases is effective in yielding imaging-based local control and long-term pain relief with clinically acceptable safety profile.

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VMAT/RAPIDARC IN OLIGOMETASTATIC SELECTED PATIENTS WITH BRAIN METASTASES: THE IRCCS "GIOVANNI PAOLO II" EXPERIENCE

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Aims: To report the IRCCS"Giovanni Paolo II" experience on palliative treatment of brain metastases, using VMAT(Volumetric Modulated Arc Therapy)/RapidArc-technique delivered to each lesion with different fractionation schedules. Our restrospective analysis evaluates dosimetric coverage of the target,local disease control and RT-related toxicity,in order to consider the benefits of partial brain irradiation in oligometastatic patients with better life expectancy.

Methods: From 2015 to 2017,9 patients were irradiated with VMAT on their brain metastases(max 4). Among them,5 patients with brain disease confirmed by neuroimaging had metastatic carcinoma and clinical characteristics (performance status,primary tumor site control) that suggested for a better life expentancy; they completed radiotherapy,without previous whole-brain irradiation. Fractionation schedules were:for 3 patients with single brain lesion DT(Total Dose)25Gy,Df(Dose per Fraction)5Gy; 1 patient with single metastasis received DT 24Gy,Df 6Gy; 1 patient with 4lesions had DT 40Gy,Df 8Gy.The most important dosimetric parameters related to PTVmetastasis were Conformation Number(CN95%) and Homogeneity Index(HI);respect of constraints for Organs at Risk(OARs) was also considered in each plan.Acute toxicity was scored according to the RTOG scoring system.Local disease control after 3months is being evaluated by neuroimaging.

Results: The calculated CN95% was acceptable:(average) 0.56.PTV had an excellent HI:(average) 0,04. Mean value of V95 is 99,6%.A good dose-sparing of healthy cerebral tissue and eyes was obtained.Ongoing follow up shows clinical results similar to survival data in literature;with regard to local control of brain disease,1 patient -still alive after 7months-obtained RC(Complete Remission)of brain metastasis;2 patients obtained RP(Partial Remission) of their lesions until their death(for systemic progression of disease);for 2 patients follow up is in progress.RT-related acute toxicity affected only 1 patient with moderate headache;satisfactory quality of life was maintained by other patients.

Conclusions: VMAT represents a good conforming technique for brain metastases, with an excellent target coverage, homogeneity of dose-distribution(as a typical stereotactic treatment)and useful sparing of healthy tissue and OARs.Even if our preliminary results on tolerance and efficacy seem to be encouraging,we still need more evidences by larger samples of selected patients and extended follow up.

CASO	Volume (TV)	TVpi	Vpi	Dp (Gy)	Dmean	V95% (%)	D2% (Gy)	D98% (Gy)	D5% (Gy)	CN95% (%)	HI	Right eye	Left eye	Brain
A	3,7	3,4	7,8	24	24	100	24,5	23,6	9,6	0,401	0,037	0.26	0.87	1.89
B	52,4	49,8	77	40	40	99,6	40,98	38,9	33,4	0,615	0,052	1.00	1.00	13.3
C	47,6	45,5	58,4	25	25	99	25,8	24,3	15,3	0,745	0,060	1.50	2.40	4.3
D	7,5	7,1	11,7	25	25	99,5	25,6	24,4	8,4	0,574	0,048	0.04	0.04	1.64
E	2,8	2,6	5,5	25	35	100	25,3	24,7	6,3	0,439	0,024	0.35	0.53	1.75
Medie	**22.8**	**21,68**	**32,08**			**99,6**	28.43	27.18	**14,6**	**0,56**	**0,04**	**0.63**	**0.97**	**4.57**

Dosimetric results for target and OARs; B patient with 4 brain metastases in unique target volume

TVpi= Target Volume prescription dose 95%
Vpi= Volume prescription dose 95%
TV = Target volume (cc)

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STEREOTACTIC BODY RADIOTHERAPY (SBRT) FOR OLIGOMETASTATIC UROTHELIAL CARCINOMA: A RETROSPECTIVE ANALYSIS OF 11 PATIENTS

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Objectives: The aim of our study was to retrospectively report on the image guided stereotactic body radiotherapy (SBRT) in the oligo-recurrent bladder cancer. Eleven patients treated in our department for urinary bladder transitional cell carcinoma with lymph node or bone recurrence were retrospectively reviewed. The primary endpoint was to evaluate the safety of SBRT, proposed as an alternative to systemic treatment in unfit patients and/or to defer the start of a second line chemotherapy.

Methods: Inclusion criteria for our retrospective study were as follows: adult oligometastatic transitional cell cancer (TCC) patients with lymph node or bone recurrence that underwent SBRT but not other local/systemic therapy. Previous radiotherapy, systemic therapy or surgery on the primary tumor were allowed. The median treatment dose was 25 Gy (range, 20-30 Gy) given over a median of 5 fraction (range, 3-15 fractions).Toxicity and tumor response were evaluated. Progression disease free-survival was also evaluated.

Results: Eleven patients for a total of 19 lesions were treated with CyberKnife or Vero System- SBRT between 2012 and 2016. Median age at SBRT was 65.3 years (range 45-80) and Karnofsky performance status (KPS) was 90 (range 70-90). Mean interval between TCC diagnosis and the first SBRT fraction was 2.8 years. Median follow- up was 20.3 months. Radiological response evaluated at the first imaging assessment was: complete response, partial response, local progression and not evaluable 11, 1, 6 and 1 lesions, respectively. The radiological progression of disease was registered in 7 patients at the median of 8.2 months (range 2.3-18.5 months) from the end of SBRT; in 6 cases it was out-field and in-field progression, while in one patient an only out-field progression was observed. At the time of the analysis, 3 pts are alive with no evidence of disease (median of 20.1 months from the end of SBRT), 2 alive with evidence of disease, 5 dead of cancer related disease and 1 was lost to follow-up. No severe acute and late toxicity were observed.

Conclusions: SBRT on lymph node or bone oligorecurrence from TCC offers a good in-field tumor control with very low toxicity profile. In small proportion of patients the starting of another systemic therapy was deferred with a reasonable control of disease. Further study are needed to establish a role of SBRT in the oligometastic recurrent bladder cancer.

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SALVAGE FOCAL CYBERKNIFE STEREOTACTIC RADIOTHERAPY TO DOMINANT INTRA-PROSTATIC LESIONS USING [11C]CHOLINE PET/CT

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Aims: To investigate the role of integrated [11C]choline PET/CT for target volume delineation in patients with recurrent prostate cancer following External beam radiotherapy (EBRT) for a salvage focal Cyberknife Stereotactic Hypofractionated Radiotherapy (SBRT) treatment.

Methods: From December 2012 to May 2016 a cohort of 36 pts with initial disease category defined as low (8), intermediate (9), high (19), in accordance to NCCN guidelines, a median age of 74 years (range 62-89) and an history of locally-recurrent prostate cancer following EBRT were referred to our Department for salvage Cyberknife SBRT. The diagnosis of a clinically evident prostate cancer recurrence was based on biochemical progression and imaging studies (CT Scan, Bone Scan and [11C]choline PET/CT). Median iPSA was 19.6 ng/ml (4.9-88 ng/ml), EBRT median dose was 76 Gy (range 74 - 79.2 Gy) and the mean time to failure was 66 months (range 11-187 months). of 66 months (range 11-187). The median pre-reirradiation PSA was 4.84 ng/ml (range 2.23-21.04 ng/ml). To reconstruct CTV and organ at risk, CT scan and MRI with T1-T2 sequences were performed and [11C]choline PET/CT images were fused. Ten pts received 3 fractions of 10 Gy (total dose 30 Gy), 24 pts received 3 fractions of 12 Gy (total dose 36 Gy) delivered to the PET positive prostate node (median volume of 14.3 cc - range 5.75-65.04).

Results: Salvage Focal Cyberknife treatment was well tolerated without any RTOG grade 3 acute or late toxicity. With a median follow up of 25 months (range 7-43) we observed the following Results: no in field recurrence, resulting in a local control of 100%. In 6 pts, a [11C]choline PET/CT detect the presence of a local recurrence (median time 15 months; range 8-22 mts) with the evidence of a new positive prostate node outside the irradiated field requiring a second Cyberknife salvage treatment. 3 pts developed lymph-nodes o bone metastases 6, 9 and 12 months after Cyberknife.

Conclusions: Cyberknife Hypofractionated stereotactic radiotherapy using [11C]choline PET/CT fusion for image guidance is a suitable technique for partial prostate dose escalation.According to available literature, [11C]choline PET/CT is not clinically recommendable to plan target volume, nevertheless our promising data suggest a potential role of [11C]choline PET/CT as an image guide tool for the irradiation of focal prostate cancer relapse. Prospective trials are needed to better define the role of differential prostate treatment on imaging defined targets.

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SUCROSOMIAL IRON SUPPLEMENT IN PATIENTS UNDERGOING CHEMOTHERAPY: A SINGLE-CENTER EXPERIENCE

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Aims: Iron deficiency and anemia represent common problems in oncologic patients treated with chemotherapy. This can cause delay of treatment, hamper adhesion to the treatment schedule and exert a major influence on quality of life. Reduced iron enteral absorption is frequently altered in cancer patients, diminishing the effectiveness of common oral iron preparations. Sideral® Forte is composed of ferric pyrophosphate contained in a matrix of phospholipids and sucresters to promote intestinal absorption and reduce gastric side effects. We aimed to use this supplement in a small group of patients with anemia and iron deficiency receiving chemotherapy in our Center.

Methods: Patients undergoing chemotherapy who developed at least Grade 1 (CTCAE v4.03) anemia and iron deficiency were proposed for sucrosomial iron integration. The supplement was given twice a day in the first two weeks and once daily thereafter. Patients were monitored during treatment with a full blood count (FBC) at every visit. An iron panel blood test including serum iron, transferrin, and ferritin level was performed at baseline, and every 4 weeks on average.

Results: 15 patients had at least one re-evaluation with a FBC. Average treatment duration was 62 days. Mean hemoglobin level at baseline was 9,92 g/dL (8,7-10,7) and 10,88 g/dL (9-12,6) at the last control. The average increment of Hb levels was +0,96 g/dL ((-0,2) - (+2,9)). Grade 2 anemia was present in 8 out of 15 patients at baseline, and in 3 patients at the most recent control. Six patients improved their anemia grade of at least one category according to CTCAE v4.03, and two patients were found not to have anemia at all at the last control. Mean levels of serum iron, transferrin and ferritin level were 34 (18-54) mcg/dL, 316 (260-416) mg/dL and 28 (13-51) ng/mL at baseline, respectively, and 49 (26-77) mcg/dL, 273 (196-367) mg/dL, and 100 (34-169) ng/mL at the last control. Average difference of levels of serum iron, transferrin and ferritin level was +16 mcg/dL, -43 mg/dL and +72 ng/mL, respectively.

The supplement was well tolerated, without any toxicity reported.

Conclusions: Sucrosomial iron integration can improve hemoglobin levels and iron deficiency in cancer patients during chemotherapy, with a good tolerability profile.

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NEW DRUGS AND RADIOTHERAPY IN THE TREATMENT OF METASTATIC MELANOMA: A CASE REPORT

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Aims: To analyze the integration between new drugs and radiotherapy in the treatment of metastatic melanoma.

Methods: In December 2015 a 41-years old female patient was treated with stereotactic body radiotherapy (SBRT) for an isolated lung metastases, unresponding to previous systemic treatment.

Results: In May 2014 a CT scan showed multiple bilateral lung metastases (maximum diameter of 1.6 x 1.0 cm) in a previous operated pT3 N0 wild-type BRAF cutaneous melanoma. Patient underwent chemotherapy with Fotemustine 100 mg/mq and Cisplatin 75 mg/mq for IV cycles with stable disease. Due to small blood count, chemotherapy was stopped and patient was treated with Ipilimumab 3 mg/Kg for IV cycles. CT scan performed in November 2015 showed a radiological complete response of all the lesions except for the one with maximum diameter that was increased (1.6 x 1.9 cm). A FDG PET scan was perfomed and confirmed only one active lung lesion. In December 2015 patient underwent SBRT on the lung lesion for a total dose of 50 Gy in 5 fraction with a radiological complete response. After a follow-up of 1 year there is a complete response with a negative FDG PET scan.

Conclusions: New drugs have radically changed the prognosis of metastatic melanoma. In addiction to the new drugs, radiotherapy can improve disease control especially in oligometastatic desease.

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STEREOTACTIC RADIOTHERAPY FOR OLIGOMETASTATIC OVARIAN CANCER PATIENTS TREATED WITH VERO™ AND CYBERKNIFE™ AT EUROPEAN INSTITUTE OF ONCOLOGY: UPDATE RESULTS IN 82 PATIENTS/156 LESIONS

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Aims: To retrospectively evaluate response and

toxicity(tox) of stereotactic radiotherapy(SRT) for oligometastatic ovarian cancer patients(pts).

Methods: Inclusion criteria were: (1)oligorecurrent/oligoprogressive disease(1–5 lesions) after/during systemic therapy; (2)salvage surgery/other local therapies not feasible; (3)patient not eligible for systemic therapy due to comorbidities, severe toxicity, no more chemotherapy(CHT) lines available or refusal of the patient. Tox and tumor response were evaluated using CTCAE and RECIST criteria. CT or PET was performed at 2-3 months (mo.).

Results: Between May 2012 and December 2016, 82 patients/156 lesions underwent SRT. We treated 112 nodal metastases (mets) and 44 visceral mets. 126 lesions were treated with VERO™, 30 with Cyberknife™. Median age was 60.4 years(range 37.4-84.1). Histology was high grade serous, low grade serous, endometrioid, granulosa, others in 55(67.1%), 6(7.3%), 7(8.5%), 7(8.5%), and 7(8.5%) pts, respectively. 81/82 pts had previously received CHT and/or hormonotherapy (HT); pts received a median of 3 CHT regimens prior to SRT(range 0–9). Concomitant systemic therapy was performed for 25 lesions(9 CHT, 20 HT). SRT consisted in re-irradiation for 4 lesions. Mean GTV was 3.15 cm3 (range 0.19–90.5). Median dose was 24 Gy(range 14-45 Gy) in 3 fractions(range 1–5). Median follow-up (FU) was 1.45 years(range 0.18 - 4.28). Radiological response at first FU was: complete response, partial response, stabilization and progressive disease(PD) in 91 (60%), 26 (17%), 24 (16%) and 11 (7%) for 153 evaluable lesions, respectively. At last FU, 28 pts were alive with no evidence of disease, 40 alive with disease, 14 died of disease. No G3-G4 acute or late tox was observed. Pattern of failure was mainly out field. Local control at last FU was observed in 115/153 evaluable lesions (75.2%). 3 year (y)-Local progression free survival (PFS) was 55%. Median PFS was 0.47 years (95%CI: 0.29-0.88), 1 y- and 3 y-PFS were 34% and 8%, respectively. Median time to systemic treatment after SRT was 7.4 mo.(range 2.1 – 49.3).

Conclusions: In our experience, SRT in oligometastatic ovarian cancer pts has shown good local control and excellent toxicity profile. It might be a good alternative to other more invasive local therapies in order to delay systemic therapy especially when temporaneously contraindicated, not tolerated, or in chemorefractory disease. The evaluation of histologies, site and volumes treated is ongoing.

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CASE REPORT. AS THE IGRT MODIFIES THE THERAPEUTIC WORKFLOW: FROM PALLIATIVE TO RADICAL

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Aims: To present a clinical case in which image-guided radiotherapy (IGRT) modifies the workflow and the purpose of the radiation treatment, from palliative to radical, in a patient with adrenal metastasis from lung cancer.

Methods: 65 years old male patient, former smoker, with lung adenocarcinoma, received surgery in April 2016 and adjuvant chemotherapy with Cisplatin and Vinorelbine until August 2016. The computed tomography (CT), performed in November 2016, showed a metastasis of 2.5 cm in left adrenal. The next positron emission tomography not only confirmed this but also highlighted a radiopharmaceutical uptake in the right adrenal. After one month, another CT detected a size increase in left adrenal lesion (5 x 4 cm) and the appearance of a right adrenal metastasis (2 cm). The patient underwent chemotherapy with Carboplatin and Etoposide but showed disease progression. In April 2017 radiotherapy consultations were conducted for these adrenal metastases, as they were the only metastatic sites since the onset of disease. Palliative treatment was performed on left (7.5 x 6.5 x 5 cm) and right (3 x 2.5 x 1.5 cm) adrenal lesions of total volume of 138 cc, with volumetric-modulated arc therapy and monoisocentric technique, for a total dose of 30 Gy in 10 fractions and daily IGRT (cone-beam computed tomography). At the eighth session, a significant reduction in the overall volume of lesions (60 cc) was appreciated. Adaptive radiotherapy followed. During treatment, the patient did not exhibit radiation-induced toxicity. A week from the end of the treatment, CT showed a further reduction in lesions (5 x 4 x 2.3 cm and 1.2 x 1.5 x 0.6 cm), with a total volume of 32 cc. Given the excellent response to treatment, a stereotactic boost of 10 Gy in single fraction was programmed.

Results and Conclusions: In this clinical case, the use of IGRT has played a decisive role in modifying the therapeutic workflow, allowing to perform unplanned adaptive radiotherapy and altering treatment purpose.

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DEFINITIVE RADIOTHERAPY IN INVASIVE VAGINAL CARCINOMA: A SYSTEMATIC REVIEW

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Aims: To systematically review the recent (last 10 years) literature on the role of definitive radiotherapy (RT) in the management of vaginal cancer (VC) with the aim to evaluate outcome and toxicity.

Methods: From Pubmed (2007-2016) database, a literature search was performed including english published prospective and retrospective articles on RT in invasive VC. The following data were recorded: number of patients, enrolment period, median follow up, treatment characteristics, and results in terms of toxicity and outcome.

Results: Based on inclusion criteria, 13 studies were selected enrolling a total of 793 patients (median 45; range: 26-138). All studies had a retrospective design and patients were treated between 1958 and 2014. Studies were heterogeneous in terms of RT dose, fractionation, and treatment techniques, use of brachytherapy (BT) boost, combination with surgery, chemotherapy, or other therapies and evaluation modalities. Particularly, external beam RT plus BT boost was used in 80.6% of patients. In 10 studies, a minority of patients received a combination of RT and chemotherapy and different RT techniques were used (AP/PA, 4 fields, IMRT, VMAT). Acute and late grade ≥ 3 toxicity rate ranged between 0.0% and 24.4%, and between 2.4% and 17.8%, respectively. Median 5-year progression-free survival was 77% (I & II stage: 25-92%, III & IV stage: 0-48%), while median overall survival was 58.4% (I & II stage: 25-83%, III & IV stage: 0-50%) respectively, with a significant difference between early stage (I & II) and advanced stage (III & IV).

Conclusions. Only few and retrospective studies have been published in the last decade on RT in VC, with a large heterogeneity in terms of treatment characteristic and evaluation criteria. Clinical results were strongly influenced by tumor stage. Prospective randomized studies are needed to improve patients outcome especially in high stage disease.

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PRELIMINARY RESULT OF INTRAOPERATIVE RADIOTHERAPY IN PRIMARY AND SECONDARY BRAIN TUMORS: A MONO-INSTITUTIONAL EXPERIENCE

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Purpose: To describe preliminary results of intraoperative radiotherapy (IORT) for brain tumors patients. IORT was performed by Novac linear accelerator using 9 MeV electron beam.

Methods and Materials: From March 2015 to March 2017, seven patients underwent wide or partial resection of the brain tumor followed by IORT at the first surgery or at the second salvage surgery after failure of conventional external beam irradiation. The IORT dose (range 10 - 20 Gy), collimator diameter (range 4 - 6 cm) and angle of inclination (range 0° - 15°) were determined by tumor volume, tumor location and previous radiation treatments. All doses were specified at 90% isodose. Patients receive IORT were as followed: four patients were atypical meningioma (grade II WHO '16), one recurrent malignant gliomas (grade IV WHO '16), one brain metastasis of lung cancer, one recurrent ependymoma.

Results: Three meningiomas received, IORT as exclusive adjuvant treatment after wide resections, with a total dose of 20 Gy. Another meningioma patient underwent partial resection followed by IORT as boost with 10 Gy and subsequently external radiotherapy (45 Gy in 25 fractions). Patient with recurrent glioma, after failure of first surgery and external radiotherapy (60 Gy in 30 fractions plus concomitant temozolomide), received second salvage surgery and IORT with a total dose of 14. Patient affected by a single brain metastasis of lung cancer performed debulking surgery followed by IORT with 20 Gy. Recurrent ependymoma received, after failure of surgery and external RT, a salvage resection and IORT with 14 Gy. With a median follow-up time of 12 months (range 2-26 months), only brain metastasis showed a local disease progression. At the time of the analysis, 2 patients out of 7 were dead and all of them died for extracranial disease. No one developed radiation necrosis on MRI scans follow-up or other late toxicity. The neurologic performance status judged by Karnofsky scale (Range 70 - 100) was not changed or improved after IORT.

Conclusions: This preliminary experience showed the safety and feasibility of IORT in patients with primary or secondary brain tumors. Clinical studies are advocated to evaluate the IORT efficacy in this setting of patients.

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DOSE-EFFECT RELATIONSHIP FOR VAGINAL STENOSIS AFTER BRACHYTHERAPY FOR VAGINAL INTRAEPITHELIAL NEOPLASIA

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Background: The rarity of Vaginal Intraepithelial Neoplasia (VAIN) does not allow to define optimal treatment approach nor to assess the vaginal morbidity due to the treatment. Brachytherapy (BT) could be a possible choice for the treatment of VAIN grade 3 (VAIN 3). It is generally assumed that vagina is radioresistant and no constraints are yet defined, but sexual dysfunction occurring after BT is an important cause of long term distress.

Aims: To report a single institution study of the application of high dose rate (HDR) BT to evaluate clinical outcomes and investigate the dose-effect relationship for vaginal stenosis.

Material and Methods: We retrospectively collected hospital records and treatment planning of 13 consecutive women treated, from August 2010 to August 2016, with HDR BT delivered with Iridium-192 source by a remote after loading system (microSelectron) in our Department . Doses in 3D planned treatment based on CT were prescribed in high-risk –CTV defined as vaginal wall. Vaginal stenosis was defined as vaginal shortening/narrowing according to CTCAE 4.1. The ICRU bladder and rectal point were used for a dose-report analysis as surrogate point of anterior and posterior vaginal wall, respectively. The PIBS (posterior-inferior border of the symphysis) points were used to derive reference points as surrogates for the dose distribution at the mid, the transition from mid to lower and at lower vagina.

Results: The age of the enrolled women ranges between 43 and 77 (median 60 years). The total radiation dose ranges between 24-42 Gy with a median value of 35 Gy (56 Gy EQD2 a/b:3) delivered in a median period of 15 days. Treatment was well tolerated in all patients and no treatment interruption was necessary. Acute toxicity was minimal. Regarding late toxicity, 4 patients developed vaginal stenosis G2 and 3 patients G3. Preliminary evaluations showed that patients with vaginal stenosis G≥2 received a dose to rectal point >32 Gy and were >61 years. All patients were alive without progression to invasion.

Conclusions: According to our study, patients with VAIN 3 seem to derive a good benefit from BT. Finding applicable dose limits to the vagina could improve the quality of life for women therefore these data needs to be further investigated

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A SURVEY OF AIRO (ASSOCIAZIONE ITALIANA DI RADIOTERAPIA ONCOLOGICA), SICO (SOCIETÀ ITALIANA CHIRURGIA SENOLOGICA) AND ISIORT (INTERNATIONAL SOCIETY OF INTRAOPERATIVE RADIOTHERAPY) ON ATTITUDE AND CURRENT PRACTICE FOR IORT (INTRAOPERATIVE RADIOTHERAPY)

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Aims: to gain understanding of the current approach of IORT being undertaken and elicit the factors driving physicians into choosing one irradiation modality over another, in particular for breast cancer.

Methods: In 2017, the Intraoperative Study Group on behalf of the Italian Association of Radiation Oncology proposed a survey. All Italian radiation oncologists involved in IORT were invited to fill questionnaire regarding their clinical practice, in particular for breast cancer. We proposed the survey also to two other societies: the SICO for breast surgeons, and the ISIORT. The questionnaire included sections dedicated to the IORT-related workload and to institutional indications for breast cancer radiotherapy. In the invitation letter, we specified that only physicians involved in IORT were required to answer the questionnaire for each single centres.

Results: To date, 109 colleagues have answered the questionnaire: 85.3% from Italy and 14.7% from other European countries. The majority are radiation oncologists (58.7%). The majority (56%) is working in National Health Services across Europe, 33% in Academic and University Hospital, while 11% in Private centres. Most centres have been using IORT for 5-10 years, while nine centres for more than 15 years. Seventy (64.2%) centres use intraoperative electrons with dedicated accelerator, 11 centres (10%) use Intrabeam and photons, 6 centres use interstitial bra-

chytherapy. For breast cancer, fifty-six percent of centres uses IORT as the sole treatment. Forty per cent of physicians are confident in using IORT as a full dose as much as IORT as "boost". Fifty-two per cent of the physicians polled believed that IORT as a full dose is the most comfortable and safest modality to perform partial breast irradiation. Fifty-five per cent of physicians do not apply IORT after neoadjuvant chemotherapy and only 28.8% include MRI in the routinely preoperative radiological work-up, even in premenopausal women. In 64.2% of centres sentinel node biopsy is provided before IORT and in 57.8% of cases an intraoperative assessment of margin status, oestrogen receptor and proliferative index is carried out.

Conclusions: Although there were wide variations in the clinical practice of IORT across the centres, the core activities were reasonably consistent. More than a half of physicians keep on offering IORT full dose, considering it the most convenient partial breast irradiation modality.

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INTRAOPERATIVE RADIOTHERAPY (IORT) IN BREAST CANCER: ANALYSIS OF 8,417 CASES FROM ISIORT DATABASE

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Aims: A joint analysis of clinical and technical data from 42 centres within the International Society of Intraoperative Radiation Therapy (ISIORT) was undertaken in order to identify the range of intraoperative radiotherapy (IORT) indications and techniques for various tumour sites. In this survey we analysed breast treatments.

Methods: Since 2007, we collected demographic, clinical and technical data related to IORT procedures in a common database. Prospective and retrospective data entry was possible. The current study analysed 8,417 breast tumours.

Results: Breast tumours represent 75.5% of all data of the ISIORT survey that encompassed 11,146 IORT procedures performed from 1992 to 2017. Median age of breast patients was 61.1 years (range 16-90). In 8,291 cases (98.5%), IORT was a component of radical treatment for primary, newly diagnosed disease and in 126 cases (1.5%), it was an attempt to rescue localized recurrent breast cancer. IORT was performed as a boost before or after EBRT in 4,107 cases (47.8%) with doses of 8–12 Gy. In 4,310 cases (52.6%), IORT was used as single radiation treatment modality with doses of 18 Gy, 20 Gy or 21 Gy. The patients enrolled in study protocols represented 33% of those treated by a single dose and 6.3% of those treated by a boost dose. IORT was delivered after and before tumour removal in 39% and 61% of cases, respectively. In 7,845 cases (93.2%), IORT was performed using electrons of 4-12 MeV energy. The most used applicators (77% of cases) were 5 or 6 cm in diameter and bevel angle was 0° in the majority of cases (88%). Five hundred and seventy-two (6.8% of patients) were treated with a 50-kV x-ray source in a single centre. X-rays treatments were delivered by a spherical applicator inserted into the surgical cavity after tumour removal.

Conclusions: ISIORT database represents the largest clinical and technical IORT data collection. Breast cancer is the most frequent IORT treatment performed in the 42 participating centres. From this analysis, it emerged that in most cases IORT was used as single shoot of 18-21 Gy, the most employed treatment modality was electron beam and the procedure was most frequently performed after tumour removal. Only a minority of patients was included in clinical trials. Further data analyses could enhance multi-institutional performance and serve as a basis for designing clinical trials in an effort to define the role of IORT in tailored multimodality therapeutic approaches.

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PARTIAL BREAST RE-IRRADIATION USING HDR BRACHYTHERAPY FOR LOCAL RECURRENCES AFTER PRIOR ADJUVANT EXTERNAL BEAM RADIOTHERAPY: UPDATED RESULTS

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Aims: To evaluate technical feasibility and toxicity using catheter-based interstitial high-dose-rate (HDR) brachytherapy as adjuvant treatment in previously irradiated recurrent breast cancer.

Methods: This is a retrospective analysis on 23 consecutive patients with histologically confirmed recurrent breast cancers after conservative surgery and conventional whole breast radiotherapy were retreated with a second conservative surgical resection and reirradiated by adjuvant interstitial HDR BRT using a remote afterloading unit between January 2011 and October 2013. The median time from first treatment until salvage surgery for local recurrence was 126 month (range 43 -336 month). None of the brachytherapy implant was performed during the quadrantectomy procedure. Number of catheters was individually chosen to adequately cover the width and thickness of the target. A dose of 34 Gy in 10 fractions, 3.4 Gy per fraction, 2 fractions per day with a minimal gap of 6h in-between was delivered. At the time of the implant, the median age of the patients was 55 years (range, 41-74 years).

Results: No complications involving the implant, such as bleeding or infection, were noted. Procedure resulted to be well tolerated for all patients. No epidermitis or soft tissue acute side effects higher than grade 2 were recorded, with good cosmetic results in all patients. After a median follow-up of 47.6 months (range, 31.8 – 73.6 months), the overall survival, local control and disease free survival was 100%, 86.9% and 82.6%, respectively. Three patients developed local and /or regional and/or distant metastases and one patient developed only lung metastases.

Conclusions: Our retrospective analysis showed that the repeated course of radiotherapy by means of HDR brachytherapy to the new surgical bed is a feasible treatment for recurrent breast cancer, offering very low-complications rate and good cosmesis. Main limitations of our study include small number of patients and relatively short follow-up.

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SINGLE 19GY FRACTION HIGH DOSE RATE BRACHYTHERAPY FOR INTERMEDIATE RISK PROSTATE CANCER: FEASIBILITY AND ACUTE TOXICITY

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Gustave Roussy

Aims: To evaluate the feasibility and the acute genitourinary (GU) and gastrointestinal (GI) toxicities of a single 19Gy fraction HDR brachytherapy in patients with intermediate risk prostate cancer with short-intermediate life expectancy.

Methods: We report a single-institution study evaluating 19 patients (pts) treated from October 2015 to March 2017. Patients received a single 19Gy fraction as HDR brachytherapy. Cytoreductive neoadjuvant short term hormonal therapy was administrated for volumes >50cc or within the discretion of the radiation oncologist. Urinary function was evaluated with the International Prostate Symptom Score (IPSS) and only pts with a score <20 were eligible. The dose constraints for prostate volume coverage, urethra and rectum followed the major published guidelines. In all pts a dose of 0.80-1mg/kg of prednisolone was administrated the day after the treatment. Acute GU and GI toxicities were evaluated according the Common Terminology Criteria for Adverse Events version 4.0 at the time of the therapy, after 1 and 3 months.

Results: Pts mean age was 73 (57-86) years and 10 pts had Gleason Score (GS) 7(3+4); 6pts had GS 6(3+3) and PSA>10ng/ml; 3pts had GS 7(4+3) with short life expectancy (comorbidities and/or age). Cytoreductive hormonal therapy was administrated in 7pts and mean IPSS was 7.8 (0-13). The mean prostatic volume was 44.1cc ±11.88cc and the mean D90%, V100, V150 were as follow: 97.3%, 88.1%, 37.9%. Mean urethral Dmax and D5cc were 114.1% and 100.0% respectively while mean rectum Dmax and D2cc were 85.3% and 61.7%. Median follow up was 6 months. Genitourinary toxicities were as follows: in the first week after the treatment 3pts had G2 toxicity, 5pts had G1 and 11pts reported no toxicity; at 1 month G2 toxicities were 2 and G1 were 6 while at 3 months one patient had G2 toxicity and 4 had G1. Only one patient had G1 gastrointestinal toxicity in the first week, at 1 and 3 months (always the same patient). No G3-G4 toxicities were reported. In 2 pts acute urine retention (G2 toxicity) made it necessary to place an urinary catheter in the first week after the treatment.

Conclusions: A single 19Gy fraction HDR brachytherapy for intermediate risk prostate cancer is a feasible treatment with acceptable acute toxicities, similar to alternative treatment options. Further follow up is still required to better evaluate the efficacy

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THE EXPERIENCE OF EUROPEAN INSTITUTE OF ONCOLOGY IN THE ADJUVANT RADIOTHERAPY TREATMENT OF SOFT TISSUE SARCOMA (STS) OF EXTREMITIES AND TRUNK: BRACHYTHERAPY, EXTERNAL BEAM RADIOTHERAPY OR BOTH

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Aims: Soft tissue sarcoma (STS) is an uncommon, extremely heterogeneous group of malignant tumors of mesodermal origin. Conservative surgery represents well-established treatment for STS of extremities and trunk. The modality of combination with radiotherapy, when indicated, is not well established yet. In this work we want to present a retrospective analysis of the radiotherapy treatments of STS in adjuvant setting done at European Institute of Oncology (EIO) of Milan.

Materials and Methods: We analyzed 3 different cohorts of patients (pts) that received different adjuvant radiotherapy treatments: group 1- interstitial brachytherapy alone (PDR or HDR), group 2- external beam radiotherapy alone and group 3- brachytherapy as anticipated boost followed by external beam radiotherapy. For every cohort we analyzed the clinical outcomes in terms of local control (LC), disease free survival (DFS) and overall survival (OS). We analyzed also the acute and chronic toxicity, with particular attention to wound complications and mobility deficit due to fibrosis.

Results: We analyzed 90 pts (median age 65 years) treated between November 2011 and September 2016: 21 in brachytherapy group, 26 in external beam group and 43 in mixed technique group. Tumor size were >5 cm for 32 and <5 for 26 patients (unknown in 32 pts), with histological grading of 1 (n = 14), 2 (n = 11), or 3 (n = 40) (unknown in 25 pts). The most frequent histology was liposarcoma. The median dose 45Gy, 59.4Gy, and 15+45Gy for group 1, 2 and 3, respectively. For all 90 patients the five year actuarial LC, DFS and OS were 92.1%, 94.4% and 89.9%, respectively. Grade 3 acute skin toxicity was present in 4 pts (1 of group 2, and 3 of group 3); 2 years chronic toxicity was available for 60 patients: muscle weakness grade 3 was present in 1 pts, 4 pts and 3 pts in group 1, 2 and 3 respectively.

Conclusions: All data confirm that in adjuvant setting radiation therapy represents an effective and well-tolerated treatment offering high local control and overall survival. Further analysis will be performed in order to identify the patients that need more aggressive approach.

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TOLERANCE EVALUATION OF EXCLUSIVE INTRAOPERATIVE RADIATION THERAPY AT DIFFERENT DOSES FOR BREAST CANCER CONSERVATIVE TREATMENT

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Aims: To evaluate toxicity in breast cancer patients treated with two different doses of Intra Operative Radiotherapy (IORT): specifically, to test whether a reduced total single dose (18 Gy) of intraoperative radiotherapy with electrons may be tailored to safely treat patients with selected early breast cancer in comparison with the standard dose 21 Gy. (NCT 01276938)

Methods: From 2009 to 2011, females eligible for breast-conserving surgery with biopsy-proven invasive ductal, cribriform, tubular, apocrine, mucinous carcinoma and with a mass of < 2.5 cm were included in this study. According to tumor major diameter pts underwent two different doses: < 1 cm (pT1a/pT1b) a single dose of 18 Gy; > 1cm < 2.5 a single dose of 21Gy. The median age at diagnosis was 65 years (range 45-85). After wide local excision, sentinel lymph node dissection, and surgically positioning of the appropriately sized applicator on the tumor bed, a 18 Gy or 21 Gy single dose was given using LIAC dedicated electrons accelerator. The collimation of the beam was achieved by a hard-docking system, consisting of 4-5-6 cm diameter perspex applicators. Used electron energy was 6-8-10 MeV. In vivo dosimetry by micro-mosfet was applied. 168 females affected by breast cancer were treated with this approach: 71 patients (pT1a\b, pN0-1a/mic, pMx,G1-G3) received 18Gy and 97 pts(pT1c\2, pN0-1a/mic, pMx,G1-G3) received 21Gy.

Results: With a median follow up of 6 years, in the 18Gy group: 65 pts (91.5%) result disease-free, 3 pts (4.2%) died for breast cancer – unrelated causes (HCC, Parkinson's disease, lung cancer) while only 2 pts (2.8%) had local recurrence. As to the cosmetic outcomes 37 pts (52.1%) show an excellent aesthetic result, 31 (43.7%) good, 2 (2.8%) acceptable and 1 (1.4%) low. As regard 21Gy: 93 pts (95,8%) result disease-free, 4 pts (4.1%) had local recurrence. As regard the cosmetic outcomes 34 pts (35%) have an excellent result, 49 (50.5%) good result, 14 (14.4%) acceptable.

Conclusions: Our results evidence the de-escalated 18 Gy as adequate single dose IORT to obtain excellent results in terms of cosmetics and local control in selected early breast cancer in comparison to the standard 21 Gy single dose.

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INTRAOPERATIVE RADIOTHERAPY WITH ELECTRONS IN BREAST CANCER, IOERT: RETROSPECTIVE ANALYSIS OF 818 CASES

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Aims: In the last years there has been growing interest to experience less extensive treatments for selected patients at low risk of locoregional and systemic recurrence of breast cancer. Personalised management is considered the future of cancer care: medicine aiming at giving patients the best treatment according to their personal medical history, their physiological status and the molecular characteristics of their tumours. To reduce the radiation treatment time and to control tumor disease in breast area with the higher risk of relapse, was proposed Partial Breast Irradiation (PBI). We report our center experience with mobile linear accelerator, the NOVAC7, as approach to deliver partial breast irradia-

tion or as tumor bed boost for the breast cancer (electron beam energy from 3 to 9 MeV).

Methods: From February 2005 to May 2017, 818 cases of breast cancer received IOERT immediately after breast resection with a single dose of 21Gy or with a dose of 10Gy, as anticipated boost. 212 patients were treated with an exclusive IORT of 21 Gy, delivering the prescribed dose to the 90% isodose. In the other 606 patients the IORT was used as tumor bed boost with dose of 10 Gy, followed by 44-50 Gy whole-breast external-beam radiotherapy.

Results: We evaluated 635 pts with a follow-up longer than 24 months: 456 treated with IOERT as anticipated boost and 179 treated with IOERT single dose. The median follow-up was 66 months for boost group and 82 months for the IOERT single dose group. To date we observed 4 local recurrences in the first group, 6 recurrences in the second, 2 patients developed a lymphnode recurrence, 37 pts developed distance metastasis 17 pts died for cancer, 25 pts died for other reasons, 28 pts were lost during the follow-up.

Conclusions: IOERT should be now considered as an alternative to EBRT for specifically selected and well-informed patients. IOERT with a single dose is feasible, well tollerated and very well accepted by patients not suffering a long cycle of radiotherapy. In our experience it resulted an appropriate technique for the PBI, providing direct localization of the tumor bed and minimizing the damage to normal tissues. Our data suggest that the anticipated boost is associated with a low incidence of local recurrence and can be considered equivalent to the external boost in terms of acute and late toxicity.

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IMAGE (MRI) GUIDED ADAPTIVE BRACHYTHERAPY (IGABT) IN LOCALLY ADVANCED CERVICAL CANCER (LACC). OUR 5-YEARS MONO-INSTITUTIONAL EXPERIENCE

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Aims: In LACC MRI IGABT seems to play a major role in the improvement of clinical outcome with no increase in morbility.We evaluated if D90 for HRCTV correlate with LRC in our 5years(yy)mono-institutional experience.

Methods and Materials: From Jan2011 to Dec2016 we retrospectively analyzed a total of 97pts with LACC FIGO Ib2-IVa that underwent to a combination of external beam radiotherapy(EBRT)and high dose rate(HDR)BT±chemotherapy(CT).EBRT was delivered by LINAC or Tomotherapy with 3DCRT or IMRT.As regards BT we first treated 24pts with a schedule of 30Gy/5Fx and then 64pts with 28Gy/4Fx.The total dose of EBRT+IGABT HDR has been calculated with a dose equivalent of 2GyEQD2 assuming / =10 for T and / =3 for the OAR, with the objective of D90 HR-CTV≥ 87GY10 and D90 IR-CTV≥60-70Gy10 and constrains as OAR D2cc rectum-sigmoid≤70-75Gy3 and D2cc≤90 Gy3 for bladder,D2cc≤60Gy3 bowel. We identified two groups of patients GroupA with D90HRCTV<87Gy and GroupB with D90HRCTV≥87Gy and,in an additional analysis, pts were stratified also according to T size (≥or<5cm).The primary endpoint was LRC in the 2groups.

Table 1.

		N° PZ	GROUP A	GROUP B
HISTOLOGIC TYPE	SCC	81 (92%)	44 (96%)	37 (88%)
	ADK	7 (8%)	2 (4%)	5 (12%)
STAGE (FIGO)	IB2	2 (2%)	1 (2%)	1 (2%)
	IIA1	4 (5%)	4 (9%)	
	IIA2	2 (2%)		2 (5%)
	IIB	67 (76%)	33 (72%)	34 (81%)
	IIIB	8 (9%)	7 (15%)	1 (2%)
	IVA	5 (6%)	1 (2%)	4 (10%)
TUMOR SIZE	< 5 CM	47 (53%)	24 (52%)	23 (55%)
	≥ 5 CM	41 (47%)	22 (48%)	19 (45%)
CT	CDDP	61 (69%)	28 (60%)	33 (79%)
	TAXOLO Q21	11 (13%)	8 (17%)	3 (7%)
	NO	16 (18%)	10 (23%)	6 (14%)
EBRT TECNIQUE	3D	11 (12%)	7 (15%)	4 (9%)
	IMRT	33 (38%)	13 (28%)	20 (49%)
	TOMOTHERAPY	44 (50%)	26 (57%)	18 (42%)
LYMPH NODES	NEGATIVE	46 (52%)	27 (59%)	19 (45%)
	POSITIVE	42 (48%)	19 (41%)	23 (55%)
	PELVIC	37 (42%)	17 (37%)	20 (48%)
	LA	5 (6%)	2 (4%)	3 (7%)
BRT	30 GY/5FX	24 (27%)	22 (48%)	2 (5%)
	28 GY/4FX	64 (73%)	24 (52%)	40 (95%)
ACUTE TOXICITY (scale CTCAE v4.0)	NO	53 (60%)	22 (48%)	31 (74%)
	BLADDER			
	G1	7 (8%)	7 (15%)	
	G2	12 (14%)	8 (17%)	4 (9%)
	G3			
	RECTUM			
	G1	8 (9%)	8 (17%)	
	G2	13 (15%)	9 (17%)	5 (12%)
	G3	2 (2%)	1 (2%)	1 (2%)
	BOWEL			
	G1	6 (7%)	6 (13%)	
	G2	12 (14%)	11 (24%)	1 (2%)
	G3			
LATE TOXICITY (scale CTCAE v4.0)	NO	77 (87%)	38 (83%)	39 (92%)
	BLADDER			
	G1	1 (1%)	1 (1%)	
	G2	5 (6%)	4 (5%)	1 (1%)
	G3			
	RECTUM			
	G1	2 (2%)	1 (1%)	2 (1%)
	G2	4 (5%)	4 (5%)	
	G3			
	BOWEL			
	G1	1 (1%)	1 (1%)	
	G2	3 (3%)	3 (3%)	
	G3			

Results: 88pts were evaluable. Median age was 58yy(range 32-89).Median FU was 25months(range 6-71).Pts characteristics, acute and late toxicity were reported in table1.Median OTT was 53days(43-71).In GroupA there were 46pts(22with T size≥5cm),in GroupB 42pts(19 with T size≥5 cm). Overall 2yy LRC was 89.8%. 2yy LRC were 84% and 83.7%(P=0.8) in groupA and GroupB respectively.2yy LRC in pts with T size≥5cm were 82.2%(groupA) and 100%(groupB) and in pts with T size<5cm were 82.4%(groupA) and 82.1%(groupB)(p=0,45). Overall 2yy DFS was 74.9%. 2yy DFS were 75.2%vs75.1% (p=0.84) for groupA and

groupB respectively. At last FU 8pts(76,4%)were disease free, 21pts(23.6%) had evidence of failure (8 local recurrence, 7 distant metastasis, 4persistence and 1 pelvic partial response). At last FU 75(85%)pts were alive and 13(14.8%)pts died (9in groupA, 4in groupB),8due to cancer (5 groupA,3 groupB) and5 non cancer related cause.

Conclusions: Even if, in our experience, we did not observe a statistically significant difference in the two groups of pts, probably due to the low number of patients we observed a positive trend for local control in pts with T size>5cm withD90>87 Gy.

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COMBINED MODALITY TREATMENT (CMT) CONTAINING INTRAOPERATIVE RADIATION THERAPY (IORT) IN LOCALLY RECURRENT RECTAL CANCER: THE CRO-AVIANO EXPERIENCE

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Aims: the management of locally recurrent rectal cancer remains a challenging issue. Aim of this study was to evaluate outcomes of a multimodality approach containing IORT for these patients (pts) treated at our Institution.

Methods: between February 1999 and August 2016, 49 pts with potentially resectable locally recurrent rectal cancer, have been treated with CMT, including preoperative RT (45-50.4Gy) and 5FU or Capecitabine-based Chemotherapy (23 previously untreated pts) or by a re-treatment program with re-RT (36-41.4Gy) and 5FU or Capecitabine-based CT (19 previously RT-CT treated pts), followed by surgical reavaluation and IORT. Seven pts underwent only surgery and IORT. Adjuvant CT was given in 18pts (37%). We retrospectively analyzed outcomes of these series of patients.

Results: most part of patients had locally advanced sintomatic disease, F2 47%, F3 49%, only 1pts had F4 and 1pts had F1 disease (modified Suzuki classification). Pain, bleeding and mucous discharge were more frequent symptoms. Symptomatic response was reported in most part of 42pts (90%) treated with CT-RT (pain relief in 85% with decreasing/modulation of ongoing oppioid drugs and bleeding cessation in all pts). Partial clinical response at (CT/MRI) was reported in 38% of pts. 41/42 (98%) of preop CT-RT pts underwent surgery with R0 (34%), R1 (53%) and R2 in (8%) margin of resection. 1 re-treated pts was unresectable at operation. IORT was given in all resected patients (dedicated LINAC in operative room) with a dose range of 10-18Gy with electrons (9-12MeV), according to resection margins and re-treatment status. Major complications were reported in 7pts (14%): 2pts (4%) in untreated and 5pts (10%) in re-treated group respectively. Seven selected pts (14%) were treated with surgery and IORT alone (15-18Gy) because of hard previously treatment. At a median follow-up of 38 months, 17(35%)pts are alive, seven of them with local persistent disease.

Conclusions: This CMT containing IORT appear feasible and safe, also for pre CT-RT treated pts (with some re-RT dose and PTV adaptation allowing a good palliative benefit and curative surgical intent in most part of pts). IORT was useful as selected RT dose escalation. More details in long-term disease control, survival and related prognostic factors will be reported.

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VERTEBRAL INTRAOPERATIVE RADIATION THERAPY (V-IORT) FOLLOWED BY VERTEBROPLASTY: A NEW MULTIMODALITY APPROACH TO SPINE METASTASIS. THE EUROPEAN INSTITUTE OF ONCOLOGY EXPERIENCE: UPDATED RESULTS

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Aims: About 50% of bone metastasis are in the spine and are suitable for radiation therapy (RT) to relieve pain and prevent fractures. A combination of vertebroplasty and Intraoperative Radiation Therapy (V-IORT) can be performed for lesions between T4 and L3 using the Intrabeam, Carl Zeiss AG mobile platform with flexible arm.

Methods: We retrospectively analyzed patients (pts) treated at the European Institute of Oncology (IEO) between November 2015 and May 2017 with V-IORT for spine metastasis. Informed consent was obtained in all patients. Although a total of 20 patients (pts) were evaluated to receive V-IORT, only 7 pts were judged suitable for the treatment, and 5 pts finally underwent procedure; 2 pts enrolled but not treated because of technical reasons were treated with External Beam RT. The treatment was performed after the evaluation of radiological images with interventional radiologists and physicists. Evaluation of previous RT data (3 pts) was performed. A preplanning evaluation with basal CT scan was mandatory to define dose and the adequate positioning of the applicator, primarily considering the

spinal cord as organ at risk. During the procedure a standard fluoroscopy was performed in 3 pts while in 2 pts a C-arm digital fluoroscopy was used. All pts received biopsy before treatment. After V-IORT all pts underwent vertebroplasty. Total treatment time was about 2 hours while irradiation time was about 2 minutes. Follow-up was performed with clinical examination and CT or PET scan after 2-4 months, when possible.

Results: Primary malignancies were breast, kidney and pancreas in 2, 2 and 1 patients, respectively. For 3 of 5 pts V-IORT was a re-irradiation at the same site. A dose of 8 Gy was delivered in all pts, prescribed at 7, 8 and 10 mm in 1, 2 and 2 pts, respectively. Three pts had visceral metastases before V-IORT and died for systemic disease progression. Two pts are still in radiological follow-up: no pain or neurological complications related to the procedure were observed. Follow-up CT scan confirmed vertebrae reconstruction without disease. In 1 pt the biopsy revealed an histologic type different from the primary tumor.

Conclusions: Our preliminary analysis confirm that V-IORT is a promising technique to treat or re-treat vertebral metastasis. The procedure is fast and safe. In particular, no neurological complications were registered. Longer follow-up and a larger court of patients are needed in order to confirm our Results:

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IMPLANT AND POSTIMPLANT DOSIMETRIC PARAMETERS IN PROSTATE LDR BRACHYTHERAPY: UPDATE FROM THE BRACHYTHERAPY SERVICE OF AZIENDA BROTZU

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Aims: Prostate cancer (PCa) is the most common malignancy in men. Brachytherapy (BRT) is a valid treatment option for low and favorable intermediate risk PCa. Postimplant dosimetric analysis is standard practice following BRT procedures, and represents an important quality assessment tool as it allows to evaluate how the dosimetric goals, estabilished during intra-operative planning, have been meet. In this study we present data about planning and post planning parameters in our patient cohort.

Methods: From January to December 2016 27 patients with low and favorable intermediate risk pCa underwent brachytherapy as monotherapy at the Urology Unit, Brotzu Hospital, Cagliari (Italy). Patients were treated with transperineal ultrasound-based 125-I permanent implantation using an intraoperative 3D conformal treatment planning system. Prescription dose (PD) to cover the target volume (TV, prostate) was 160Gy. Postimplant dosimetry was evaluated on CT scan 4 weeks after implant. Dosimetric parameters for TV and Organ at Risk (rectum and urethra) were registered for all the 27 patients both on intra and post operative planning.

Results: Mean age at implant was 68 (6.4SD) The mean prostatic intraoperative and postimplant volume was respectively 29cc (8.39SD) and 28cc (7.6SD) and the mean number of implanted seeds was 58 (9.5SD). No seeds were missing. Prostate (P) coverage softly decreased in post (D90 174.9Gy ±6.29 SD, meanV100 95.5% ±3.37 SD, meanV150 44.2% ±8.58 SD) on respect to intra plan evalutation. (D90 191.5 Gy ±6.29 SD, V100 98.6% ±3.37SD, V150 50.8 ±8.58). As sumarized in table (Table 1), rectum and urethra dosimetry did not differ significantly between INTRA and POST planning evalution. On the all, post implant dosimetry on target and OARs was adequate and compatible with low PSA failure and acceptable toxicity as reported in literature. Post implant dosimetry on target and OARs were adequate and compatible with low PSA failure and acceptable toxicity as reported in literature.

Conclusions: Postimplant dosimetry has to be performed for all patients after BRT. It plays an important role in the assessment of implant quality and the evaluation of the dose delivered to target volume an surrounding tissues. Post implant dosimetry could improve the confidence on prostate BRT as a safe and effective treatment option for selected patients affected by pCa.

Table 1. Mean and median values for implant and post implant parameters for TV and OARs with the associated standard deviations.

	PLANNING		Post PLANNING	
Parameters	Median	Mean ± SD	Median	Mean ± SD
PD_{90}(Gy)	192	191.5 ± 6.29	174	174.9 ± 6.29
PV_{100} (%)	99.4	98.6 ± 3.37	96.68	95.5 ± 3.37
PV_{150} (%)	51.9	50.8 ± 8.58	41.45	44.2 ± 8.58
PV_{200} (%)	20.6	20.6 ± 4	18	19.8 ± 4
PV_{90} (%)	/	/	98.95	98.5 ± 1.5
PD_{100} (Gy)	/	/	119	116.4 ± 15.57
RD_{2cc} (Gy)	119.5	115 ± 24	116.75	119.4 ± 24
$RD_{0.1cc}$ (Gy)	182.4	182 ± 24	230	234.4 ± 24
RD_{10} (Gy)	123	124 ± 18.35	102.8	104.3 ± 20.45
RV_{100} (cc)	0.44	0.5 ± 0.3	0.68	0.72 ± 0.3
UD_{10} (Gy)	200	200 ± 10.13	205	201 ± 10.13
U. D_{20} (Gy)	194.5	193 ± 7.63	187	186 ± 7.63
UD_5 (Gy)	202.5	204 ± 11.6	215	211 ± 11.6
UV_{150} (cc)	0	0.01 ± 0.03	0	0.5 ± 1.5

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EXCLUSIVE BRACHYTHERAPY IN POST-OPERATIVE ENDOMETRIAL CANCER PATIENTS: CLINICAL OUTCOMES OF MONOINSTITUTIONAL EXPERIENCE

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Aims: Objectives of this study were to evaluate, overall

survival, disease-free survival and local relapse-free survival in a cohort of patients with diagnosis of endometrial cancer underwent high-dose-rate adjuvant vaginal brachytherapy (VBT)

Methods: Between September 2007 to December 2016, seventy-three patients with endometrial cancer were retrospectively analyzed. The median age was 65 years (range 35-80). Surgical treatment was performed in all patients and consisted of total hysterectomy and bilateral salpingo-oophorectomy (TH/BSO) without node dissection in 35 patients; or TH/BSO with bilateral pelvic lymph nodes dissection and lumbo-aortic lymph nodes dissection in 33 patients and 5 patients respectively. The pathological stage was defined according to the International Federation of Gynecology and Obstetrics (FIGO-2009) surgical staging system. The overall stage distribution was as follows: IA (42/73) IB (31/73). All 73 patients presented endometrioid pathological subtype. Grade 2 was the most frequent histological grade, seen in 35 patients (47.9%), whereas 30 patients(41%) presented grade 3 and 8 patients (11%) presented grade 1 The myometrial invasion (MI) >50% was present in 33 patients (45.2%). The VBT regimens were 21 Gy in 3 fractions of 7 Gy/die. Overall survival (OS), disease-free survival (DFS) and local relapse-free survival (LRFS) were evaluated.

Results: The median follow-up was 45.7 months (range 3 – 110). Mean overall survival was 41.6 mounths (range 3-110). The median DFS and LRFS was 41.06 months (range 1.07-105.73) and 15.06 months (range 4.8 – 51.16) respectively. The 5 years OS was 86.5%. Local recurrence was observed in two patients. (2.7%) Five patients (6.8%) presented distant disease (lung metastases, hepatic and lymphnodes metastases). No toxicities above grade 1 were observed. Six patients (8.2%) are died at the time of analysis: 3 patients died for intercurrent causes without evidence of disease.

Conclusions: Data support that adjuvant exclusive vaginal brachytherapy in patients with early stage endometrial cancer showed good outcomes in terms of overall survival, disease local control and local relapse free survival.

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LONG TERM OUTCOMES OF HIGH DOSE RATE BRACHYTHERAPY BOOST IN BREAST-CONSERVING SURGERY: PERIOPERATIVE VS INTRAOPERATIVE MODALITY

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Aims: To evaluate survival and outcomes of two HDR brachytherapy modality boost: perioperative (PERI) vs intraoperative (INTRA). Methods: From January 2001 to February 2005, 75 pts. with breast cancer were treated with intraoperative (29) or perioperative (46) implant consisting of 3 fractions of 350 cGy each, 6 hour apart, before or after Whole Breast Radiotherapy (50 Gy/5 weeks). To provide coverage of tumor bed implant done with afterloading catheters at the time of quadrantectomy or after the external beam, clips to mark the walls of the excision cavity, markers at the extremities of each catether plus an other marker on the apex of the implant out of the breast (skin points). All pts. underwent CT to evaluate the needles insertion that was always 3 cm at least around surgical cavity (when surgical clips available) or 3 cm around surgical scar. Implants planned with a semi-3-D technique aided by simulator, target volume determined by surgical clips and dose to the skin by the catether markers. Survival comparison with Kaplan Meier method

Results: Median follow up: 8,2 years (1-16 years). Age: median 57 (26-77). Survival comparison median 10,24 years (PERI) vs 2.74 (INTRA), P=0.95 (not significant). In PERI group 11/46 pts. had relapse or metastasis (24%) vs INTRA 8/29 (27%). The rate of relapse was similar 6.5 INTRA vs 6.8 PERI. Lymph node status of relapse or metastasis not significant (9 pts. N0 9 pts. N+). Ten years local relapse-free rate was 90 INTRA vs 89% PERI.

Conclusions: In brachytherapy boost irradiation to tumor bed, no difference in local and loco-regional recurrence, metastasis-free and overall survival observed comparing these different boost techniques.

Table 1.

PET-GTV (T+N)	
Volume (cc)	Mean 62.20 cc (Range 40.75-86.9 cc)
Median D95 (%)	97.84% (Range 95%-102.6%)
Median D5 (%)	102.79% (Range 99.6%- 104.4%)
PTV2	
Median D95 (%)	98.11% (Range 95.7%-103.4%)
PRV Spinal Cord max	Mean 43.9 Gy (Range 34.3 Gy- 47.6Gy)
PRV Brainstem max	Mean 39.8 Gy (Range 29.9Gy-58.2Gy)
Ipsilateral Parotid (mean dose)	Mean 23.2 Gy (Range 16.2Gy-24.8Gy)
Contralateral Parotid (mean dose)	Mean 23.5 Gy(Range 19.5Gy- 26.0Gy)

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ABSORBED DOSE CORRELATES WITH METABOLIC RESPONSE TO RADIOEMBOLIZATION OF LIVER METASTASES WITH RESIN 90Y-MICROSPHERES

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Aims: The aim of the present study was to investigate

possible correlation between absorbed dose and tumour response by means of a Tumour Control Probability (TCP) in liver metastases treated with radioembolization (RE) with resin 90Y-microspheres. To assess response, the analysis of parameters from FDG-PET/CT has been preferred to RECIST criteria based on CT, as often, metabolic response has been proven to anticipate morphologic response.

Methods: Patients with chemo-refractory liver metastases from solid tumours scheduled to receive RE underwent FDG-PET/CT scan before and 6 weeks after RE. 99mTc-MAA (75-111 MBq) were injected 2 weeks before RE to simulate treatment and perform provisional dosimetry based on SPECT fused to contrast CT. Response assessment was performed according to PERCIST criteria. The variations (%) of PET parameters versus basal examination were evaluated to establish Complete-Response (CR), Partial-Response (PR), Stable-Disease (SD), Progressive-Disease (PD).

Results: 22 patients and 29 lesions were suitable for analysis. Patients had hepatic lesions from colon-rectal (11), breast (7), ovary (1), endometrial (1), parotid (1) cancer, cholangiocarcinoma (1). All patients received a single treatment of RE, with a median activity of 1.7 GBq (range 0.6-2.9) of 90Y-microspheres. Median (range) tumour absorbed doses was 100 (30-443) Gy; average dose +/- standard deviation was: 129+/-100.

Metabolic response rate of lesions as assessed with PERCIST was: CR=31%; PR=28%; SD=24%; PD=17%. Two different TCP curves were obtained by probit regression when considering: i) PR or CR as endpoint1; ii) CR only as endpoint2 ($p<0.01$ in both cases). For tumour doses >170 Gy only CR were observed. TCP of 20%, 50%, 75%, 90% were obtained at: i) 51, 80, 104, 125 Gy; ii) 81, 121, 153, 183 Gy, respectively.

Conclusions: Despite the variety of primary tumours, the relatively low cohort of patients, and the implicit uncertainty of the previsional dosimetry with 99mTc-MAA, our preliminary data provided evidence of correlation between response based on PET/CT parameters and absorbed dose. These encouraging results need to be confirmed with more ample dataset and possibly differentiation depending on tumour type. Other PET/CT parameters for response such as the metabolic tumour volume, and tumour lesion glycolysis are being considered for comparison with PERCIST and possible improved correlations.

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EFFICACY AND SAFETY OF ELECTRONIC BRACHYTHERAPY FOR NONMELANOMA MALIGNANT SKIN NEOPLASMS: PRELIMINARY RESULTS OF A PROSPECTIVE PILOT TRIAL

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Aims: Surface electronic brachytherapy (EBT) is an emerging alternative radiotherapy (RT) solution to external beam electron RT and high-dose-rate radionuclide-based brachytherapy for skin cancers. It can also be used as an alternative treatment to surgery for selected patients (pts). This prospective, single-center, non-randomized, pilot trial evaluates the clinical efficacy, safety and cosmetic results of a new EBT system, named Esteya®. Preliminary results are presented. Methods: Between November 2016 and March 2017, 14 consecutive pts (mean age: 85 years, range: 55-96) with nonmelanoma malignant skin neoplasms have been enrolled and analyzed. Two pts presented primary squamous cell carcinomas (SCC) of eyelids and 42.9 % recurrent SCC of the scalp and face, 28.6 % showed recurrent basal cell carcinomas of the nose and 14.3% cutaneous lymphomas. Only lesions with a maximum diameter < 2,5 cm were treated with radiation dose of 40 Gy (5 Gy fraction, 2/week). Pts with cutaneous lymphomas received conventionally fractionated RT of 36 Gy (2 Gy fraction, 5/week). Acute toxicity has been measured according to CTCAE (Common Terminology Criteria for Adverse Events) v4.03 scales and RTOG-EORTC scales were used to assess cosmetic Results: Results: All pts underwent clinical examination and photographs during RT, 4 weeks, 8 weeks, 3 months, and 6 months after treatment. Toxicity started after the 4thfraction and worsened between the end and 6 weeks after RT. All pts presented erythema: moderate to brisk grade was scored in 71.4% cases (G2 CTCAE). Moist desquamation and crusting were shown by 2 pts, 1 patient presented moderate edema. Late toxicity was scored in 41.8 % pts: 2 pts showed slight pigmentation changes (G1 Late RTOG-EORTC) and 3 pts (25%) presented moderate telangiectasia (G2). A clinical complete response was observed in 91.7% of cases, 1 patient presented residual disease and 1 experienced marginal/in-field recurrence. Out-field recurrence was observed in 1 patient. Conclusions: Our preliminary results show that Esteya® is an effective, simple, safe, and comfortable treatment associated with good cosmetic outcomes for nonmelanoma malignant skin neoplasms. Even if a longer follow-up, a bigger sample size and more studies are needed to confirm these preliminary findings, EBT can be an alternative solution for elderly pts, for pts refusing or presenting contraindications for surgery or when surgical treatment would result in a more disfiguring outcome.

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CONCORDANCE BETWEEN PREOPERATIVE DIAGNOSIS AND SURGICAL SPECIMEN IN SINGLE DOSE IOERT FOR BREAST CANCER

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Aims: The main limitation about the use of IOERT in accelerated partial breast irradiation is the lack of histological information at the time of therapy. Our aim is to demostrate that an accurate preoperative diagnosis of a breast lesion with mammography, ultrasound, MRI and core-biopsy is essential for designing an optimal treatment algorithm in order to achieve a careful selection of patients who may benefit from electrons partial breast irradiation. The Core needle biopsy is accurate in diagnosing breast carcinoma and has a specificity of 96%–100%. CNB examination providing istological typing and biological characterization is very predictive and therefore it could replace surgical speciment (SS) in determining ER, PgR and HER2/neu status; CNB should be mandatory before an exclusive treatment to identify suitable patients.

Methods: From 2010 patients elegible for IOERT were diagnosed using core-biopsy and selected according ASTRO criteria. We examined the concordance of histological types, tumor size, hormone receptors, and human epidermal growth factor receptor 2 (HER2) status between CNB and SS in 43 cases treated from 2014 to 2016 with a single dose of 21Gy delivered to the 90% isodose.

Results: Preoperative diagnosis has high concordance with SS in the evaluation of histological types , tumor size and the molecular profile of invasive breast cancer. CNB provides an accurate evaluation of the molecular profile of invasive breast cancer, especially ER and HER2/neu status. In the present study, concordance rates between pre-operative evaluation and SS for histologicol type was 100%, tumor size was 97,7%, the concordance rate for ER PgR and HER2/neu were high.

Conclusions: The molecular profile of breast cancer is critical in the management of patients with breast carcinoma and should be considered the most important aspect in cancer treatment. Traditionally the results obtained from CNB has been considered ambiguous and not representative of the whole tumour, as the sample obtained is small and the distribution of antigens could be varied within the tumour. Our data suggest that the core-biopsy has high concordance with surgical specimen in the evaluation of the molecular profile of invasive breast cancer, so leading the CNB provide an accurate selection of the patients for favorable luminal A biology. IOERT is an attractive APBI approach and should be now considered as an alternative to EBRT for specifically well-selected and informed patients.

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VARIABILITY DURING MULTIPLE HDR BRACHYTHERAPY APPLICATION TO LOCALLY ADVANCED CERVICAL CARCINOMA.

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Aims: This study aimed at examining variability, during multiple high dose rate (HDR) intracavitary brachytherapy (ICBT) applications, as regards applicator geometry and reconstruction, tumor and organs at risk (OARs) contouring. In planning, DVH variability between BRT-HDR fractions with or without CT simulation (CTS) were analyzed as well.

Methods: Sixteen patients with locally advanced cervical cancer underwent first concurrent CHT and EBRT (DTF:45-50.4 Gy) and then HDR-ICBT fractions of 5-6 Gy at weekly intervals. Through the TPS fusion function, “surface matching”, the variation of applicator geometry was observed. This allowed a fusion of the images which showed the same structure, the intrauterine tandem (IT), in all CTSs carried out on the patient. Then the first CTS was fused with the next at the first BRT fraction. Of these fusion CT images, the distance between the tip end of the IT and the distance between the ovoids both in cranio-caudal and latero-side direction were measured. Instead of carrying out a CTS with subsequent planning in every BRT fraction, the optimization of the BRT treatment following the first fraction was given up and positions and dwell times of the radiation source in the first BRT fraction were used for the following ones. The DVHs obtained during these assumed BRT fractions were compared with the DVHs of each BRT fraction actually performed. D100 and D90, the V100 and D2cc of OARs were taken into consideration.

Results: Relevant differences, in terms of geometrical variations, were observed in each CT carried out on the patient at every BRT fraction when comparing mean values (MV) and standard deviations (SD) for every parameter. At contouring, the difference between CTV and OAR volumes in cc was remarkable. At planning, in comparing real with assumed treatment for each patient, significant variations were found also in MV and SD of D100 and D90, the V100 and D2cc of OARs.

Conclusions: The study observed a series of variables in the different phases of BRT treatment. All these data not only evidentiate the differences existing between the positioning of the applicator at different BRT fractions, at contouring of volumes and at planning DVHs, but they confirm, in quantity and quality, that it is fundamental to study target and OARs before every BRT fraction with CTS and subsequent planning.

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RECTAL DOSE EVALUATION DURING VAGINAL CUFF BRACHYTHERAPY USING RECTAL TUBE

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Aims: Rectal toxicity, both early and late, is a substantial problem in gynaecological brachytherapy (BT) , occurring in the majority of patients within the first 2 years after treatment. Strategies are needed to limit high doses to the rectal mucosa without reducing the overall target coverage. Aim of our study, following an occasional observation, is to evaluate if the rectal tube (Rtube) we use in our Institute for in vivo dosimetry (IVD) allows also a reduction of the rectal dose.

Methods: In our Institute, adjuvant vaginal BT is Image Guided (CT/MRI) with a multichannel endovaginal applicator, chosen taking into account both the comfort of the patient and the best contact of the applicator surface with the vaginal mucosa. For all patients, rectal wall IVD is performed with a dedicated Rtube (diameter: 8.3 mm) integrated with dosimeters and rigidly fixed to the endovaginal applicator. Over the time, for technical/ clinical problems, two CT scans (acquired within a time interval of 10 minutes) were obtained in 11 patients: one without and one with Rtube. Each treatment plan was generated and delivered using CT-images with Rtube in order to calculate dose to target and OARs (TPS: Oncentra BT System). Vaginal cuff, bladder, rectum and sigmoid were contoured by a single radiation oncologist and the contours were reviewed by all members of the BT team. Plan optimization was performed according to International guidelines. As CT-images with/without Rtube showed an evident displacement of rectum wall, we try to transfer the treatment plan generated on CT images without Rtube. For both plans, bladder and rectum DVHs were assessed considering the near maximum dose to 2cc of each OARs, D2cc (%). Results are reported as mean (±SD). The Wilcoxon test for pair samples was used for comparison. Differences were considered statistically significant at $p < 0.05$.

Results: Generally Rtube does not increase rectum volume. Mean target dose D90/ V90 is 98%±2/ 99%±4.2. No significant variation was found for bladder D2cc with/without Rtube: (68.7±5.9/ 68.7±4.2)% , respectively. D2cc for the rectum systematically increased in all calculated plans without Rtube: (68.9±5.7/ 86±6.7)%. Differences were found statistically significant (p=0.031).

Conclusions: These preliminary results show that the use of Rtube for in-vivo dosimetry does not affect target coverage and allows a significant reduction in dose to the rectum in terms of 2cc.

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INTRAOPERATIVE RADIOTHERAPY ELECTRON BOOST FOR PATIENTS WITH EARLY BREAST CANCER: PRELIMINARY RESULTS OF IRCCS "GIOVANNI PAOLO II" IREB PROTOCOL

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Aims: To report preliminary results of IREB (Intraoperative Radiotherapy Electron Boost) protocol adopted by IRCCS "Giovanni Paolo II". This study evaluates feasibility, tolerance and cosmetic outcomes of an intraoperative anticipated electron boost (10Gy), delivered with IORT (Intraoperative Radiotherapy) to patients with early breast cancer subjected to conservative breast surgery and subsequent EBRT(External Beam RT) (50Gy in 25 fractions).

Methods: From July 2014 to December 2016, 31patients with early breast cancer (stage I-II) were treated with IORT(DT-Total Dose 10Gy to tumor bed), using Novac 7 Accelerator; among them,26 completed IREB protocol with EBRT(DT 50Gy to whole-breast; Df-Dose per Fraction 2 Gy).All patients were older than 50 years, had invasive breast cancer,negative surgical margins,absence of multicentric disease and neoadjuvant treatments. Physical and dosimetric parameters were evaluated: UM(Monitor Units) and delivery time of intraoperative anticipated boost,Dose-Volume Histogram(DVH) of EBRT plans.Post-IORT toxicity,acute toxicity (according to the RTOG scoring system) and cosmetic outcomes were assessed for each patient. Local recurrence and metastases were also evaluated during the follow up.

Results: The mean age of the patients was 62 years; right breast were treated in 54% of them. 22 patients had CDI (ductal invasive carcinoma),2 CLI (invasive lobular) and 2 had mixed histology.25 patients had over-expressed hormonal receptor; Ki67 mean value was 19%. For IORT treatments, mean value of UM was 523,77, delivered in 41,6 sec. DVH analysis shows complete submission of EBRT plans to regular constraints for heart and lungs:mean value of V25 for heart is 3,33% (regular <10%) and V20(mean) for lung is 8,7%(<20%). Mean follow up is 12 months (15 patients): no local recurrence occurred and only the triple-negative patient has metastases. After IORT,73% of patients had not any toxicity; 8% sieroma,4% fibrosis,4% phlogosis,11% delayed healing;during EBRT, low-grade toxicity has been observed.One month later, among patients who continued follow up, 44%(10) had satisfactory cosmetic results;17% fibrosis, 9% erythema, 9% sieroma, 4% (1 patient) mastitis.

Conclusions: Intraoperative anticipated boost delivered with IORT could be considered a safe alternative

to external boost,with the benefits of reduced treatment's duration and increased patients' compliance;we need long-term results on a larger group of selected patients, without unfavourable prognostic factors.

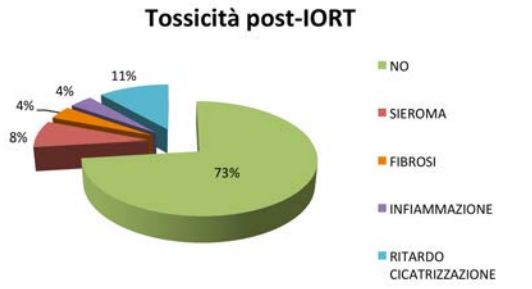

Figure 1. Risultati tossicità dopo trattamento IORT.

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SINGLE SHOT INTRAOPERATIVE RADIOTHERAPY FOR BREAST CANCER, FOLIGNO CITY HOSPITAL EXPERIENCE

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Aims: To evaluate local relapse after single shot intraoperative electron radiation therapy (IOERT) for breast cancer

Methods: Between april 2009 and may 2015 58 patients were treated with single shot IOERT at Foligno City Hospital after breast conserving surgery and sentinel node biopsy. Median age was 73 years (range 54-86). Twelve patients (20.7%) were pT1b stage, 37 pT1c (63.8%) and 9 pT2 (15.5%), all patients but 3 had negative sentinel nodes and underwent axillary dissection with no evidence of further lymph node metastases; in 2 patients sentinel node micrometastases were found but no axillary dissection was performed. Fifty patients had a ductal infiltrating carcinoma, 1 a lobular infiltrating carcinoma, 5 a mucinous infiltrating carcinoma, 1 a tubular infiltrating carcinoma and 1 a low grade ductal carcinoma in situ. Tumor grading was not known in 4 cases (6.9%), G1 in 7 cases (12.1%), G2 in 39 cases (67.2%) and G3 in 8 (13.8%). Three patients were treated for bilateral breast cancer with same histology and stage. All patients were treated with a single shot 21 Gy dose to tumor bed with an electron dedicated machine (LIAC) in the operating room. Energy and reference isodose was chosen after measuring the thickness of the target tissue and ranged from 6 (86.8%) to 8 (13.2%) MeV, reference isodose varied between 85 and 100%. Applicator diameter was chosen after measuring tumor diameter on surgical specimen, a minimum radial margin of 2 cm was given (range 50-80 mm), beveled applicators were not used. In all cases the surgeon positioned a steel/plastic shield between chest wall and target breast tissue.

Results: Three patients were lost at follow up, the remaining 55 patients had a median follow up time of 50 months (range 9-94). No one developed local recurrence, 6 patients died: 1 of metastatic disease (bones and lungs, no local recurrence), 2 of rectal cancer, 1 of anal cancer, 1 of contralateral metastatic breast cancer and 1 of non oncological disease.

Conclusions: In selected cases single shot IOERT fo breast cancer is feasible and yields a low percentage of local and distance recurrence.

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PBI WITH IORT TECHNIQUE: OUR EXPERIENCE

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Aims: The Intraoperative Radiotherapy (IORT) is a thecnique of partial breast irradiation and is considered to be exclusive treatment in a subgroup of patients who are conservatively treated and considered low risk of local recurrence. The aim of this work is to evaluate acute and late side effects and aesthetic results in patients treated with IORT.

Methods: From October 2015 to April 2017, 10 pcs aged between 51 and 77 aa were enrolled. 9 pcs have been diagnosed with infiltrating ductal carcinoma; For 1pz the diagnosis was of mucinous carcinoma.3 pcs have presented G1 cell differentiation grades and 7 pcs G2.8 pcs have been shown to be in the definitive histological examination luminal A and 2 luminal B. These latter were subsequently started at systemic therapy . All the pcs have been treated with IORT. A mobile accelerator for the operating room was used for the treatment using a miniature X-ray source of 50 Kv and 40 mA. The CTV is represented by the fabric that delimits the operating cable adapted to the source. The prescribed dose is 20 Gy at the surface of the applicator and is equivalent to BED at irradiation of about 60 Gy to 5 mm of tissue from the surface of the spherical applicator. Above that distance, the dosage should drop rapidly, respecting the surrounding tissues. The average duration of treatment was approximately 30 minutes. No adverse events occurred during the treatment. Treatment was well tolerated by patients

Results: All the pts carried out periodic inspection visits for an average 12-month follow-up. The skin toxicity evaluated according to the RTOG toxicity scale was found to be G0 and the aesthetic result satisfactory as can be seen from photographic documentation

Conclusions: IORT treatment with low energy photons selected in pcs is a safe treatment, skin toxicity is very limited and the aesthetic result is satisfactory.

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TO AVOID DOSIMETRIC UNCERTAINTIES ABOUT A POSSIBLE MOVEMENT OF THE APPLICATOR, AFTER POSITIONING, CENTERING AND EXECUTION HDR BRACHYTHERAPY IN CERVICAL CANCER

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Aims: The purpose of this report is to avoid dosimetric uncertainties about a possible movement of the applicator. Occasionally, movement patient from the couch used for the treatment in the bunker and the centering room and back , can caused dose variation of brachytherapy reference points. At our institution, this problem is not covered, because the treatment and the TC scanning are performed in the same bunker, so as to avoid any risk of applicator movement.

Methods: From genuary 2016 to april 2017, in our institute 21 women with bioptically diagnosy of local advanced cervical cancer were treated with 3 fraction HDR brachytherapy intracavitary implants after pelvic EBRT with volumetric arc therapy ± Chemiotherapy associated. Brachytherapy dose High risk CTV as per GEC-ESTRO guidelines delivered 21 Gy in 3 fractions (700cGy for single fraction), in about 13 days overall. ICRU- GEC-ESTRO 89 (rewiew 2016) prescription points (A, B, P, bladder, and rectum) were used.

Figure 1.

Results: All patients have received spinal anesthesia, so no sedation , presence of anesthetist and nurse in the room during the entire planning time for monitoring parameters and discharge on the same day. At each implantation, all patients had a urinary catheter in situ and received bowel enema before undergoing planning CT simulation. Medical and physical planning time has had maximum duration of 1 hour, currently in phase of acceleration to get to less than 30 minutes. Each brachytherapy insertion had a different plan generated prior to treatment delivery used Oncentra Brachy treatment planning. Dose volume histogram was generated and treated volume to the prescription dose was recorded for each fraction, assessing the importance of a reduction in the size of the ovoid during the treatment cycle, depending on response to brachytherapy. All cases (BT treatment) were performed in the same bunker of TC scanning so as to avoid any risk of applicator movement and what surely implies greater comfort for patients. There were no acute side effects (G0 RTOG scale), longer times to exclude late toxicity.

Conclusions: In conclusion, the possibility of using a single bunker to tc scanning and execution HDR brachytherapy treatment allows us to prevent unintentional movement of the applicators and greater comfort for the patient.

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RADICAL HIGH DOSE RATE BRACHYTHERAPY FOR RECURRENT BASAL CELL CARCINOMA OF THE HAND: CASE REPORT

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Aims: Non-melanoma skin cancer consists of two major histologic subtypes, basal cell carcinoma (BCC) and squamous cell carcinoma. Most BCCs occur in the head and neck region, followed by trunk and extremities. Although BCC-related mortality is low, both tumour growth and treatment can cause considerable functional and cosmetic morbidity. Aim of our study is to demonstrate that High-Dose-Rate Brachytherapy (HDR-BRT) allows minimal irradiation of normal tissue and ensures the best possible chance of rapid healing and the smallest chance of late radiation morbidity.

Methods: In January 2014, a 58 year old female patient was reported to our Department, with diagnosis of recurrent ulcerative lesion over left ring finger since seven years, already treated with multiple drugs. The lesion was biopsied and diagnosed as BCC. The patient refused surgical amputation and has been candidate for HDR-BRT. For CT scan simulation, a mould is constructed to allow precise placement of the radioactive sources in relation to the tumour: impression of finger was made with alginate material all around the circumference of ring finger inside plastic cylinder. On the outer surface of the cylinder have been positioned catheters to be used for delivering radiation, bolus 8 cm thickness was overlapped to the plastic cylinder. The number (15) and location of catheters were determined by the radiation oncologist and physicist. The treatment volume was defined by a combination of clinical examination and MRI hand study. The dose given was

4000 cGy on the skin surface in 20 fractions, 2 fractions a day with a minimum interval of 6 hours.

Results: Patient had an acute reaction to HDR-BRT, consisting of desquamation, crusting and cutaneous erythema grade 2 (RTOG toxicity scale). Late side-effects, such as telangectasia and skin atrophy were grade 1 sec. RTOG. There was no deficit in the range of movements in the treated finger; similarly, fine touch sensitivity was not shown to be significantly different between both the hands. Three years after the end of treatment, there are no evidence of recurrence.

Conclusions: From this experience, we conclude that HDR-BRT, as a treatment for BCC of the hand, produces local tumour control; morbidity is low, cosmesis and hand function after treatment are excellent.

Figure 1.

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DOES VAGINAL BRACHYTHERAPY INCREASE ACUTE TOXICITY IN PATIENTS TREATED WITH PRIOR PELVIC NODAL EXTERNAL BEAM RADIOTHERAPY?

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Aims: Adjuvant treatment in early stage endometrial cancer usually consists of vaginal brachytherapy (VB), pelvic external beam radiation therapy (EBRT), or a combination of the two techniques. We compared toxicity outcomes across these various radiation treatment modalities.

Methods: Between October 2015 and May 2017, we retrospectively analyzed 20 patients with endometrial cancer who underwent hysterectomy with or without lymphadenectomy and adjuvant High Dose Rate (HDR)-vaginal BT +/- adjuvant EBRT. The total dose prescription for the EBRT was 45 Gy (25 fractions of 180 cGy/die), and the dose of HDR-vaginal BT was 15 Gy in 3 fractions (every other day) after EBRT. If the patient had not been submitted to EBRT the dose of HDR-vaginal BT was 21 Gy in 3 fractions (every other day). Acute toxicities were evaluated according to CTCAE vs 4.02.

Results: Most patients were treated with combination EBRT + VB (55%) compared with VB (45%). The proportion of patients who received EBRT was higher for those who did not have a lymph node dissection or with fewer dissected lymph nodes. In the patients treated with EBRT, grade 2 acute toxicity was observed in 3 patients (27 %), and it was diarrhea. In the patients treated with VB, toxicities greater than grade 1 were not observed. No grade 3 or higher acute toxicities were observed.

Conclusions: Our experience confirms that VB treatment in early stage endometrial cancer patients has lower toxicity than pelvic external beam radiation therapy, with the benefit of performing a shorter overall treatment time.

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STEREOTACTIC BODY RADIOTHERAPY: COMPARISON BETWEEN TWO IGRT SYSTEMS

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Aims: To compare the residual setup errors measured with ExacTrac X-ray 6 degree-of-freedom (6D) and kilo-voltage cone-beam computed tomography (CBCT) for patients receiving stereotactic body radiotherapy (SBRT) at Fondazione IOM in collaboration with REM Radioterapia.

Methods: At our center, on a Novalis STx treatment unit, from January to May 2017, 23 patients with extracranial tumors were treated with SBRT for a total of 30 lesions (5 patients having more than one lesion) and 83 treatment sessions. Prescribing doses ranged from 24 to 60 Gy in 3 fractions or 20 Gy in a single fraction and planning techniques were dynamic conformal arc therapy or hybrid intensity modulated radiotherapy, with non-coplanar fields. All patients were initially located using personalized immobilization systems and setup corrections were determined and corrected with the ExacTrac system by means of registrations of ExacTrac X-ray images with the corresponding digitally reconstructed radiographs using the ExacTrac 6D fusion. At the end of each treatment session, with the couch at 0°, the residual setup error was determined by means of registrations of CBCT images with the planning CT using online 3D fusion and for each of the 83 sessions, displacements were evaluated to analyze the residual setup errors.

Results: A modest difference in residual setup errors was found between ExacTrac system and CBCT. The average of the observed residual displacements for the three directions of the space, in absolute value, was 1.5

mm in vertical and in lateral directions, 1.2 mm in longitudinal direction.

Conclusions: This work showed the good agreement on the setup accuracy between ExacTrac X-Ray 6D and CBCT for patients treated with SBRT. The two systems present comparable precision, but ExacTrac offers additional benefits such the ability to quantify all rotational errors, fastest automated positioning in 6D even for non-coplanar fields and furthermore smaller doses, representing a valid alternative to CBCT with complementary and additional informations in image-guided stereotactic radiotherapy.

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MARGIN NEEDED TO COMPENSATE PROSTATE AND SEMINAL VESICLES MOTION IN PROSTATE CANCER IGRT

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Aims: seminal vesicles (SVs) motion results in deformation and tilt and cannot be compensated with a simple shift. For this reason an adaptive off-line re-planning IGRT protocol (REPLANNING) to define ITV was routinely used in our Department. The aim of this study was to evaluate the residual motion of SVs and prostate CTV after matching CBCT on bone structures. We also investigated the possibility of using a standard anisotropic CTV-PTV margin in order to avoid extra time needed for re-planning.

Patients and Methods: We analyzed prostate and SV movement in 62 patients treated with REPLANNING where the first five CBCTs were used to create an adapted ITV (re-PTV) to compensate for organ motion. The distance between CTV and re-PTV, was measured as maximum shift on the planning CT, in all the directions (anterior, posterior, left, right, inferior, superior), for prostate and SV, separately. We tested anisotropy of prostate and SV motion using one-way ANOVA and post hoc analysis with Bonferroni correction.

Results: Descriptive statistics of prostate and SV motion is reported in table 1 in terms of median, range, and 95th percentile. SVs showed different and statistically significant greater mobility than the prostate in anterior (up to 2.8 cm), posterior (up to 1.9 cm) and caudal (up to 2.7 cm) directions. SVs even had statistically significant greater mobility than the prostate in anterior, posterior and caudal directions (corrected p-value<0.001) with a difference in mean value of 0.36±0.09 cm, 0.23±0.06 cm and 0.38±0.08 cm, respectively. Anisotropic motion effect was found with one-way ANOVA for both prostate and SV (p-value<0.001). With post hoc analysis, for SVs, a greater motion in the anterior direction respect to lateral and cranio-caudal direction was found (corrected p-value<0.05) , with an average difference in mean value of 0.40±0.03 cm.

Conclusions: The adaptive off-line re-planning IGRT protocol remains our best choice to define a personalized ITV. In fact a margin larger than 1 cm (in almost all directions) and up to 2.5 cm (in anterior direction for SVs), which is needed to cover 95% of cases, resulted too large to be applied to all patients.

Table 1.

	Direction	95th Percentile (cm)	Median (cm)	Range (cm)
Prostate	Anterior	1.10	0.48	0 - 1.3
	Posterior	1.10	0.56	0 - 1.8
	Cranial	1.6	0.5	0 - 1.7
	Caudal	0.76	0.1	0 - 1
	Right	0.78	0.3	0 - 1
	Left	0.98	0.4	0 – 1
Seminal vesicles	Anterior	2.49	0.8	0 - 2.8
	Posterior	1.50	0.9	0 - 1.9
	Cranial	0.82	0.49	0 - 0.81
	Caudal	1.92	0.5	0 - 2.7
	Right	1.2	0.35	0 - 1.6
	Left	1.24	0.5	0 - 2

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EVALUATION OF THE IMPACT OF INTRA-FRACTION ORGAN MOTION ON THE DOSIMETRIC COVERAGE OF ITV BY THE ANALYSIS OF A PRELIMINARY DATA SET OF 200 CBCT IMAGES ACQUIRED IN 15 PATIENTS (PTS) TREATED ACCORDING TO A SBRT PROTOCOL FOR PRIMARY AND METASTATIC THORACIC TUMORS

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Aims: To evaluate the impact of intra-fraction organ motion on the dosimetric coverage of ITV analyzing 200 CBCT images acquired in 15 pts treated with SBRT for primary and metastatic thoracic tumors.

Methods: Between 2013 and 2017, 15 pts, 10 males and 5 females, median age 76 yrs (range: 35-89 yrs) received SBRT for primary or metastatic thoracic tumors: 12 primary lung cancer, 2 mediastinal lymph-node metastasis, 1 lung metastasis. All pts had a 4D-CT high-resolution simulation in 10 respiratory phases for ITV definition. Median ITV-PTV margins were 5 mm. All pts received IG-IMRT with 2 modulated arcs. Doses were prescribed according to ICRU 83 (median PTV dose) and 99% of PTV had to be encompassed by 90% isodose. Total doses: 20 Gy x 3 in 1 pt, 12 Gy x 4 in 3 pts, 10 Gy x 5 in 5 pts, 7.5 Gy x 8 in 1 pt, 6 Gy x 8 in 5 pts. Before CBCT acquisition 2 planar (AP-LL) set-up EPID images were taken for preliminary set-up analysis. In absence of rotations, CBCT images (N=88) were acquired for on-line set-up corrections applied before

each 1st SBRT treatment arc. Intra-fraction motion was evaluated by CBCT images acquired before starting and at the end of the 2nd treatment arc. Structure matching on CBCT was automatically done first on bone, then on soft tissue. On-line set-up corrections between 1st and 2nd arc were applied for errors≥ 3mm. For all pts, mean differences between planned and shifted ITV position along the 3 spatial axes (CC, AP, LL) were calculated on 112 CBCT images: 74 taken between 1st and 2nd arc, 38 at the end of 2nd arc. For each pt, isodose distribution was recalculated on the TPS after correction of the isocenter position of the 2 arcs applying the mean differences found. Finally, differences in ITV median dose, V90, V95, and D98 were calculated.

Results: Mean ITV displacements after the 1st arc were -0.7 mm±1.4 mm, -0.4 mm±1.3 mm, 0.0 mm±1.0 mm for CC, AP and LL directions, respectively; at the end of 2nd arc were -0.1 mm±1.3 mm, -0.6 mm±1.2 mm, 0.1 mm±1.1 mm. Differences between planned and delivered ITV median dose ranged from +0.6% to -1.8%; V90≥99.8%, V95: 86.7%-100%; D98≥ 92.7%.

Conclusions: Our analysis of 200 CBCT in 15 pts, aimed at evaluating intra-fraction organ motion during VMAT SBRT of thoracic targets, shows that, with ITV-PTV margins of 5 mm, ITV dosimetric coverage is minimally influenced by intra-fraction ITV displacement, provided that on-line corrections are applied before each treatment arc.

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DEFORMABLE REGISTRATION AND DOSE WARPING OF RECTUM IN PROSTATE CANCER PATIENTS TREATED WITH MODERATELY HYPOFRACTIONATED RADIOTHERAPY DEVELOPING LATE RECTAL TOXICITY ≥ G3 (CTCAE).

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Aims: To evaluate the impact of dosimetric uncertainties on late rectal toxicity developing in prostate cancer (PC) patients (pts) treated with hypofractionated RT.

Materials and Methods: We analyzed the plan of 9 pts treated for PC with hypofractionated Intensity-Modulated Image-guided RT (IGRT) with Tomotherapy that showed late rectal toxicity≥ grade G3, according to CTCAE scale. All patients but one were treated with simultaneous integrated boost (SIB) with following doses: 70Gy to 8pts and 73.6Gy to 1patient on prostate, 58.8Gy to 4pts and 60Gy on seminal vesicles and 50.4Gy to 7pts on pelvic nodes in 28 fractions. Eight pts received hormonal therapy before and during the RT. Six pts underwent abdominal surgery before RT. Two pts had diabetes. Median age was 68 years. Pts were classified (ISUP2014) into: 1pts G2, 2pts G3, 5pts G4 and 1patient G5. An automatic daily re-contouring of rectum, rigid/deformable registrations and dose warping was carried out to simulate dose and volume variations during therapy. Support vector machine, K-means clustering algorithms were used to create an unsupervised predictive tool to detect incorrect setup and/or morphological changes as consequence of inadequate patient preparation, supporting clinical decision-making.

Results: All pts showed late rectal toxicity between 9 and 37 months after the end of RT. Eight pts showed late rectal bleeding G3 while 1patient G4. Meaning results for all pts: the rectum has a volume (V) of 77.7±36.9cc and dose (D) of 40.5±5.5Gy. For volumetric and dosimetric evaluations during the therapy, a normalization was carried out considering the values of V and D of the first day the 100% and reporting the gradual divergences during the treatment such as a fraction of this percentage. 50% of pts analyzed in this study shown an abnormal V trend of the rectum with an average value of 182%; an overfilling of the rectum seems to be systematic. 78% of pts shown a mean increment of 2.6% of the received average dose.

Conclusions: By combining daily IGRT images with rigid/deformable registration and dose warping, it is possible to apply a machine learning approach to the clinical setting obtaining useful information for a decision regarding an individualized adaptive strategy. From this preliminary study focused on rectum, it seems to be a correlation between toxicity and volumetric/dosimetric variations during the treatment.

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ASSESSMENT OF A ROBOTIC COUCH (PROTURA™) IN CBCT IMAGE-GUIDED STEREOTACTIC RADIOSURGERY FOR BRAIN METASTASES: PRELIMINARY RESULTS

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Aims: To evaluate the spatial displacement patient positioning with a 6 degree of freedom (6DoF) couch in CBCT image-guided stereotactic radiosurgery (SRS) for brain metastases (BM).

Methods: A total 82 analyzable setup cases for brain SRS using 6DoF robotic couch (Protura CIVCO Medical Solutions) were evaluated. Patient was immobilized with a thermoplastic mask that covers head. CBCT was acquired and registered to the reference CT imaging by OBI (Varian Medical System) to improve the setup accuracy. CBCT image registration was based on clinical practice bony matching, by applying a rigid 3D translation. After 3D translation step, a rotational adjustment was performed automatically by OBI system. This adjustment was made by using the 6DoF robotic couch and validated by followingclinical bone matching. The resulting translational and rotational

positioning shifts were analyzed by using the Euler formalism. A paired Student t-test ($p<0.05$) was performed to evaluate differences between 3DoF and 6DoF setup correction Methods:

Results: For linear movements in 3D registration, the mean lateral, longitudinal, vertical positioning shifts were (2.4±2.0), (1.3±1.6) and (1.5±2.7) mm, respectively. In 6DoF correction, we observed no statistically significant difference between 3D rigid and robotic registration ($p=0.36$) due to too small angular movements carried out by the couch to correct setup errors. In fact, the mean angular shifts were (0.6±0.8)°, (-0.1±1.1)° and (0.4±1.0)° for pitch, roll and yaw rotations respectively. Maximum angular shift was 2.0° both for pitch and roll; 3.0° for yaw. For every cases, displacement 6DoF vector was obtained and compared with the 3DoF one: no significant difference was observed (4.4±2.5 mm vs 4.3±2.4 mm). Moreover we considered 53 cases with a single BM (diameter <40 mm) and we evaluated the residual setup errors arising if no rotation was applied: the mean value of the considered group was (0.2±0.1) mm, with 0.6 mm maximum value. The analysis for patients with multiple BM is ongoing.

Conclusions: Setup errors are in the same range as those reporting in literature. In our study, maybe due to lesions size and shape of BM, no significant difference between 3DoF and 6DoF was found. Further analysis are ongoing to evaluate the dosimetric relevance of positioning errors and 6 DoF correction relevance in BM SRS. In summary, the robotic coach permitted a full correction of setup inaccuracies in 54 of 82 cases (66%) and a partial correction in the remaining 28 cases (34%).

P272

FRAMELESS, SURFACE IMAGE-GUIDED RADIOSURGERY FOR THE TREATMENT OF BRAIN METASTASES

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Aims: The aim of the present study is to describe the use of a frameless surface imaging-guided radiosurgery (SIG-RS) technique to treat brain metastases in combination with cone beam-CT (CB-CT).

Methods: We prospectively analysed 62 consecutive patients (pts) with brain metastases treated with SIG-RS at our institution. Patients underwent MRI and non-contrast simulation CT (1 mm axial slice intervals) with a customized open-face thermoplastic mask. Both MRI and CT were co-registered using a rigid auto-registration tool on treatment planning system. The gross tumor volume (GTV) was delineated based on MRI findings. The planning target volume (PTV) was then generated by adding a 1.5 mm margin to the GTV. Radiation dose prescription to the 80% isodose ranged from 18 to 24 Gy in a single fraction (47 pts) and 24 Gy in 3 fractions (15 pts). The DICOM objects RTSTRUCT and RTPLAN containing the isocentre coordinates and the CT body surface were exported from the TPS to the AlignRT system. The AlignRT surface imaging system was used for patient initial set-up and for monitoring the position during treatment. The initial set-up was confirmed with a CB-CT prior to treatment. The isocenter displacements along the main axes detected by the two modalities were analysed to evaluate the level of agreement (LOA) between the two methods by means of a Bland-Altman analysis.

Results: A total of 92 treatment procedures were collected. Shifts calculated based on CBCT after the initial setup with AlignRT were 0.5 ± 1.1 mm, 0.7 ± 1.3 and 0.0 ± 1.3 mm in the lateral (LL), anterior-posterior (AP), and superior-inferior (SI) directions, respectively. The LOA intervals at the level of 95% between the AlignRT initial setup and the CB-CT detected errors resulted respectively [-2.2 mm, 2.7 mm], [-1.8 mm,3.2 mm] and [-2.5 mm, 2.5mm] in the lateral, anterior-posterior (AP), and superior-inferior (SI) directions. The residual shifts registered during the treatment by means of the surface monitoring function provided by Align RT were less than the threshold of 1.5 mm in the AP direction and less than 1 mm in the other directions.

Conclusions: The results obtained show that the use of the AlignRT for patient set-up is a safe and accurate. The mean discrepancy compared to CB-CT is millimetric with a maximum LOA of 3.2 mm in the AP direction. SIG-RS may help to ensure patient set-up before RS delivery in combination with CB-CT and to verify the correct position throughout the treatment in case of multiple fractions.

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EXTREMELY HYPOFRACTIONATED RADIOTHERAPY USING BEACON TRANSPONDERS IN INTERMEDIATE-RISK PROSTATE CANCER: PRELIMINARY RESULTS OF TOXICITY AND EFFICACY

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Aims: In the last decades, an improved diagnostic accuracy has led to an increased incidence of early stage prostate cancer (PC). The traditional radiotherapy lasting 7-8 weeks could be considered an overtreatment. We designed a study with a short course radiotherapy. We report preliminary results on feasibility and early side effects of a protocol using a hypo-fractionated SBRT delivered with Volumetric Modulated Arc Therapy (VMAT) with Flattening Filter Free (FFF)

beams and gated by beacon transponders

Methods: Patients with intermediate disease, good urinary performance (IPSS≤ 7) were enrolled in this prospective study study. Patients were first submitted to pelvic MRI. 3 beacons transponders were positioned transrectally within the prostate parenchyma by an urologist. Simulation CT-scan was performed 7-10 days after. MR images were registered with those of simulation CT in order to better define prostate parenchyma and organs at risk. A SBRT was prescribed, with a total dose of 38 Gy delivered in 4 fractions, every other day. The beacon transponders placed in the prostate emit a non-ionizing electromagnetic signal that is tracked in real time by a GPS system, in order to guide treatment beams. Toxicity was registered according to CTCAE v4.0

Results: Acute Toxicities were as follow: 3 patients (12%) presented G1 proctitis. Genito-urinary toxicity was observed in 52% of patients (n=15): in particular, 10 patients had G1 cystitis (34%) with 5 of these presenting even G1 increased urinary frequency (17%), G2 cystitis was observed in 5 patients (17%) with a G2 urinary frequency observed in two of these patients (7%); in only one patient a G2 urinary retention was observed and it was treated with transient catheterization and oral and rectal medications. No acute gastrointestinal ≥ G2 or genito-urinary ≥ G3 toxicity was found. No other toxicities were observed. At a median follow-up of 15 months (range 6-36, calculated from the time of diagnosis), only one patient presented an outfield relapse of disease, that was treated with androgen deprivation therapy (ADT). No other biochemical recurrences or disease progressions were observed

Conclusions: According to our results, this treatment appears clinically feasible with a tolerable toxicity profile and encouraging results in terms of disease control. Longer term evaluation are required to assess ultimate efficacy and late toxicity rates.

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A MONO INSTITUTIONAL REPORT ON IMAGE GUIDED RADIOTHERAPY FOR PROSTATE CANCER WITH DAILY CONE BEAM CT (CBCT): ACUTE TOXICITY AND SETUP ERRORS ANALYSIS

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Aims: The aim of this study was to evaluate the acute toxicity profiles of a moderate hypofractionated regimen with daily Image Guidance in prostate radiotherapy and the feasibility to reduce the PTV margin.

Methods: 23 patients treated in 2016 were included in this study: 7 low risk, 12 intermediate risk and 4 high risk. The average age was 73 years. Patients received a dose of 70,2Gy in 27 fractions using 3DCRT (39.1%), IMRT (39.1%) and VMAT (21.8%). All patients were treated in supine head first position using external immobilization, including knee and feet rest. Patients received dietary advice to minimize rectal distension and satisfactory bladder filling. The acute genitourinary (GU) and gastrointestinal (GI) toxicities were recorded according to RTOG/EORTC acute radiation morbidity scoring criteria. PTV was defined by adding 1cm margin around the CTV, except posteriorly at the rectum where 0.6cm was used. 729 daily CBCT imaging with online correction were analyzed. Analysis of the displacement along the three major axis was obtained by the XVI system respecting the isocenter position, using a clip box and mutual information algorithm. Online corrections were applied prior to treatment for every fraction in case the error was >0.5cm.

Results: The average number of cone beams per fraction is 1.12. The 35% of the patients was taken off the bed because of insufficient bladder or rectal preparation, corresponding to the 3% of all the fractions. The mean overall errors of all directions are 0.4mm longitudinal, 0.8mm lateral and 0.4 vertical. In 43% of the fractions the couch was moved to correct the position. The average 3D vector length was 5.7mm before the correction and 2.7mm after.(Tab) The displacements are within the currently PTV used margins, even in the absence of any correction. At the end of treatment acute toxicities were recorded for the GU (G0, 13/23 [56.5 %]; G1, 7/23 [30.5%]; G2, 3/23 [13 %]) and the GI (G0, 19/23 [83%]; G1, 3/23 [13%]; G2, 1/23 [4%]). At three months only 3 patients showed Grade 1 GI toxicity [13%] and 5 patients showed Grade 1 GU toxicity [22%]. Only one patient at three months showed Grade 2 GU toxicity [4%]. No G3 or G4 acute toxicity has been reported in our series.

Conclusions: The use of daily online IGRT with CBCT allows reduction in the CTV to PTV margin to be achieved safely and is beneficial in term of predicted acute GU and GI toxicity. This alludes the possibility of dose escalation.

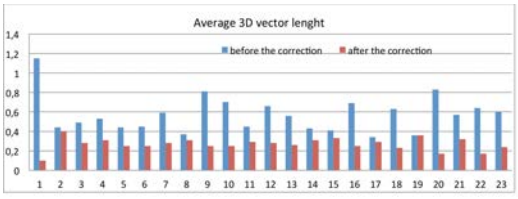

Figure 1.

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4D GATED IMAGING IN EXTERNAL RADIOTHERAPY, FROM PLANNING TO TREATMENT VERIFICATION AND DELIVERY: PHYSICAL AND CLINICAL ASPECTS

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Aims: 4D gated imaging is very useful during the treatment planning in order to identify the Internal Target Volume (ITV) of the Gross Tumour Volume (GTV) during respiratory excursions. IGRT allows daily verification of margins and set-up. 4D-IGRT has been recently implemented also for treatment verification. The aim of the present work is to analyse 3 features of a 4D CT cone beam (CTCB) system for patient positioning: image quality, dose to patient, consistence of GTV - ITV margin from Planning Multislice CT (MSCT) to IGRT CTCB.

Methods: Two XVI systems with SymmetryTM software installed on two Elekta SynergyTM accelerators were used. We used an independent software (Velocity – Varian Medical Systems) to perform image registration of the 10 single phases CTCB with the MSCT. We also used a set of TLD inserted in an Alderson Rando phantom to measure equivalent dose due to the imaging. 10 patients with lung lesions were studied. 29 fractions were considered and 290 rigid image registration were obtained.

Results: The equivalent dose due to each 4D MSCT was approximately 2,5 times higher than that due to 3D-MSCT.CBCT dose determinations are mixed up due to a change in FOV dimension in 4D modality (small) as compared to 3D (medium) and to a different gantry rotation range. 4D/3D dose ratio is nearly 2 in the isocenter region, while on the surface regions is varying from 0,6 (dorsum) to 2 (laterally) up to 4,5 (anterior body surface).

The range of tumor motion measured with CBCT was bigger (at least in one fraction) than that resulting from MSCT (in 3/9 patients in l-l direction; in 4/ 9 in c-c direction and in 7/9 in the A-P direction).

Conclusions: The 4D-CTCB system allows a daily based ITV definition. In 1/3 of the analysed fractions the ITV margin that would have been defined with the 4DCTCB would have been bigger than the planned one. In every case the daily ITV was within the defined PTV (ITV- PTV margin is 6 mm in our Department). Therefore if a ITV-PTV margin reduction is desired, the use of 4D matching is a useful tool. Dose delivered with a 4DCTB is generally higher than with 3D. The use of 4D-CTCB has therefore to be possibly personalized; e.g., for stereotactic treatments the excess dose due to the 4D imaging can be neglected; for normo-fractionated treatments it might be envisaged to use 4D-CTCB less frequently, possibly according to the variations of the effective tumor motion range observed in the first treatment sessions.

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ROLE OF FDG-PET/CT METABOLIC FEATURES AS PROGNOSTIC AND PREDICTIVE FACTORS IN LUNG PRIMARY OR SECONDARY TUMORS UNDERGOING STEREOTACTIC RADIOTHERAPY (SBRT)

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Aims: To evaluate the prognostic impact and predictive role of the maximum standardized uptake value (SUV max), the metabolic tumor volume (MTV), the total lesion glycolysis (TLG) and SUV max lesion/SUVmax liver (rPET) and their correlation with local control, overall survival (OS) and disease-free survival (DFS) in patients treated by stereotactic body radiation therapy (SBRT) for primitive or secondary lung tumors undergoing pretreatment F-FDG PET/CT imaging

Methods: Between September 2009 to December 2016, 70 patients with 85 medically inoperable pulmonary lesions were treated with SBRT and underwent a F-FDG PET/CT before the treatment. Median age was 73 yrs. Twenty-nine lesions were primitive lung cancer while 55 were lung metastasis and 1 lesion was unknown. SBRT schedules were 60/55/50 Gy in 5 fractions or 54 Gy in 3 fractions. The effects of clinicopathological factors including primary tumor SUV-max, MTV , TLG and rPET on OS, DFS and local control (LC) were evaluated. Kaplan–Meier survival curves were generated and compared with the log-rank test.

Results: With a median follow-up of 26 months, the median OS and PFS were 39.7 and 30.1 months, respectively. The 12- and 24-months OS were 94% and 76%, respectively , with a 12- and 24-months PFS of 81% and 60%, respectively. On univariate analysis SUV max of tumor, with a cut-off of 10, showed a mild correlation with OS, even if statistical significance has not been achieved (p=0.611). Multivariate Cox analysis showed that non analysed parameters were related to OS [(SUVmaX p: 0.446); TLG (p: 0.294); MTV (p:0.568)] and PFS [(SUVmax p: 0.648); TLG (p: 0.414); MTV (p: 0.981)]. Wilcoxon test showed that no correlation was observed between SUVmax (p: 0.6988), MTV (p: 0.6761), TLG (p: 0.8495), rPET (p: 0.8417) and local control.

Conclusions: The prognostic value of SUVmax and other PET related factors in patients with lung lesions remains controversial. Our study not reveal relationshi-

ps between PET parameters and specific clinical outcomes, probably due to smaller sample. Anyhow the PET parameters will be of use in evaluating the aggressiveness of tumors; this is especially important in patients with lung cancer treated with SBRT, as pathologic information, a robust biomarker of tumors, is limited in SBRT. It is expected that there will be more investigations of the correlation between PET imaging findings and outcome.

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EVALUATION OF INTER-FRACTION SET-UP ERROR DURING VMAT-IGRT TREATMENT OF PROSTATE CANCER

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Aims: The objectives of this study were to obtain indication about our set-up errors related to the frequency of CBCT (daily vs. 5 CBCT vs. 10 CBCT) and to assess whether the CTV-PTV margin we use is safe on the basis of the positioning errors.

Methods: From January 2016 to December 2016, at our Department of Radiotherapy, 24 patients underwent radical radiotherapy for prostate cancer, with daily CBCT, for a total of 866 computed tomography studies. At CT simulation patients were positioned supine on the couch with knee-ankle immobilization Combifix system. The CTV correspond to GTV and includes whole prostate from the apex to the base and the seminal vesicle. The PTV margin was calculated from CTV 10 mm isotropically except for a 5 mm posteriorly. A VMAT plan was created for each patient based on PTV using Monaco TPS System with a single arc. Prescribed doses were 76 Gy/38 fr. for 20 pts, 78 Gy/39 fr. for 2 pts and 70.20 Gy/26 fr. for 2 pts; beam energy was 6 MV. Before each fraction, patients were aligned based on 3 pelvic tattoos on the skin with a system of wall-mounted alignment lasers. The treatment was done by an Elekta Linear Accelerator equipped with Cone Beam CT (CBCT) and a motorized bed (Hexapod) with six degrees of freedom, 3 translations and 3 rotations, the latter with a tolerance range up to a maximum 2.9 degrees.

Results: 866 CBCT scans were evaluated. For translations and for rotations we calculated the population standard deviation (Σ) (average systematic value "inter-patient") and the random population standard deviation (σ) (deviation standard variability about repeated measures of each patient). There's no statistically difference for systematic error between daily, 5 scans or 10 scans We found instead statistically difference for the random error just between daily CBCT and 5 scans for translations only, in AP and SI direction. With Van Herk et al. model [2.5Σ+0.7σ] we calculated CTV-PTV margin (cm) necessary to guarantee the CTV inclusion into 95% isodose for 90% of patients. (Table1).

Conclusions: This retrospective study of the inter-fraction set-up error using CBCT data shows that a smaller number of imaging provides adequate information to predict the range of inter-fraction set-up error on following days without daily imaging. On the basis of van Herk et al. model we needs to revalue our CTV-PTV margins.

Table 1. PTV Margin expansion compared with systematic and random error (cm)

	AP	SI	L
Σ	0,21	0,20	0,24
σ	0,07	0,05	0,05
Security margin	0,57	0,54	0,64
CTV-PTV margin	1 A; 0.5 P	1	1

AP antero-posterior; SI: super-inferior; L: lateral; Σ: population standard deviation; σ: random population standard deviation

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PRELIMINARY RESULTS OF USE THE HEXAPOD EVO RT SYSTEM FOR AN ART (ADVANCED RADIATION THERAPY): OUR EXPERIENCE

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Aims: The accuracy in the delivery of radiation therapy is subordinate a the patient positioning and organ motion. The HexaPOD evo RT System is Elekta's advanced robotic patient positioning platform providing six degrees of positioning freedom. The aim of this work is to evaluate the improvement clinical workflow and to realize a realy adaptive-radiation therapy

Methods: HexaPOD evo RT System is a robotic patient positioning system to correct for any misalignments detected by X-ray volume imaging (XVI). From February to May 2017 we evaluated the set-up of 50 pts using IGRT cone beam CT and HexaPod system; the anatomical districts studied were: 30 pts male pelvis, 7 pts female pelvis, 8 pts abdominal region and 5 pts thoracic region. The set up control was performed daily. The rotation values found were on average 4.5 degrees in the pelvic area and 3 degrees in the thoracic abdominal. The iGUIDE software automatically moves the HexaPOD evo RT Couchtop to the corrected isocenter position as defined by the XVI system. On all pts the checks were carried out online and corrections were made before the treatment. The margins that are used in the definition of PTV aim to correct system definite errors and random or set up errors. Through the use of HexaPod we have reduced these uncertainties and through on-line verifications and corrections it has always been possible to bring the patient-couch system back to the isocenter and thus make a true adaptive radiation therapy.

Results: We observed that in all patients the use of HexaPod did not increase the duration of the single

treatment session and the corrections made in the six sizes allowed to minimize the uncertainties arising from set up errors by providing 3D volume imaging at the time of treatment, highlighting any positional discrepancies before treatment begins.

Conclusions: The use of HexaPod has greatly reduced random and set up errors. This will be followed by a study to reduce the margins used in the expansion from CTV to PTV and to limit the dose as much as possible to the OARs especially in VMAT or stereotactic treatments, where the escalation dose path is currently limited by the involvement of the structures healthy adjacent to the target.

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THE ROLE OF OSMS IN INTERFRACTION MOVEMENTS, A SINGLE INSTITUTION EXPERIENCE

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Aims: To determine patients' movements using modified-mask stereotactic radiotherapy performed by volumetric arc therapy (RapidARC) with Optical Surface Monitoring System (OSMS).

Methods: AlignRT® is a laser scanner system based on three cameras which is able to reconstruct body surface details thus allowing to track regions of interest of patients. This feature enables the system to assess translational (Lateral, Longitudinal, Vertical) and rotational (Rotation, Pitch, Roll) deviations identified as Real Time Deltas (RTDs). Initial set-up was performed in all patients before each treatment by orthogonal KV images followed by Cone Beam Computed Tomography (CBCT); subsequently an OSMS reference surface was captured delineating the portion of face not covered by the modified-mask. The reference surface was then used to track patients' movements during the delivery. RTD were recorded about every 0,5 seconds to monitor translational and rotational deviations. A final CBCT after the completion of the delivery was performed as a further confirm of the RTDs recorded.

Results: In our preliminary analysis we focused on differences between the initial CBCT and the range of values registered by the OSMS. WE observed 33 fractions of 8 treatment plans delivered by Edge® linear accelerator (Varian, Palo Alto, CA). The average change in position from reference captured treatment was respectly for CBCT : x (Lat.) = 0,0003 mm, y (Long.) 0,0066 mm and z (Vrt.) = 0,0084 mm with magnitude of 0,01 mm, Rot = - 0,0181 deg, Pit = 0,0212 deg, Rol =0,0454 deg, whereas for OSMS was : x (Lat.) = -0,0011 mm, y (Lng) = -0,01mm and z (Vrt.) = 0,02 mm with magnitude of 0,022 mm, Rot = -0,01 deg, Pit = 0,02 deg, Rol = -0,07 deg.

Conclusions: In conclusion, interfraction patient motion assessed by OSMS is consistent with kV and CBCT image guided. We are looking forward to obtain an adequate amount of data to assess also the role of OSMS in intrafraction movements.

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ADAPTIVE VMAT FOR HIGH RISK PROSTATE CANCER IN THE IGRT ERA: DOSIMETRIC IMPLICATIONS

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Aims: to quantify internal margins and the resulting Clinical Target Volume (CTV) to Planning Target Volume (PTV) adaptive margins after Image-Guided Radiotherapy (IGRT) in Volumetric-Modulated Arc Therapy (VMAT) for high-risk prostate cancer. Dosimetric parameters for CTV coverage and exposition of organs at risk (OARs, ie rectum and bladder) according to their daily filling were also analysed.

Methods: PTV was obtained adding 0.7 cm margin to prostate plus seminal vesicles (CTV) in all directions, except posteriorly, where a 0.5 cm margin was used. A daily Cone-Beam CT (CBCT) for image guidance was acquired before VMAT for the first week of treatment, then weekly: the translational and rotational displacements were registered and then corrected through the robotic couch. Image fusion was performed to transfer the prostate, seminal vesicles, bladder and rectum contours onto each CBCT. Contours were edited to match the new anatomy of each CBCT. Using these structures, average CTV, and average OARs were generated and internal margin was calculated. Dose distributions and DVHs were obtained and weekly CBCT scans were used to monitor the PTV coverage.

Results: A total of 100 CBCTs were evaluated: we retrospectively analysed 10 consecutive patients with high-risk prostate cancer treated at the Radiotherapy Unit of San Donato Hospital – Arezzo with IGRT VMAT to prostate and seminal vesicles (median dose 76 Gy, range 74-80) from January to April 2014. The CTV displaced ≤4 mm in the majority of cases. In 95% of the weekly CBCT scans, the CTV was located within the average PTV. The bladder was found to be smaller for 76.3% of CBCTs evaluated. This reduction in volume correlated to an increase in the cumulative bladder doses, while increases in volumetric rectum dose correlated with increases in rectal volume.

Conclusions: IGRT adaptive VMAT allowed for reduction of the PTV margin to 4 mm without decreasing CTV coverage during treatment, improved OARs sparing and treatment accuracy in high risk prostate cancer.

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COMPARISON OF FOUR TECHNIQUES FOR SYNCHRONOUS IRRADIATION OF BOTH BREAST AFTER CONSERVATIVE SURGERY

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Purpose: Optimize the dose to both residual mammary glands (PTV) by observing the dose constraints on the OARs by choosing the optimal technique according to the conformation of the volumes to be treated.

Materials and Methods: We present four different synchronous irradiation techniques to treat four patients with bilateral breast cancer. All of them were treated with standard fractionation (50Gy / 25 fractions) plus electron boost on tumor bed (10Gy in 5 Fractions). The four techniques used were the following: Two 3D Techniques: 1°) TANGENTIAL FIELDS; 2°) FIELD IN FIELD (FF); Two IMRT techniques: 1°) TOMOTHERAPY HI-ART; 2°) VMAT. By examining the dose volume histograms of the four techniques and comparing the homogeneity of the optimal therapeutic doses delivered to PTV and the doses received by the OARs, it was found that in all techniques used the PTVs had a good mean dose of 48Gy, with Respect for all costrains for OARs in all the techniques tested. It was calculated for the PTV of each plane HI (homogeneity index) = D2% -D98% / D50%:

FF: (PTV) HI = 0.15%; Dmax (107%) = 53.59Gy; Low doses OARs: Lung lung: V10Gy = 10.3%; V20Gy: 9.64; Heart: V25Gy = 4.6%; Dmean: 6.2Gy

F.TANG.:(PTV) HI = 0.29%; Dmax (107%) = 53.58Gy; Basse doses OARs: Lung Sum: V10Gy = 12.7%; V20Gy: 8.9; Heart: V25Gy = 1%; Dmean: 4.35Gy

VMAT: (PTV) HI = 0.12%; Dmax (107%) = 53.5Gy; Basse doses OARs: Total Lung: V10Gy = 30%; V20Gy: 5.6; Heart: V25Gy = 1.3%; Dmean: 7Gy

TomoTherapy: (PTV) HI = 0.13%; Dmax. (107%) = 54Gy; Low doses OARs: Lung amount: V10Gy = 20%; V20Gy: 2; Heart: V25Gy = 2%; Dmean: 10Gy

Conclusions: From this analysis it has been shown that the optimal technique to be used for the synchronous irradiation of bilateral residual breast gland is the 3D Field in Field respect to modulated intensity techniques, for reducing the percentage of low doses to LUNGS and HEART (OARs).

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INTEROBSERVER ANALYSIS OF MANUAL MATCHING FOR IMAGE GUIDED RADIOTHERAPY (IGRT) OVER A LARGE NUMBER OF TREATMENT FRACTIONS PERFORMED BY APPROPRIATELY TRAINED OPERATORS WITH DIFFERENT PROFESSIONAL BACKGROUND

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Aims: Radiotherapy treatments are more frequently delivered to small volumes with high precision requirements. Daily online image guided radiotherapy (IGRT) based on cone beam computer tomography (CBCT) may provide this precision but requires appropriate operator performance. This retrospective offline interobserver evaluation analyzes the variation in manual image matching between several appropriately trained operators with different professional background.

Methods: In an offline retrospective approach, a total of 30 daily CBCT datasets of a single patient with locally advanced lung cancer (PTV volume 197 cc) were manually matched by 1 board certified radiation oncologists (RT) and 16 radiotherapy technicians (TSRM) after automatic prematching either based on a grayscale or bone algorithm, resulting in a total of 480 matching procedures. We considered RT analysis as the gold standard. The interobserver variability was estimated as a difference between TSRM and RT measurements.

Results: The mean interobserver variabilities were in latero lateral direction (LL), anterior posterior direction (AP) and cranio caudal direction were 0 mm (+/- 1 mm), 0.2 mm (+/- 1.1mm), 0.1 mm (+/-1.0 mm). The differences between all the TSRM and RT measurements were less than 2 mm in 97 % LL, 98% AP and 99% CC of the evaluations.

Conclusions: Interobserver variation between 17 appropriately trained operators with different educational background was minimal (no systematic variation and low random variation) over the whole treatment course of a typical patient with advanced lung cancer. This result should be confirmed over a larger number of clinical paradigms and patients.

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IMPACT OF A MRI SAFETY AND CLINICAL ELIGIBILITY QUESTIONNAIRE ON SELECTION PROCEDURES FOR PATIENTS CANDIDATE FOR MRI-RADIOTHERAPY

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Aims: Our radiotherapy (RT) Department has implemented a hybrid machine (MRIdian, ViewRay®, Cleveland, Ohio, USA) that allows to deliver radiation treatments while acquiring real time MR imaging for patient repositioning and motion management. Aim of this study is to analyze the impact of an MRI safety and clinical eligibility questionnaire on patients (pts) selection procedures.

Methods: 84 pts candidates for RT have been enrolled between February and May 2017. For pts enrolled between February and March (Group 1) the selection procedure was applied through a clinical visit before simulation evaluating the existence of absolute MRI exclusion criteria (i.e: pacemaker; surgical clips MRI-unsafe or with unknown MRI safety; claustrophobia) and/or other clinical incompatibility issues. A MRI safety and clinical eligibility questionnaire has been introduced for the selection of pts evaluated between April and May (Group 2). The questionnaire has been administered as a first selection procedure: the clinical visit took place only for the pts in which the questionnaire did not detect any MRI incompatibility or compliance issues. The remaining pts were addressed to traditional RT.

Results: For Group 1, 51 pts were evaluated and 68% (34 pts) of them was then simulated on the MRIdian machine. For the 16 pts for whom MRI simulation was not possible we observed different exclusion causes: clinical incompatibility with positioning and prolonged treatment time (pain or functional impairment) (7), claustrophobia (7) and anatomic conditions hampering simulation procedures (2). The 33 pts of Group 2 were then screened with the questionnaire and 81% (27 pts) of them was allowed to undergo MRI simulation. Their causes of incompatibility observed during the clinical visit were mainly: underestimated claustrophobia (3), compromised general conditions (1) and presence of undeclared pacemaker (1) and decorative tattoos with unknown MRI behavior (1). Overall, 26 (30.9%) patients resulted not eligible for MRI with claustrophobia as main cause of exclusion (38.5%).

Conclusions: An ad hoc questionnaire resulted to be a useful tool in selection procedures for pts candidate for MRI-RT, allowing significant time saving in treatment procedures. Claustrophobia resulted to be the most significant exclusion criterion and appeared to be often underestimated by pts. These results encourage the use of a MRI safety and clinical eligibility questionnaire in the centers equipped with MRI-RT technologies.

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MODDICOM: AN OPEN SOURCE LIBRARY FOR RADIOMIC INVESTIGATIONS

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Aims: Radiomics is the discipline that extracts and analyzes high-dimensional quantitative features from medical images(MI) in order to build decision support tools to help oncologists in their daily clinical practice. It has the potential to detect spatial and temporal heterogeneity of solid cancers correlated to a clinical outcome. There are already tools which extract and analyze quantitative information from MI, but these are not free and open source(OpS) and few of them are designed to automatize the computation on a large set of DICOM studies. For these reasons we propose Moddicom, an OpS and free library specifically designed to extract a large amount of standardized radiomic features (RF) from CT, PET and MRI, based on the R software.

Methods: The Moddicom library was developed in R and C++ environment, by using also the DICOM libraries DCMTK. The entire package is easily usable as a standard R package. The Moddicom modules to facilitate the RF extraction are shown in Figure 1. The geoLet module allows easy loading of a large amount of DICOM images from a given path while the RF extractor, called geoLet.features, allows the extraction of a standardized set of RF from the previously loaded MI. In addition, the feature extraction algorithm has been validated by an international ring of collaborative centers.[1]

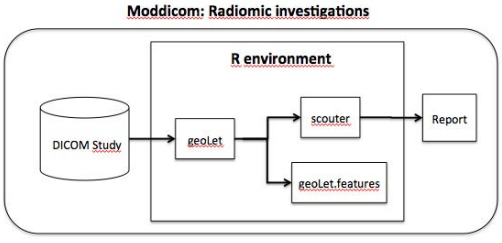

Figure 1.

Results: In the current version, Moddicom automatically extracts 94 features from MI divided into the following families: 17 first order histogram, 15 morphological, 25 grey level co-occurrence texture, 16 grey level run length, 16 grey level size zone and 5 fractal features. In the last two years, our multidisciplinary lab

extensively used Moddicom to analyze 182 MRI and 60 PET for rectal cancer, 160 MRI for gynecologic cancer, 60 CT for lung and 58 dorsal vertebral bodies. During this period, the software has been updated in order to improve performance and offer researchers a comfortable environment. The package, working on Windows, Linux and Mac OS can be downloaded from gitHub(https://github.com/ kbolab/moddicomV2).

Conclusions: Moddicom is able to extract a large amount of standardized RF automatically from CT, PET and MRI. Potentially, it can discover statistical relations between RF and clinical outcomes. Moddicom is a free and easy-to-access tool for any department interested in performing Radiomics investigations on its own MI.

Reference

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APPROPRIATENESS FOR DOSE INTENSIFICATION IN RECTAL CANCER RADIOTHERAPY: INTERNAL MOVEMENT EVALUATION OF GROSS TUMOR VOLUME (GTV) AND MESORECTUM BASED ON CONE BEAM COMPUTED TOMOGRAPHY (CBCT)

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Aims: Correlation of total radiation dose with complete pathological response was reported in rectal cancer. A greater interest in dose intensification on small volume is emerging, thanks to the availability of conformational techniques, as IMRT and VMAT and in the perspective of an organ-saving surgery. An appropriate evaluation of target movement is recommended. This study aimed to provide an estimation of the internal movement (IM) of GTV and mesorectum in patient treated with neoadjuvant radio-chemotherapy for rectal cancer, using three-dimensional cone-beam CT (CBCT).

Methods: Fourteen patients, (M:10, F:4), underwent CT scan simulation in prone position with controlled bladder filling. CBCTs were performed once a day during the first 5 fractions, then once or twice a week during the all treatment, by Elekta X-Ray volume imaging system (XVI). The IM was estimated for GTV (tumor site and corresponded rectum) and mesorectum. Both were delineated on MRI imaging co-registrated with CT scan simulation and with all CBCTs. Bladder was also delineated to evaluate the impact of its volume on GTV and mesorectal IM. Co-registrations were performed on RayStation platform (RaySearch Laboratories, Stockolm, Sweden) by bone landmarks and corrected for set-up error. IM evaluation was obtained as mean shift in postero-anterior (P-A), cranio-caudal (C-C) and left and right (L-R) directions and volumes variability were calculated by DICE index.

Results: A total of 133 CBCTs were performed and retrospectively analyzed. Measured movement of the GTV was -0.13cm (+/- 0.1) and 0.15cm (+/- 0.08) for L-R direction. In P-A direction, mean shifts were 0.12cm (+/- 0.11) and -0.19cm (+/- 0.14), in C-C direction were 0.28cm (+/-0.27) and -0.36cm (+/- 0.23). Mesorectal IM resulted in -0.12cm (+/- 0.08) and 0.13cm (+/- 0.04) for L-R direction, 0.17cm (+/- 0.11) and -0.19cm (+/- 0.10) in P-A direction, and 0.27cm (+/- 0.16) and -0.25cm (+/- 0.15) in C-C direction. Concerning bladder, movements were less than 0.6cm, except for caudal shift calculated as -1.12cm (+/- 0.56). Mean DICE index for GTV, mesorectum and bladder was 0.58, 0.75, 0.48, respectively.

Conclusions: GTV and mesorectum IM, in our study with patients in prone position, was less than 4mm in all directions. Although a worst DICE was obtained for bladder volume, this did not influence target movements. CBCT resulted effective for IM assessment and could represent a valid method for appropriate treatment intensification.

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ASSESSMENT OF THE EFFECT OF SETUP ERROR ON DOSE DISTRIBUTION TO TARGET VOLUME AND OARS IN HEAD AND NECK VMAT USING DAILY IGRT

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Aims: To assess the effect of patients setup errors identified with daily pretreatment CBCT imaging on dose distribution to target and OARs in H&N cancer treated with volumetric modulated arc therapy (VMAT).

Methods: A retrospective study on setup error measurements was conducted on 246 CBCT images. The patient set up errors were defined as the offset between CBCT and planning CT in LR, SI and AP directions. To evaluate the effect of patients setup errors on dose distribution, the isocenter of the original VMAT plans was shifted to simulate the dose to targets and OARs without online correction on planning CT. The magnitude of displacements in each direction was obtained using daily CBCT shifts. The same original VMAT plans were applied without alteration of optimized beam profiles. Dose-volume histograms (DVHs) were recalculated and were compared with expected planning DVHs; a difference ≥3% from planned dose was considered dosimetrically significant.

Results: A total of 246 CBCT scans were analyzed. The magnitude of displacement in the LR, SI and AP direction between 1-3mm was 65%, 66.5%, 42%

respectively and between 3-5mm was 35%, 33.5% , 58% respectively. The effect on dose distribution showed that if no correction was applied, the mean dose on parotid glands would be increased by 6.4%, on brain stem by 3% and on spine by 4% with a moderate difference in target coverage from planned dose.

Conclusions: Online correction of setup errors using daily IGRT increase accuracy of H&N VMAT reducing the difference between planned dose and delivered dose.

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IMAGE-GUIDED RADIOTHERAPY IN SICILY: A SURVEY BY THE SICILY GROUP OF THE ITALIAN ASSOCIATION FOR RADIATION ONCOLOGY

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Aims: In 2017, a survey was conducted to analyze the available resources and their use in the radiation treatment of patients with malignancies in Sicily, on behalf of the Sicily group of the Italian Association of Radiation Oncology.

Methods: A questionnaire was sent to 15 of radiotherapy centers active in the region. Items investigated the techniques performed in each center (3D-CRT; IMRT, VMAT, TBI, Brachitherapy, Stereotactic radiotherapy brain and body, IORT) , the inclusion criteria for the various techniques, how to access structures, integration with chemotherapy and new drugs, the presence of multidisciplinary teams.

Results: 15 questionnaires were returned. Treatment techniques were intensity-modulated radiotherapy with image-guided radiotherapy in 9 centers (60%). There was a good consistency on the use of radiotherapy in different settings, whereas integration with chemotherapy and new drugs was present in all centers of radiotherapy.

Conclusions: This survey provides important data on the use of radiotherapy resources for patients with cancer in Sicily. The data offer the opportunity to further investigate issues that could better standardize cancer treatment and allocate resources across the region.

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EQUIPMENT, STAFFING AND PROVISION OF RADIOTHERAPY IN LOMBARDY, ITALY: RESULTS OF THREE SEQUENTIAL "SNAPSHOT" SURVEYS PERFORMED IN 2012-2016

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Background: Several efforts are being implemented at the European level to measure availability and provision of up-to-date radiation treatments. As a contribution to the detailed knowledge of current professional standards, a Working Group was activated in Lombardy to measure and monitor time trends of several items related to radiotherapy (RT) provision

Methods: A "snapshot" survey involving all RT oncology centers within Lombardy was initially performed in 2012 and repeated in 2014 and 2016.Centers were asked to provide detailed information concerning all individual patients being treated in the "index day", and to report data on available local capital and human resources. To evaluate workloads, total numbers of patients treated yearly at each center were also enquired.

Results: Response rate was 100% in all three surveys. We observed an increase in the number of centers (from 30 to 34 in 2016, including one particle therapy facility) and MegaVoltage Units (MVU) from 76 to 87. Mean number of MVU per center was 2.5 range 1 to 6. Patients on treatment and staffing in terms of absolute numbers of professionals increased correspondingly. Average age of MVU increased from 5.3 to 7.5 years and patients on waiting list also increased, likely due to expanding clinical indications to radiation treatment and to increasing numbers of patients coming from other regions. Conformal 3-dimensional (3D) RT courses (from 56% to 42% of all courses delivered in the "index" day) were progressively replaced by VMAT treatments (from 32% to 42%), while conventionally IMRT courses remained stable (7%). Treatments with

CyberKnife and with linac-based SRT also increased but remained a minority (1.3% and 0.9% in 2016, respectively). Waiting times were satisfactory overall but significant differences between centers were noted. Analysis of workload was made difficult by several confounding factors. Radiation oncologists treated on average 152 RT courses per year and radiation therapists 100 RT courses per year, but again differences were large.

Conclusions: The methodology of "snapshot" survey proved feasible and provided valuable information about radiation oncology provision and accessibility. Overall the delivery of radiation treatments was deemed adequate, but critical items exist in terms of equipment aging, waiting times and heterogeneity between centers. A formal cooperation with regional policy makers was initiated to plan future resources in a evidence-based perspective.

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IMAGE GUIDED INTENSITY MODULATED RADIOTHERAPY (IG-IMRT) USING MODERATELY HYPOFRACTIONATED RADIOTHERAPY FOR INTERMEDIATE/HIGH RISK PROSTATE CANCER (PCA): OUTCOME AND TOXICITY ANALYSIS IN 161 CONSECUTIVE PATIENTS (PTS) TREATED AT TWO DIFFERENT ITALIAN CENTERS OVER A SPECTRUM OF FRACTIONATION REGIMENS

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Aims: Dose escalated RT plays an important role in improving clinical outcome for PCa pts. Recent studies showed that hypofractionated radiotherapy (HRT) shortens treatment at isoeffective prescription doses, but some concerns regarding tolerance remain. Aim of the study is to investigate tolerability and clinical outcomes of dose escalated RT regimens using IG-RT hypofractionation for PCa pts.

Methods: From 2008 to March 2016, 161 pts with PCa underwent radical RT using moderate HRT. Median age was 73 years. Sixty-one pts had intermediate risk PCa, 48 high and 52 very high risk, according to Version 1.2017 NCCN Guidelines Risk Stratification. Gleason Pattern Score (GPS) was <7 in 40 pts, equal to 7 in 68 and superior in 53; median GPS was 7. At diagnosis all pts had an elevated PSA: 76 had initial PSA value (iPSA) <10 ng/mL, while in 55 pts it was between 10.1-20 ng/mL and in 30 >20 ng/mL. Upon clinical staging (based on TNM stadiation - AJCC 2010) 16.8% of pts had cT1, 41.2% cT2, 23.3% had cT3a and 18.8% had cT3b. After complete radiological staging pathological pelvic nodes were found in 12/161 pts (7.4 %).

Results: All pts were treated with HRT (2.3-3.82 Gy/day,17-32 total fractions) with or without Total Androgen Deprivation (ADT) using IG-IMRT with Tomotherapy® or VMAT. Median total prostate RT dose was 70 Gy. One hundred-fifteen of 161 pts received RT in association to neoadjuvant, concomitant and even adjuvant ADT. Target volume encompassed just prostate in 21 pts and prostate and seminal vescicles in 56; pelvic abdominal RT was performed in 84 pts with prophylactic intent due to high risk of pelvic nodal involvement (based on Roach algorithm). At a median FUP of 34.7 months 140 pts (81.7%) were alive. Three- and 5-year actuarial OS were 91.8%(ES±2.6%) and 79.3%(ES±5.00%), respectively. Actuarial Biochemical Relapse Free Survival was 84.8%(ES±3.7) and 77.8% (ES±5.2) while Metastasis Free Survival was 92.8% (ES±2.4%) and 88.5% (ES±4.4%). Eight pts had ≥Grade 2 acute toxicity (3 pts had gastrointestinal discomfort and 5 pts had urinary symptoms) while 20 pts had ≥ grade 3 late symptoms (12 pts with GI toxicities and 8 pts with GU symptoms)

Conclusions: HRT using IG-IMRT resulted in good oncological outcome and toxicity profile. Three and 5-year bRFS and correspondingly OS are excellent and confirm recently published results of randomized controlled trials over a wider range of fractionation regimens

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RE-IRRADIATION OF LOCALLY RECURRENT PROSTATE CANCER (LRPC): RESULTS OF EFFICACY AND SAFETY

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Aims: Re-treatment of locally recurrent prostate cancer with external beams radiation therapy remains controversial because of fear of major complications and side effects. In this study we report our experience on re-irradiation in 17 patients previously irradiated for prostate cancer.

Methods: Patients with a biochemical relapse and with a PET-Choline revealing the presence of a local recurrence of disease were included in this study. Re-irradiation consisted of a stereotactic treatment delivered by image guided radiation therapy (IGRT)-volumetric modulated arc therapy (VMAT) technology in 5 daily fractions. Toxicity was recorded according to the CTCAE criteria (v 4.0).

Results: Seventeen patients received re-irradiation. Previous treatment consisted on a median total dose of 74 Gy on prostate or prostatic bed (range 66-76). Ten patients had also received radiotherapy on seminal vesicles, four patients on pelvic lymph-nodes. As a re-irradiation, a median total dose of 25 Gy (range 25-30) was delivered in a median number of 5 fractions (range 5-6). An immediate biochemical response was observed in

all cases. Median PSA after treatment was 0,77 ng/ml (0,19 – 6.0, p=0,004). The sole acute toxicity reported was genito-urinary, mainly represented by pollakiuria and dysuria grade 1 (n=9, 52.9%) or grade 2 (n=2, 11.8%). One patient (5.9%) had a grade 3 hematuria, was hospitalized and submitted to continuous bladder irrigation. A late grade 1 GU toxicity was observed in 3 patients (17.7%). No other toxicities were observed. At a median follow-up of 22 months (range 6-36, calculated from the time of recurrence diagnosis) 8 patients (47.1%), experienced a biochemical recurrence, confirmed by a positive PET-choline in 5 cases (29.4%). Median BFS was 24 months, 1- and 2- year BFS was 85.1% and 35.5% respectively. Median LC was 24 months, 1- and 2- year LC was 91,7% and 44,6% respectively. All patients are still alive, 5 of them with measurable disease. Median OS was 96 months from the initial diagnoses (range 59-151)

Conclusions: With the technological novelties offered by modern radiotherapy, re-irradiation of patients still affected by prostate cancer, and previously treated with radiation therapy, confirms its safety and efficacy. Therefore, it can be considered a valuable option for local recurrence of this disease

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IT'S POSSIBLE TO TREAT OBESE PATIENTS WITH CYBERKNIFE SISTEM?

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Aims: The Cyberknife (CK) is a modern robotic system of radiosurgery and stereotactic radiotherapy for intra and extracranial primary and secondary tumor treatment. One of the limitations of the system is obese patients treatment. Obesity is an increasing disease in the western civilization, so often this type of patient has to be treated. Aim of the study is to demonstrate that in some cases it is possible to treat these patients with the CyberKnife System.

Methods: Since November 2012, the Cyberknife system is in use at radiotherapy of INT Pascale in Naples. The CyberKnife is a frameless image-guided radiotherapy system involving a 6-MV linear accelerator mounted on a robotic arm which possesses six degrees of freedom. The imaging system consists of two diagnostic x-ray sources mounted to the ceiling paired with amorphous silicon detectors to acquire live digital radiographic images of the tumor or tumor surrogates including bony anatomy or implanted fiducial markers. The system moves around a "virtual sphere" with points called "nodes" corresponding to positions from which the manipulator delivers radiation. Before delivering the beams, it is necessary to check that the patient is within the fixed and dynamic security zone defined by the Collision Detection Program (PDP). This security tool allows to verify if the patient is within the 106.2 cm height limits for treatment of intracranial target, 111.3 cm for upper abdomen targets and 107.9 cm for inferior abdomen targets. The maximum capacity of the couch of CK is of 159 Kg. In 2016 we treated with CK 267 patients, of whom 10 patients, affected by obesity (1-2nd grade).

Results: Of ten patients, 5 candidates for chest treatment have entered the safety zone, 4 abdominal treatment candidates have entered the safety zone after a 2-month low calorie diet, one patient with a 2nd-3rd grade obesity, was not treated with CK because it exceeded the limits given by the PDP.

Conclusions: The obese patient can be treated with CK if it does not exceed the weight of 159 kg and if it pass the PDP test. Changing lifestyle and diet has a positive impact on the likelihood of these patients being treated.

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HTA TITLE AND BREAST CANCER IN OLDER WOMEN: HYPOFRACTIONATED RADIANT TREATMENT AND ACCELERATED PARTIAL TREATMENT (APBI) CAN MAKE THE NATIONAL HEALTH SYSTEM MORE SUSTAINABLE FOR THE SAME CLINICAL EFFICACY?

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Introduction: The shortage of resources puts the Italian healthcare system (SSN) at risk. In radiotherapy (RT) this is even more apparent depending on available technology.

Objectives: This contribution reflects on accelerated or partially accelerated (APBI) treatments in older women with early breast cancer in terms of social impact and sustainability of SSN.

Materials and Methods: Were compared with 4 radiotherapy schemes: partial RT accelerated breast cancer treatment (APBI) requiring 10 sessions, a 16-day RT hypofraction, an irradiation schedule for an in situ form without boosting the operating bed , Which consists of 25 sessions, and finally a standard flush plan with a standard boost and a boost of 30. Schedules RT were analyzed using two indicators: working time for technical personnel and kilometers traveled by the clinician to reach the center (Exemplifying the distance between home and hospital within 10 km).

Results: In RT APBI Radiotherapy UOC engages 30 minutes in tomotherapy session (total 300 minutes) while the total infirms 200 km. With the hypo-fractionation of the entire breast, the UOC engages 20 minutes in a Linear Accelerator (Linac) (320 minutes total) and the total in 320 km. In the third RT regime, the UOC commits the Linac for a total of 500 minutes and the woman travels over 500 km. Finally in the fourth type

of RT the UOC occupies the Linac 600 minutes and the woman travels 600 km. In terms of kilometers, women, with the same clinical and cosmetic results, travel about a third of kilometers. The UOC of RT, even though having advanced technology, has the machines occupied for a total halved time.

Conclusions: Breastfeeding RT is promising in social terms, both for the woman and for the SSN, without giving up organs preservation.[1]

Reference

1. SM Shirvani, Int J Rad Oncol Biol Phys, Vol. 95, No. 2, pp. 605, 2016, Early-Stage Breast Cancer in Older Women: Implications for Payment and Policy Reform.

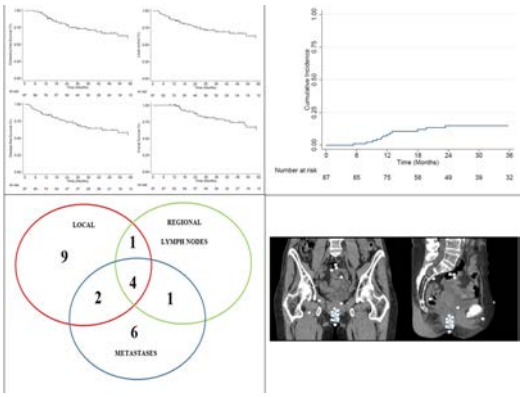

Figure 1.

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IMAGE-GUIDED IMRT WITH SIMULTANEOUS INTEGRATED BOOST AS PER RTOG 0529 FOR THE TREATMENT OF ANAL CANCER

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Purpose: To report on clinical outcomes of simultaneous integrated boost IMRT and concurrent chemotherapy as per RTOG 0529 protocol in anal cancer patients.

Methods: Clinical stage T1-T4 N0-N3 anal cancer patients were submitted to concomitant chemo-radiation. Patients with cT2N0 disease were prescribed 50.4Gy/28 fractions to the gross tumor PTV and 42Gy/28 fractions to the elective nodal PTV. Patients staged as cT3–T4/N0–N3 were given 54Gy/30 fractions to the macroscopic anal PTV, while clinical nodes were prescribed 50.4Gy/30 fractions if <3cm or 54Gy/30 fractions if >3 cm; elective nodal PTV was prescribed 45Gy/30 fractions. Two cycles of concomitant 5-fluorouracil and mitomycin C were planned for all patients. Oncological outcomes, acute and late toxicity profiles and pattern of failure were reported.

Results: The 3-year colostomy-free survival rate was 64% (95% CI 0.52-0.75). The 3-year local control, disease-free and overall survival rates were 69% (95% CI 0.57-0.79), 71% (95% CI 0.59-0.80) and 79% (95% CI 0.66-0.87), respectively. The cumulative incidence of colostomies was 15.1% (95% CI 8.15-23.88) at 24 months. The cumulative incidence of cancer-specific deaths was 16.4% (95% CI 8.60-26.47) at 36 months. Major acute toxicity consisted of hematological (G3-G4: 26%) and cutaneous (G3-G4: 16%) events. Only one case of > G3 late toxicity was documented.

Conclusions: Simultaneous integrated boost IMRT and concurrent chemotherapy as per RTOG 0529 protocol seems to be safe and feasible with consistent oncological outcomes and a mild acute and late toxicity profile in anal cancer patients.

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USE OF RMN PELVIS IN THE TREATMENT OF PROSTATE CANCER

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Aims: RMN in recent years has gained a fundamental role in the staging of prostate cancer: it allows to study better than any other investigation the integrity of the prostate capsule, the involvement of seminal vesicles and the lymph node status. For these reasons, it is not possible to carry out this investigation before setting up an exclusive radiotherapy treatment. This work aims at fusion of RMN pelvis images and TC Simultation for a better definition of target treatment and risk organs.

Methods: We evaluated from January to April 2017 12 pts with prostate cancer. All pts were staged by prostate biopsy and transrectal ultrasound: 5 pts were T2c clinical stage (intermediate risk) and 7 pts T3a (high risk) stage. We submitted all patients to RMN pelvis examination with mdc and the results obtained were the following: in 7 pts the T3a disease clinical stage was confirmed and the 5 pts previously identified as T2c actually showed capsule infiltration and they also became T3a. It therefore emerges that 5 pts had been downstaging and therefore received inadequate treatment at the real stage of the disease. All the pts have been classified as high-risk cT3a. By fusion between RMN and the Simulation TC, some critical issues related to the equipment used (A) other relative to the pz (B): A) the difference between the couch of the RMN (concave) and the Simulation TC (plane) with consequently no match between the set ups of the pz; different angle of inclination between the gantry of the RMN and that of the TC; no reproducibility of the pz set up; B) execution of the two methods with bladder filling and non-overlapping rectal emptying.

Results: The RMN has allowed us to have a proper staging and better identification of prostate apex and penile bulb not always correctly visible to TC; contrary

to the various physical condition of the pz and the non-reproducibility of the set up makes the imaging fusion is unsatisfactory.

Conclusions: To improve the result of imaging fusion it is possible to act on the pz by uniformizing its physiological state during the execution of the two methods, and on the equipment using gaps that make reproducible the pz or workstation setups that allow to melt an elastic image .

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COMPARISON IMAGES FUSION SYSTEMS: OUR EXPERIENCE

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Aims: The imaging fusion of TC Simulation and diagnostic images such as RMN, PET, TC provides more information on anatomic and metabolic details of tumors, resulting in better definition of volumes to be irradiated. The UOC of Oncology Radiotherapy of the Pugliese-Ciaccio of Catanzaro has four imaging fusion systems. We wanted to compare the fusion of images through the supplied workstations

Methods: The UOC of Oncology Radiotherapy of the Pugliese-Ciaccio of Catanzaro has the following melting systems: Oncentra and Monaco (Elekta), Pinnacle (Synergy Theme) and Prosoma (EL.SE). The first three systems are used in daily clinical practice as TPS while Prosoma is used for Virtual Simulation. We rated 10 pts from January to May 2017; of these 3 pts were affected by cerebral tumor, 4 pts from prostate cancer, 2 pts from lung cancer and 1 pts from pancreatic tumor. The Imaging fusion for pts with cerebral tumor was performed between TC simulation and RMN with mdc, for the pts with prostate cancer RMN with mdc in 3 pts was used, and 1 pts PET with Colin was used; for the lung cancer patients's we used PET with FDG and in 1 pt with pancreatic tumor we used as reference image TC abdomen with mdc. The imaging fusion of each pts has been studied on the four workstations supplied.

Results: All systems perform a images fusion satisfactory for the purpose to define the Clinical Target volume and the Planning Target Volume when diagnostic imaging with overlapping pts setups are used, such as RMN cerebral with mdc and TC abdomen with mdc in the study of brain and pancreatic lesions, respectively; In contrast, in all systems the fusion between simulation TC and PET showed a medium error along the y axis of 1.5 cm despite the good overlap of the anatomical structures used as a reference. The Monaco and Pinnacle systems have a higher rate of fusion than the Oncentra and Prosoma systems.

Conclusions: The imaging fusion process, while being a valid support for the PTV definition, has limits for improvement in the development of shared protocols that allow to acquire TC simulation and diagnostic tests with similar parameters both for equipment used and to set up and patient's physiological conditions

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ACCURACY EVALUATION OF TWO NON-INVASIVE FIXATION FRAME FOR BRAIN TREATMENTS WITH HELICAL TOMOTHERAPY

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Aims: The study focused on the accuracy evaluation of frame-less radiosurgery (RS) and hypo-fractionated treatments (HFT), delivered with helical Tomotherapy (HT), by means of two different mask-based fixation systems.

Methods: Firstly, an anthropomorphic phantom was scanned to evaluate the positioning accuracy of the tomotherapy Image Guided Radiotherapy (IGRT) system. The Megavoltage Computed Tomography (MVCT) was acquired and automatically registered with the planning CT via the automatic registration algorithm. After the application of the suggested shifts, the phantom was scanned a second time and the shifts in each direction as well as the rotations were recorded; the vector displacement (v) was calculated as the square sum of the shifts in each directions (X, Y, Z). Analogous procedure was applied to 11 and 10 patients underwent intracranial HFT and RS respectively. The second MVCT, performed at the end of the treatment, were analyzed in order to evaluate the intra-fraction motion. 25 and 18 MVCT for HFT patient immobilized with fixed with a Five Point Mask (FPM) and with Double Shell Positioning System (DSPS) were analyzed respectively. For RS patients 4 and 6 MVCT with FPM and DSPS were analyzed respectively.

Results: The mean v, obtained with the phantom acquisitions, was 0.4±0.2 mm, showing that HT-IGRT system is able to achieve positioning accuracy typical of RS (v<1mm). Moreover, the mean rotational variations could be considered negligible. In hypo-fractionated patients, v was 0.8±0.3mm (range: 0.4-1.5mm) for the FPM, and 0.6±0.4mm (range: 0.1-1.4mm) for the DSPS, showing that both masks minimized the intra-fraction motion to an extent of 1mm with a lower mean value for the DSPS (with no statistically difference: $p<0.573$, Mann-Whitney Test). No dependence of v on the treatment time was observed for both masks. No differences were found for RS patient: mean v was 0.9±0.4mm (range: 0.3-1.2mm) and 1.0±0.5mm (range: 0.5-2.0mm) for the FPM and for the DSPS respectively.

Conclusions: Our study demonstrates that mask-based fixation systems combined with HT-IGRT system have a high intracranial positioning accuracy. Zeverino et al (DOI:10.1700/1146.12640) reported similar value of positioning accuracy: v of 0.6±0.9 mm (range: 0.3-1.7mm) for invasive immobilization systems used in combination with IGRT. Therefore, mask-based fixa-

tion systems could be used as an alternative of the invasive immobilization system for high-precision treatments, like RS.

Table 1. Shifts in each direction, vector displacement (v) and rotations.

Hypo-fractionated Treatments								
mask		shift (mm)			v (mm)	Rotation (°)		
		X	Y	Z		PITCH	ROLL	YAW
FPM	mean± std	0.1±0.2	-0.3±0.6	0.0±0.5	0.8±0.3	0.3±0.3	0.2±0.4	0.0±0.3
	range	(-0.3÷0.7)	(-1.3÷1.3)	(-0.7÷1.4)	(0.4÷1.5)	(0.0÷0.6)	(-0.4÷1.5)	(-0.9÷0.6)
DSPS	mean± std	0.0±0.3	-0.1±0.6	0.0±0.2	0.6±0.4	-0.2±0.5	0.0±0.2	-0.1±0.3
	range	(-0.9÷0.6)	(-1.3÷0.8)	(-0.4÷0.5)	(0.1÷1.4)	(-1.4÷0.4)	(-0.6÷0.4)	(-0.8÷0.4)
Radiosurgery Treatments								
mask		shift (mm)			v (mm)	Rotation (°)		
		X	Y	Z		PITCH	ROLL	YAW
FPM	mean± std	-0.2±0.3	0.7±0.4	0.1±0.4	0.9±0.4	0.0±0.4	0.2±0.4	0.5±0.5
	range	(-0.7÷0.0)	(0.1÷1.2)	(-0.3÷1.2)	(0.3÷1.2)	(-0.4÷0.6)	(-0.1÷0.7)	(0.0÷0.9)
DSPS	mean± std	-0.1±0.4	0.5±0.8	0.0±0.6	1.0±0.5	0.3±0.5	0.1±0.3	-0.3±0.4
	range	(-0.5÷0.6)	(-0.5÷1.5)	(-1.1÷0.8)	(0.5÷2.0)	(-0.5÷0.7)	(-0.1÷0.6)	(-0.6÷0.1)

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CORRELATION BETWEEN ACUTE TOXICITY AND DAILY BLADDER DOSE-VOLUME HISTOGRAMS IN PROSTATE CANCER TREATMENTS

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Aims: To confirm a correlation between the risk of acute genito-urinary (GU) toxicity and some bladder DVH parameters of patients treated for prostate cancer and underwent daily IGRT with CBCT.

Methods: A retrospective analysis to investigate dosimetric predictors for acute GU toxicity, according to RTOG scale, has been performed on 51 patients irradiated after prostatectomy surgery in Maugeri Clinic (Pavia). The patients have been divided in two groups: in the first, 27 patients presented G1-G2 toxicity (TG) within 3 months after RT, while 24 (control group CG) have not reported any disease. All the patients have been simulated with empty rectum and filled bladder and irradiated with 6MV VMAT technique. Dose prescription was 2-2.2Gy/fr for 30-35 fractions. Bladder has been contoured in every daily CBCT and DVH has been evaluated on each structure. For both the patient groups a weekly analysis on the dose received by 56 and 5cc of bladder has been performed considering a threshold of 8.5Gy and 12.5Gy respectively as a latter works suggest [Carillo *et al*., Radiother. Oncol., Apr. 2014]. A cumulative dose on all the treatment weeks has been evaluated. The presence of statistically significant differences in terms of frequency of patients exceeding the thresholds between groups was assessed by the Fisher's exact test; for cumulative dose the two samples t-test or the Mann-Whitney test were applied as appropriate.

Results: 56cc of bladder in patients of TG received more than 8,5Gy in 62,2% of the treatment weeks and similarly this threshold was reached 67,5% in CG. The constraint D5cc=12.5Gy/w has never been exceeded in both groups except in only 1 week for a patient of CG. No statistically significant difference in terms of frequency of individuals receiving a weekly cumulative dose by 56cc exceeding the threshold of 8.5Gy was observed between the two groups (p-value>0.05). Among patients who received 56cc of bladder volume, a significantly higher level of cumulative dose over all weeks was observed in TG compared to CG groups (p-value=0.049). Likewise, the cumulative dose received by 5cc volume was higher in TG compared to CG but without evidence of a statistically significant difference (p-value=0.073).

Conclusions: A weak evidence of correlation was observed considering the cumulative dose received by 56cc of bladder. As in literature reported this constraint can be important to minimize possibility of GU acute toxicity in patient treated for prostate cancer.

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SAFETY OF INTENSITY MODULATED RADIATION THERAPY WITH DOSE-PAINTED DW-MRI BASED HYPOFRACTIONATED SCHEME IN RECURRENT HIGH-GRADE GLIOMAS: PROSPECTIVE PHASE I/II TRIAL

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Aims: Today for recurrent gliomas no standard of care exists. Recurrences have a life expectancy of a few months and re-irradiation has proven to be safe in terms of toxicity and in increasing OS. The integration of diffusion-weighted imaging and developments in radiation technology allow highly accurate targeting of biologically relevant tumour volumes. This could enable a presumable increase in local control reducing the radio-induced toxicity. The aim of our prospective phase I/II study (GLIORAD_15-18) is to evaluate feasibility, efficacy and toxicity of a hypofractionated stereotactic radiotherapy, with MRI based dose painting, for recurrent GBM in patients previously treated with standard therapy.

Methods: 3 patients, with recurrent GBM previously treated with surgery followed to STUPP protocol and evaluated by the neuro-oncology team, were prospectively recruited in 18 months. Multiparametric MRI was performed to define the target volume and to simulate the plan dose redistribution guided by the apparent diffusion coefficient (ADC) used as biomarker for tumor cellularity. To perform DPBN (Dose Painting By Numbers) planning procedure guided by ADC data

with RapidArc technique, home-made MATLAB software and automatic scripting procedure on a commercial treatment planning system (Eclipse TPS) were realised. According to the protocol, an inhomogeneous dose ranging from 30 to 50Gy (BED10>120Gy) was delivered to the target in order to change the recurrence pattern without excessive radiation necrosis in the target. Endpoints of this study were: the side effects, the rate of responses in accordance with the RANO criteria, QoL, OS and PFS. The local Ethics committee approved the protocol and informed consent was obtained for all patients.

Results: Patients received hypofractionated stereotactic IMRT planned by CT and standard and diffusion MRI. Treatment delivered in 5 consecutive fractions with a minimum dose of 6Gy for session and a dose of 10Gy to no more than 1cm3 of irradiated tissue. One patient died two months after re-irradiation for causes no related to radiotherapy. Two patients alive with follow up of 1 and 11 months presently ongoing second line chemotherapy. None of three patients developed acute and sub-acute radio-induced toxicity.

Conclusions: Preliminary results show the feasibility and safety of re-irradiation with MRI guided dose-painting in recurrent GBM not associated to significant morbidity or side effects.

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RADIOTHERAPY FOR EXTREMITY SOFT TISSUE SARCOMA: TECHNOLOGICAL AND RADIOBIOLOGICAL OPTIMIZATION

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Aims: Soft-tissue sarcomas are malignant tumors of the extraskeletal connective tissues that are characterized by an aggressive trend to spread thorugh surrounding soft tissues. Doses in conventional postoperative radiotherapy for extremity soft tissue sarcoma potentially exceed normal tissue tolerances. Intensity-modulated radiotherapy(IMRT) is an RT technique which offers the opportunity to better conform the RT field to the target volume whilst sparing critical normal tissue. Aim of the study is to evaluate if volumetric modulated arc therapy(VMAT)can decrease the probability of RT side effects (fibrosis, neuropathy, oedema). This study compares 3D-conformal radiotherapy (3D-CRT) with modulated arc therapy(VMAT)in optimising target volume coverage and minimising dose to OAR(skin and neurovascular bundle).

Methods: Twentyone patients undergoing post-operative radiotherapy for extremity STS were evaluated. The PTV was defined using pre-operative imaging, surgical notes, pathology results, PTV1 was formed by adding a 5 cm margin to the CTV longitudinally and 3 cm circumferential. The neurovascular bundle was contoured manually and the skin automatically. The Optimized PTV was defined removing skin and neurovascular bundle from PTV. For each patient, two plans were created: a 3D-CRT plan and a VMAT one. The plans were designed to achieve 95–105% of the prescription dose to PTV and to maximally spare the OAR. The first phase of statistical analysis consisted of searching radiobiological parameters through maximum likelihood estimation using doses and probability from literature. TCP and NTCP models were used for plan comparison.

Results: 21 patients were assessed (7F;14M). For each patient we created 2 plans: 3D and VMAT with a median dose at PTV of 59.4Gy. Statistical analysis shows higher TCP for 3D vs VMAT plans (90.6% vs 90.06% $p<0.0001$, difference percentage less than1%). Fibrosis is more likely in 3D vs VMAT plans 1.57% vs 0.7% $p<0.00001$), even Oedema and Peripheral neuropaty are more likely in 3D vs VMAT (2.99% vs 1.77% $p<0.000001$ and1.4% vs0.49% $p<0.001$ respectively).

Conclusions: The comparison between 3DCRT and VMAT shows a reduction of TCP <1% using VMAT. The probability of adverse effects (Neuropathy, Fibrosis and Oedema) is low, But using VMAT NTCP is halved at least. Even if there is a reduction of 1% of TCP (local control is about 90%) VMAT allows a high reduction of toxicities likelihood for skin and the neurovascular bundle instead of 3D CRT.

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EFFECTS OF RADIOTHERAPY (RT) ON CARDIAC IMPLANTABLE ELECTRONIC DEVICES (CIEDS): EXPERIENCE OF A SINGLE CENTRE IN A PROSPECTIVE COHORT OF PATIENTS (PTS) TREATED WITH IMAGE GUIDED RT (IGRT).

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Aims: The number of implanted CIEDs is increasing, as well as the use of RT and the evolution of RT techniques for the treatment of cancer. So, is more and more frequent that a patient with CIED undergoes RT. It is well established that RT can determine electromagnetic interference with CIED but available data on the frequency and cause of CIED failure during radiation therapy are limited and the management of these kind of pts is unclear. Although there is no clear cut-off point nor a clear linear relationship, in general, chances of device failure increase with increasing doses but an adsorbed dose at the device lower than 2 Gy is considered safe (low risk). Aim of this study is to evaluate the effects of RT on CIEDs in a prospective cohort of pts managed according to a multidisciplinary task force defined protocol.

Methods: All patients undergo an 'in clinic' control of the device before the first session and at the end of

the RT cycle, while an ECG is performed before and after every RT session only in PM-dependent or ICD patients; anti-tachy therapies have never been disabled. Only patients receiving a maximal dose absorbed by the device higher than 2 Gy or when the efficacy of RT would have been compromised by the device itself, were considered candidates to surgical repositioning of the device.

Results: Between June 2010 and December 2016, we enrolled 70 consecutive patients treated on chest, abdomen or head and neck district, most of them receiving volumetric Intensity Modulation RT (IMRT)/IGRT . In those patients who received RT on the abdomen, the maximum absorbed dose was significantly less than in the others ($p < 0.0001$); nevertheless, we did not observe any statistically significant difference in the analyzed electrical parameters (P and R wave amplitude, pacing threshold, lead impedance and residual duration of the battery estimated by the device itself). We observed only two complications (2.83%): in one patient, the RV pacing threshold increased by 1.5 fold (threshold post-RT 1.2 V @ 0.5 msec), in the second one we found a drastic reduction in the battery life (preRT estimated life 1.5 yrs, postRT < 0.5 yrs., needing an urgent device replacement). In both case the maximal absorbed dose at the device was lower than 2 Gy.

Conclusions: Radiotherapy is a safety treatment even in patients with PM or ICD. A standardized protocol is useful because it allows a prompt detection of eventual damages even in pts generally defined at low risk.

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IN VIVO DOSIMETRY REQUIRES HIGH WORKLOAD?

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Aims: *In vivo* Dosimetry, IVD, final step of a Quality Assurance protocol in Radiotherapy should be included in a clinical routine. Such activity is strongly recommended, in Italy, by the ISTISAN. Although modern technologies tend to reduce workload, it remains a time-consuming employment. However, some methods, if well organized, are particularly simple and require little work. This paper reports the IVD results obtained by the SOFTDISO software (SW) (Best Medical Italy).

Methods: SOFTDISO reconstructs in quasi-real time the dose at the isocenter (Diso), with inhomogeneity correction, in the patient from the transit signal acquired by the Electronic Portal Imaging Device (EPID) and the -analysis for the day-to-day EPID images. The SW commissioning requires only few measurements. SOFTDISO is interfaced with TPS (Pinnacle 9.10, Philips) and Portal Imaging device (IviewGT, Elekta) via DICOM. It uses CT scans and the RTPlan to buildup patient data generation. Data are recorded in DICOM-RT files in IviewGT database and through automatic synchronization the operator can explore data Results.

Results: About a week of team work by medical physicist, product specialist and system administrator is used to interface, through DICOM nodes, all the SW (SOFTDISO, PINNACLE, IviewGT). Another week is needed to train radiation therapists for a proper procedure. The SW measure commissioning required no more than 1 hour. To load a new patient on SOFTDISO it takes about 3 minutes. The patient load on the IviewGT require 2 minutes. The IviewGT database syncronizes, at night, whit the SOFTDISO database. From software interface you run automatic synchronization for each patient (<1 minute) and the system shows the results of the analysis. It display, in green, the tests within tolerance levels previously defined and in red the tests out of tolerance (Figure 1). The staff member should only analyze the latter in detail, saving time.

Conclusions: In our center, approximately 8 of the 20 patients treated per day are subjected to IVD investigation. The daily workload has been estimated in 2 minutes for patient. For the new patients this time grow up to 7 minutes. A further time is required to discuss the out of tolerance test among medical physicists and radiation oncologists. This time depends on the complexity of the problems encountered. The current IVD workload is about half an hour per day once the learning phase is over.

Figuere. Figure shows a typical result after automatic syncronization. In green the test within tolerance levels in red the test out of tolerance. In this case, on 20 January 2017, you will investigate the R value for the field 227a and not for the field 055a saving time.

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RADICAL RADIOTHERAPY IN PROSTATE CANCER PATIENTS WITH SYNCHRONOUS BONE OLIGOMETASTASIS AT DIAGNOSIS: A MONOINSTITUTIONAL EXPERIENCE

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Aims: To report the clinical results, obtained in a monoinstitutional experience, in prostate cancer (PCa) patients (pts) with synchronous oligometastatic bone

disease treated with radiotherapy with "radical" intent.

Methods: From May 2009 to December 2015, 16 oligometastatic (for the purpose of this analysis, no more than 2 bone metastases) PCa pts underwent radiotherapy on bone metastasis (2Gy equivalent dose, EQD2 >40 Gy, / =2.2), on the pelvic ± LA nodes (median EQD2 52.2 Gy, as prophylactic irradiation), to the prostate and seminal vesicles (74.2 Gy/28 fr and 65.5 Gy/28 fr, EQD2 88 Gy and 77.7 Gy respectively, / =1.5), in association with androgen deprivation therapy (ADT). All patients were treated with an IGRT technique (Tomotherapy®). Patients' characteristics are reported in Table.

Results: After a median follow up of 37.6 (1.2-78.2) months, 3 patients have deceased owing to prostate cancer progression, while 13 are still alive. Seven pts experienced a biochemical and clinical relapse (1 in the irradiation field and 6 out of field), but 2 patients who interrupted ADT more than 3 years ago are still free from progression. Acute and late toxicity were very mild, with only one late G3 rectal toxicity, solved by Argon Plasma applications. With respect to bone, no Grade≥1 toxicity were reported. The median biochemical relapse-free survival (bRFS) and distant progression-free survival (calculated from the first day of RT) were 27.2 and 30.1 months respectively.

Conclusions: A "radical" approach to oligometastatic prostate cancer with a synchronous irradiation on all sites of disease seems to show promising results in terms of both biochemical control and distant progression-free survival, with a good toxicity profile. We hope that these good results could be confirmed with a longer follow up and a largest number of patients.

P303

ROLE OF INTERIM 18F-FDG-PET/CT FOR THE EARLY PREDICTION OF CLINICAL OUTCOMES OF LUNG AND OESOPHAGEAL CANCER DURING RADIOTHERAPY OR CHEMO-RADIOTHERAPY A SYSTEMATIC REVIEW

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Aims: Non-Small Cell Lung Cancer (NSCLC) and oesophageal cancers are aggressive diseases. The possibility to early stratify patients as responsive and non-responsive with a non-invasive method is extremely appealing. The uptake of Fluorodeoxyglucose (18F-FDG) in tumours, provided by PET images, has been proved to be useful to assess the initial staging of the disease, recurrence, and response to chemotherapy or chemo-radiotherapy (CRT). In the last years, efforts have been focused on the possibility to use ad interim 18F-FDG-PET/CT (PETint) to evaluate response already during radiotherapy (RT). This review assembles the comprehensive literature to evaluate where and whether PETint may offer predictive potential in NSCLC and oesophageal cancer, since controversial findings have been reported.

Methods: several searches were completed on Medline and Embase database, combining different keywords. Original papers published in English language from 2005 to 2016 with studies involving PETint in patients with NSCLC and oesophageal cancers treated with RT or CRT were selected.

Results: Twenty-one studies, reporting on 627 patients were selected for NSCLC, while 13 studies, reporting on 697 patients, were selected for oesophageal cancers. The timing for the acquisition of PETint did not find agreement among researchers, being distributed from two to six weeks after the start of RT, corresponding to doses ranging from 14 Gy to 50 Gy. Globally for NSCLC, all the studies showed that PETint is useful to identify responder groups and different survival rates. For oesophageal cancers, eight studies have shown an association between a variation of PET parameters and tumour response, whilst five could not confirm the predictivity of PETint. The feasibility of biologically adaptive radiotherapy was investigated in 7 studies for NSCLC and 1 for oesophageal cancers, showing a great potential for loco-regional control in NSCLC and more sparing of normal tissues.

Conclusions: All the analysed papers denoted PETint as promising and challenging examination for early assessment of outcomes during CRT, sustaining its predictivity in NSCLC, while more controversial findings for oesophageal cancer do not allow to definitively establish its predictive and prognostic value. The reasons that possibly have caused contradictions, such as the lack of univocal PET parameters and timing of acquisition, demand further research with prospective and uniform protocols and methods of analysis.

P304

ACUTE DERMATITIS IN BREAST CANCER PATIENTS DURING RADIATION THERAPY: TREATMENT AND PREVENTION

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Aims: Radiation therapy is an important role in breast cancer treatment, both in the postmastectomy setting and as an integral component of breast-conserving surgery. Radiation dermatitis is the most common acute side effect of radiotherapy to the breast.It is frequently associated with pain, pruritus, burning, and discomfort, which affects the patient's quality of life (QOL) and negatively affects treatment adherence.The radiation skin reaction is a combination of radiation injury and the subsequent inflammatory response. Ionizing radiation damages the mitotic ability of stem cells within the basal layer preventing the process of repopulation and weakening the integrity of the skin. Skin toxicity is evident one to four weeks after beginning treatment and can persist for several weeks post treatment. The severity of the reaction varies from mild erythema to moist desquamation and rarely to radionecrosis. Chemotherapy based on taxanes, antracyclines with "recall" effect can produce a worse cosmetic effects after radiotherapy.The aim of this study was to focus on the effectiveness of hyaluronic acid, calendula officinalis, and CM-beta glucan (Fairest RT ® cream) in reducing skin toxicity in patients affected by breast cancer treated with RT.

Methods: From September 2016 to March 2017 at Department of Radiotherapy of "Casa Sollievo Della Sofferenza" Hospital in San Giovanni Rotondo, 50 patients (pts) affected by breast cancer were treated with adjuvant radiotherapy after breast-conserving surgery or radical mastectomy. The total dose delivered was 50 Gy +/- boost 10-14 Gy with conventional fractionation. 35 pts with breast conservation surgery received whole breast irradiation with two tangential fields using either 4 or 6-MV photons.While in 15 pts with radical mastectomy RT was delivered to the chest and supraclavicular nodes with a single field using 6-10 Mev electrons.Moreover in these 15 pts a bolus was applied to the chest wall daily. Among all 50 pts, 16 pts were treated with taxan based chemotherapy before RT and 34 pts were treated with concomitant hormonal therapy. Patients were instructed to begin applying Fairest RT® cream twice a day, during radiotherapy and one month after the end of RT. Fairest RT ® cream is triaction cream with soothing, hydrating and repairing action containing hyaluronic acid, calendula officinalis and CM-beta glucan. The acute skin reactions were classified according to RTOG scores weekly.

Results: 25 pts developed a grade 2, 20 pts grade 1 and 5 pts grade 3 acute radiodermatitis. There was no significant difference between patients curated with chemotherapy before RT and patients curated with concomitant hormonal therapy. The acute skin reaction was observed starting from at control at week 3 for patients treated with radiotherapy conserving surgery and at week 2 for patients on the chest wall after radical mastectomy. 5 patients with larger volume of the breast developed epitheliolisis. All pts with mastectomy experienced grade 2 dermatitis. No hypersensitive reaction to the cream has been reported.

Conclusions: The prophylactic and curative use of the cream containing hyaluronic acid, calendula officinalis, and CM-beta glucan is appropriate to reduce the incidence of high grade skin reaction and to improve quality of life during radiotherapy.

P305

STEREOTACTIC BODY RADIATION THERAPY (SBRT) FOR ELDERLY PATIENTS AFFECTED BY ISOLATED METASTASIS FROM DIFFERENT PRIMITIVE TUMORS

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Aims: To retrospectively evaluate the outcome of Stereotactic Body Radiation Therapy (SBRT) in the treatment of elderly patients affected by isolated body metastasis from different primitive tumors.

Methods: 70 patients with isolated body metastasis were treated. Median age at diagnosis was 73 years (range 65-88). The most common SBRT fractionation scheme was 5x7 Gy (total dose 35 Gy). The primary end points were Local Control (LC) and Toxicity. Secondary end points were Overall Survival (OS) and Cancer Specific Survival (CSS). Response to radiotherapy was assessed according to RECIST Criteria v1.1. Toxicity was registered according to Common Terminology Criteria for Adverse Events (CTCAE) v 4.0. We performed survival analysis with the Kaplan-Meier method. The correlation between time actuarial incidence and clinical parameters was studied.

Results: Median Follow-up was 19,13 months . Local control at 2 and 3 years was 87%. The 2-year OS and CSS were 84% and 87%, respectively, while the 3-year values were 73% and 76%. PFS at 2 and 3 years was 73% and 58%, respectively. On univariate analysis, KPS > 90 is statistically correlated with improved OS and CSS ($p<0,05$). Treatment related Grade >2 late toxicity was recorded in 6 patients. Actuarial 2 year late toxicity > 2 was 11%, while 3 year finding was 17%.

Conclusions: Ablative Radiotherapy represents a safe, effective and minimally invasive treatment modality for elderly oligometastatic patients who are judged unfit for systemic therapy.

P306

RADIOTHERAPY IN ELDERLY PATIENTS WITH GASTROINTESTINAL TUMORS OF THE UPPER ABDOMEN: A SYSTEMATIC REVIEW

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Aims: To evaluate feasibility and outcome of radiotherapy (RT) in the complex setting of gastrointestinal (GI) tumors of the upper abdomen in elderly patients.

Methods: A systematic review of the literature about patients aged ≥ 65 years, who underwent RT for GI neoplasms of the upper abdomen was performed using the PRISMA methodology.

Results: A total of 9 papers, amounting to 4255 patients, were included in the analysis. RT was prescribed as single modality treatment or in combination with surgery and/or chemotherapy. Irradiation was delivered by megavoltage external-beam RT with conventional fractionation, hypofractionated RT based on stereotactic technique, or proton therapy. RT dose ranged between 22 and 70 Gy (median 50 Gy) and was delivered to different targets depending on tumor and treatment aim and setting. Treatment-related severe (G ≥ 3) toxicity was reported in 4 out of 9 studies (total number of patients: 109) with 24 cases of acute toxicity (22.0%) and 3 cases of late toxicity (2.8%). When considering outcome in all patient group, overall survival ranged from 6.4 to 69 months (median 22.6 months) in patients who received radiation treatment, and from 14.3 to 31.3 months (median 24.2 months) in patients who were not radio-treated. Median 2-years survival rates were 49% (range 6.6-75.5%) and 50.4% (range 31-58%) respectively. Anyway, considering only studies comparing RT-treated and non-RT-treated patients, median survival and 2-years survival were 28.3 months (range 22.6-69), and 56% (range 49-75.5%) respectively in treated patients vs 24.2 months (range 14.3-31.2, p=0.200) and 50.4% (range 31-58%, p=0.486) in non-treated patients.

Conclusions: RT of upper GI tumors in elderly patients seems to be tolerable and safe, particularly in terms of late toxicity, both alone or combined with other treatment modalities. It may contribute to prolong survival even when other therapies are excluded because of age and/or comorbidities. Further analyses and prospective trials enrolling elderly patients are needed to better define the risk/benefit ratio in this relevant group of neoplasms.

P307

OUTCOMES IN ELDERLY PATIENTS WITH HIGH GRADE GLIOMA TREATED ACCORDING TO STUPP SCHEDULE: RETROSPECTIVE MONO-INSTITUTIONAL STUDY

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Aims: To evaluate overall survival (OS) and disease free survival (DFS) in elderly patients (65 year and older) compared with patients younger than 65 affected by high-grade glioma (HGG) treated according to Stupp schedule.

Methods: From 2001–2016, we retrospectively evaluated a total of 73 patients with malignant glioma (anaplastic astrocytoma and glioblastoma) treated with surgery and postoperative radiochemotherapy temozolomide (TMZ) based according to Stupp schedule. A total of 44 of 73 patients received also sequential TMZ. The prescribed radiotherapy dose was 60 Gy over 6 weeks in daily fractions of 2 Gy for 63 patients;10 patients received a prescription dose <60 Gy (range 28-56 Gy). Prognostic factors considered were: performance status (according to Karnofsky scale), extent of surgery, MGMT status, hemoglobin levels before radiotherapy starting. Acute al late toxicities were recorded according to RTOG scale. The Log-Rank test was applied to estimate differences in overall survival and disease free survival among two analyzed groups (<65 years vs ≥65 years). Chi-square test was applied to estimate difference in terms of toxicity among the two groups.

Results: Of the 73 analyzed patients, 41 were younger than 65 and 32 patients were 65 years or older. The median OS was 12 months (95% CI, 13-45 months) in elderly patients and 22 months (95% CI, 24-41 months) in patients younger than 65 (p value: 0.133). Median DFS for patients ≥65 years and <65 years was 5 months (95% CI, 3-25 months) and 13 months (95% CI, 10-25 months) respectively (p value:0.192). About acute toxicity, the main observed adverse effect was leuco-thrombocytopenia (41% of all patients), 34% of the observed toxicity affected elderly patients (25% of these were grade 4) and 7% in patients < 65 years (p value 0.004). No relevant late toxicities were observed.

Conclusions: Management of HGG elderly patients is controversial. Several authors suggest a poor benefit of Stupp schedule in patient > 65 years. From this study not significant differences in terms of OS and DFS were observed between <65 years vs ≥65 years patients, both receiving Stupp schedule. However, in spite of TMZ safety profile, a greater acute toxicity occurred in

patients ≥ 65 years, suggesting more caution during elderly patients treatment.

P308

ANALYSIS OF PREDICTORS OF POOR COMPLIANCE TO CONCOMITANT RADIO-CHEMOTHERAPY (RT-CHT) IN ELDERLY HEAD AND NECK PATIENTS

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Aims: Head and neck older patients undergoing concomitant RT-CHT sometimes need to discontinue chemotherapy during RT. Aim of this work is the analysis of predictors of poor compliance to concomitant chemotherapy.

Methods: We performed a retrospective analysis of 32 head and neck patients older than 65 years, that underwent concomitant chemo-radiotherapy in our department, from January 2012 to December 2016. We collected clinical information (age, sex, weight, BMI, use of induction chemotherapy) and blood tests (neutrophil, lymphocytes and platelet counts, hemoglobin, neutrophil to lymphocytes ratio:NLR). We selected as an endpoint the number of concomitant chemotherapy cycles (with a cut-off of ≤4 cycles). Clinical and ematochemical parameters were then correlated with the endpoint (≤4 cycles of chemotherapy) with an univariate analysis (Chi-Square) and a multivariate analysis (Binary logistic regression). ROC curve was also generated.

Results: A total of 32 patients were included in this analysis, with a median age of 69 years (mean 70 years, range 65-75 years). At univariate analysis (Chi-Square Test) the use of induction chemotherapy (p:0.036), the weight (p:0.048), the BMI (p:0.046) were significantly correlated with the suspension of chemotherapy. At multivariate analysis only the use of induction chemotherapy resulted significant, with a R2:0.281, and an AUC:0.725 (95%CI:0.54-0.90).

Conclusions: The knowledge of the predictors of an uncomplete concurrent chemotherapy regimen could improve the selection of patients that may benefit from other strategies of therapy, such as concurrent cetuximab, or adjuvant chemotherapy after the radiation therapy course.

P309

CETUXIMAB AND RADIOTHERAPY IN ELDERLY PATIENTS AFFECTED BY LOCALLY ADVANCED SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK (HNSCC): SINGLE CENTER EXPERIENCE

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Aims: Despite absence of a randomized study comparing the combination of cisplatin or cetuximab with RT, bio-radiotherapy is a possible treatment in locally advanced HNSCC (LAHNSCC) in light of data provided by Bonner et al. In current pratice, the use of CTX is a suitable option in patients inelegible to receive cisplatin due to comorbidities and frail general conditions. The aim of our study is to report the efficacy of CTX-RT in elderly patients affected by LAHNSCC.

Methods: We performed a retrospective, single-center analysis consecutively treated at our Department. Following the definition of the National Institutes of Health, patients with age> 65 years were defined as old. Baseline comorbidities were evaluated according to the Charlson's Comorbidity Index (CCI). RT was administred with a 3D conformal technique unti lJanuary 2012, then IMRT was the only treatment modality in place. A total dose of 66 – 70Gy was administered either with a conventional fractionation (2 Gy per fraction in 7 weeks) or with an IMRT-SIB technique (highest dose per fraction: 2.12 Gy) over 33 fractions. Concurrently, CTX was given at a loading dose of 400 mg/mq one week before the start of RT, then of 250 mg/mq weekly (max: 8 cycles). DFS was defined as the time from the end of CTX-RT to first radiological confirmation of disease progression or death. OS was defined as the time from the end of CTX-RT to death from any causes.

Results: Between February 2007 and March 2017, 23 patients were included in our analysis. The median age at diagnosis of was 70 years (range: 65-80). The median age-adjusted CCI was 7 (range: 5-10). Treatment and patients' characteristics are summarized in Table 1. The median number of CTX cycles was 6 (range 2-8). The median relative dose intensity (RDI) of CTX was 75% (range 25-100). At a median follow-up of 18 months (range 0-42), the median DFS was 3 months (range 0-22), the median OS was 9 months (range 0-16). 3 (13%) patients died due to toxicity related treatment, 3 (13%) from other causes, 6 (26,1%) due to disease progression. At the time of analysis 11 patients are alive.

Conclusions: The association between CTX-RT is associated with poor tolerance in patients unfit for chemotherapy. Considering the significantly shorter life expectancy patients unfit for chemotherapy, CTX-RT seems to be a rational therapeutic option but prospecti-

ve cohorts in unfit population would help target which patients obtain significant benefits from CTX-RT.

Table 1.

Charateristics	Patients (total number: 23)
Sex	
Male	19 (82,6%)
Female	4 (17,4%)
ECOG	
0	10 (43,5%)
1	8 (34,8%)
2	5 (21,7%)
Pack years	
0	3 (13%)
≤10	1 (4,3%)
10-20	7 (30,4%)
>20	12 (52,3%)
Primary localisation	
Oropharynx	10 (43,6%)
Larynx	5 (21,7%)
oral cavity	3 (13%)
hypopharynx	2 (8,7%)
nasopharynx	1 (4,3%)
synchronous tumors	2 (8,7%)
Stage	
III	6 (26,1%)
Iva	12 (52,3%)
Ivb	2 (8,7%)
Unkokwn	3 (13%)
RT tecnique	
3DCRT	8 (34,8%)
IMRT	15 (65,2%)
RT Total dose (Gy)	
70	13 (56,5%)
69.96	3 (13%)
66	6 (26,1%)
40	1 (4,4%)