Randomized study of hypofractionated Radiotherapy vs ultraboost on Dominant Intraprostatic Lesion for prostate cancer

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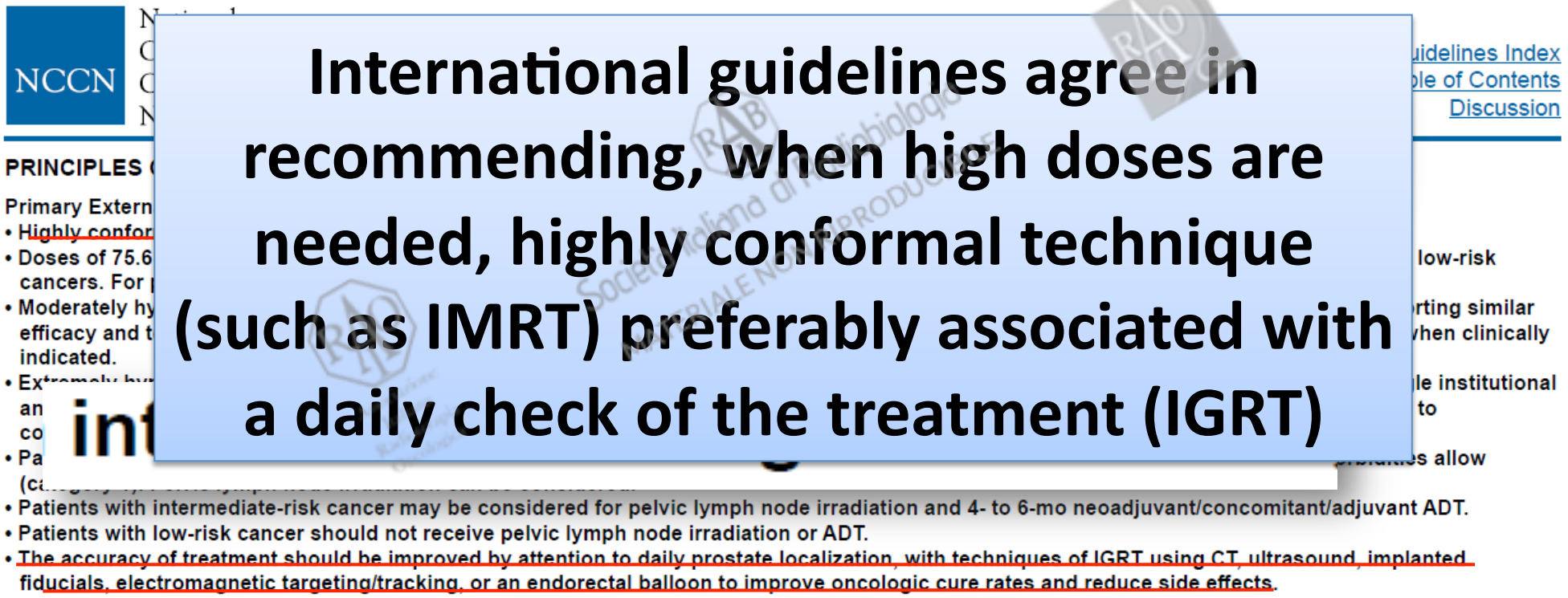
Fondazione del Piemonte per l'Oncologia — CANDIOLO

ISTITUTO DI CANDIOLO

Background

Tumor control probability is related to the RT dose



International guidelines agree in recommending, when high doses are needed, highly conformal technique (such as IMRT) preferably associated with a daily check of the treatment (IGRT)

Background

Int J Radiat Oncol Biol Phys. 2002 Jul 1;53(3):595-9.

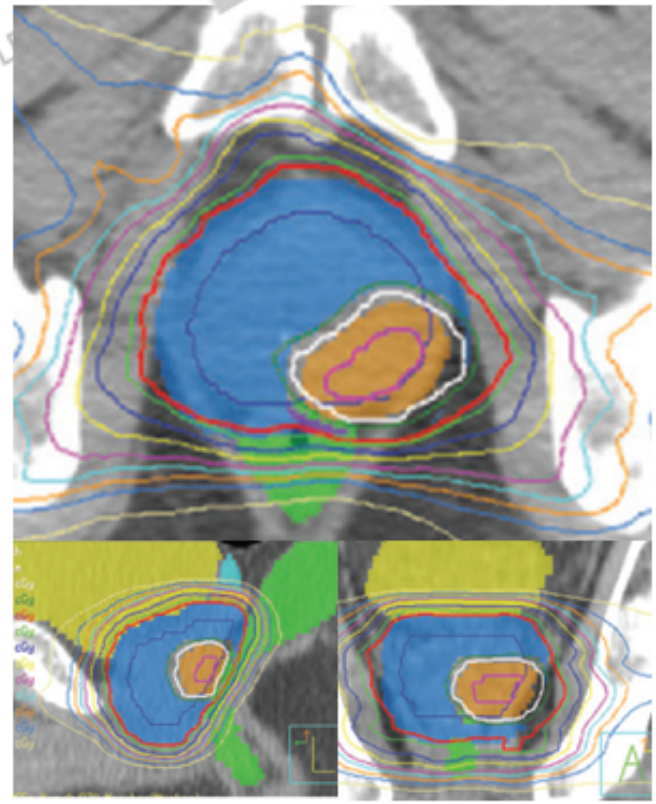
Analysis of intraprostatic failures in patients treated with hormonal therapy and radiotherapy: implications for conformal therapy planning.

Cellini N[1], Morganti AG, Mattiucci GC, Valentini V, Leone M, Luzi S, Manfredi R, Dinapoli N, Digesu' C, Smaniotto D.

CONCLUSION: The results of this analysis seem to confirm some histologic findings observed in patients undergoing prostatectomy for local recurrence after radiotherapy that suggest that local recurrence usually originates in the primary tumor rather than in focal prostatic intraepithelial neoplasia. This observation might justify the application of conformal therapy procedures aimed at identifying the gross tumor volume, in the phase of boost, exclusively with the primary tumor.

Literature data confirm, in prostate cancer, local recurrence usually occur in the primary tumor (DIL), rather than in focal prostatic intraepitelial neoplasia.

Selective irradiation of DIL by dose escalation



Dominant Intraprostatic Lesion (DIL)

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Direttore Pietro Gabriele

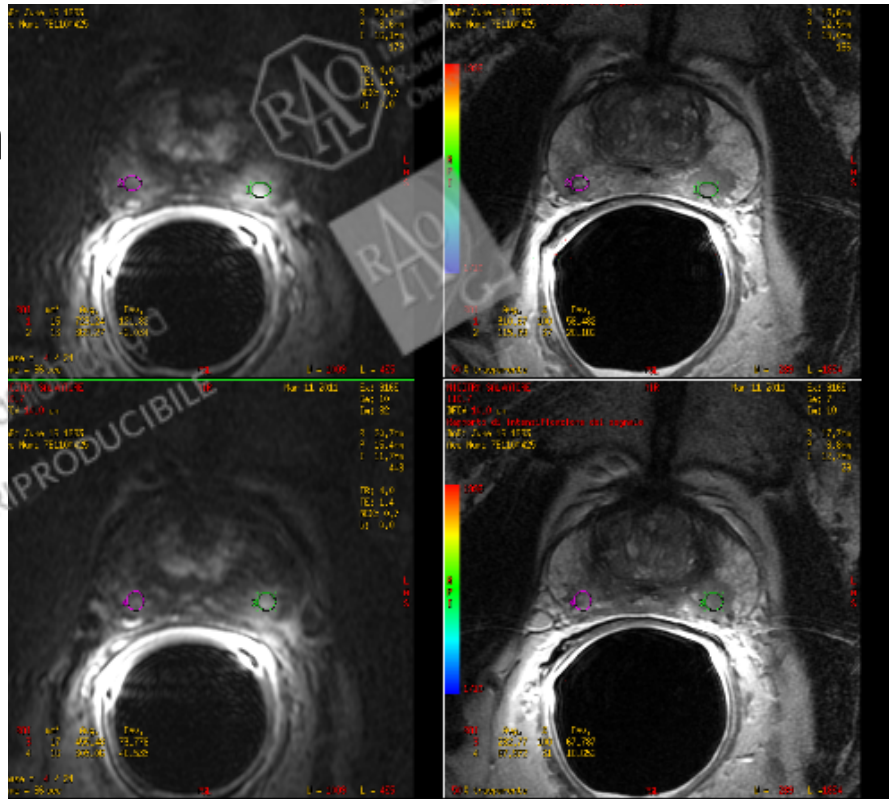
Helical Tomotherapy guided by Multimodality Imaging:a tool for a "safe" dose escalation for prostate cancer.

GRUPPO di LAVORO:

Aim of DIL study

Primary endpoints

- Dosimetric and clinical feasibility of dose-escalation (in terms of acute and late toxicity)
- Role of MRI in identifying DIL
- Correlation between pre-treatment imaging parameters (position of DIL(s), volume, etc.) and toxicity.



Secondary endpoints

- Outcome (Biochemical control)

- Correlation of outcome with quantitative analysis of MRI images

DIL-study design

Intermediate and high risk prostate cancer patients with DIL(MRI)

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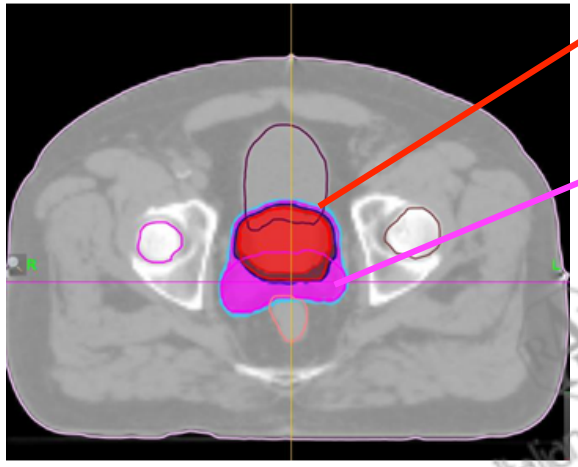
No-DIL (ND)

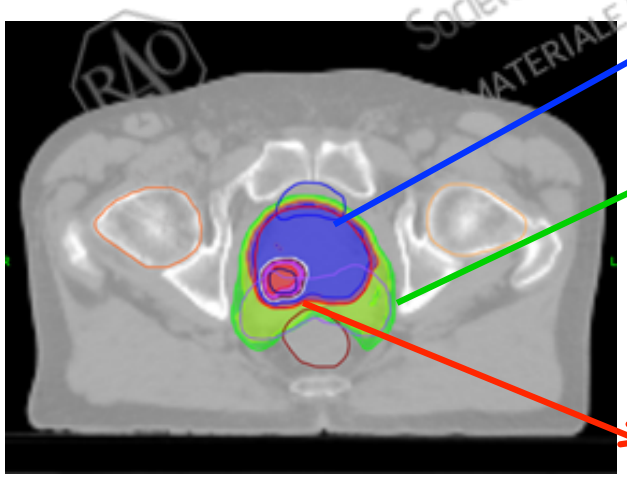


Prostate: 75.2Gy/32 fr (2,35/day)
(α/β=3 → EQD2=80.5Gy)

SV: 67,2 Gy/32 fr (2,1/day)
(α/β=3 → EQD2=68.5 Gy)

± Pelvis: 54.4Gy/32 fr (1,7/day)
(α/β=3→ EQD2=51.2 Gy)

DIL (D)



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(α/β=3→ EQD2=51.2 Gy)

DIL: 83.2 Gy/32 fr (α/β=3→ EQD2 93.2 Gy)

+ ADT (neoadjuvant, concomitant and adjuvant) 6 mth/2y

Inclusion criteria

- Histologically confirmed diagnosis
- **Intermediate / high risk class**, according to 2011-NCCN-guidelines (T2b-T2c-T3a N0M0 and / or Gleason score> 7, and / or PSA> 10 ng / ml
- Karnofsky Performance Status (KPS) = 90-100;
- **Evidence of DIL, by multiparameter MRI**
- Patient compliance to Tomotherapy
- Informed consent

Exclusion criteria

- KPS < 90;
- **previous TURP/HIFU**
- **Severe comorbidity**: severe heart disease, patients with pacemakers, ulcerative colitis, Crohn's disease, decompensade diabetes, severe hypertension, severe obesity, psychiatric disorders
- **> 2 DIL**
- **Ratio DIL volume/prostate gland volume > 20%**
- **Distance between DIL and rectum < 3 mm.**

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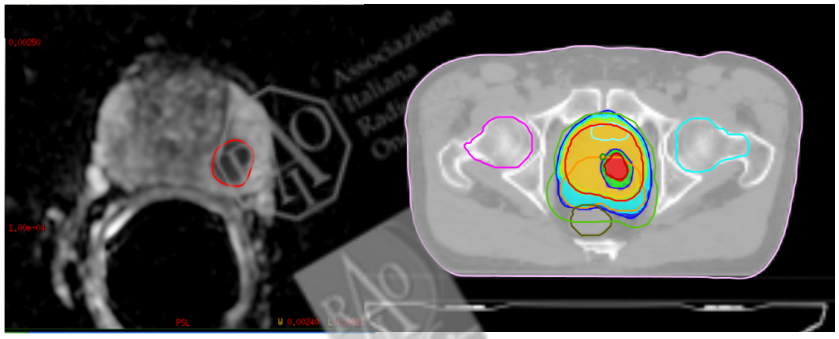
Material and methods

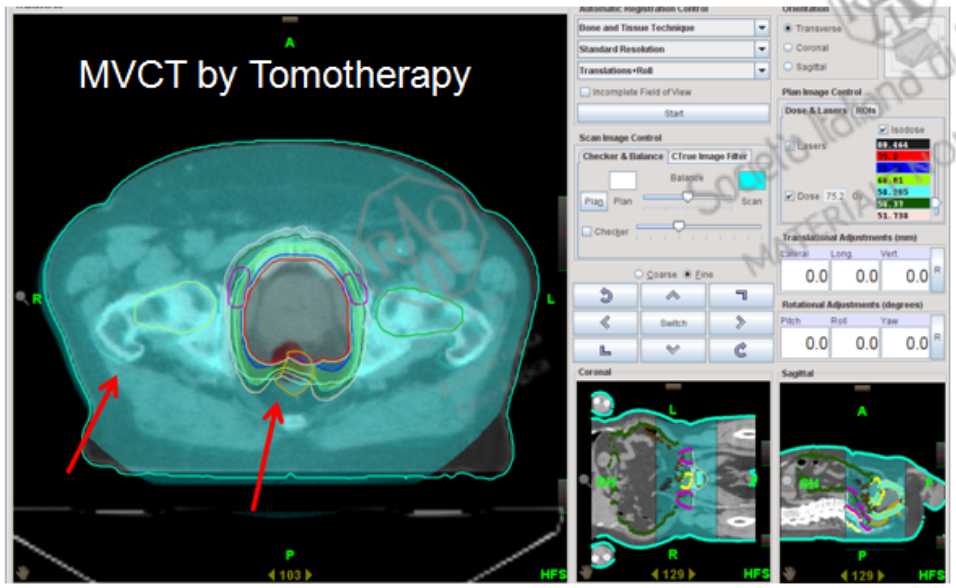
- March 2012 - May 2016: 38 patients enrolled
- All patients submitted to multiparameter MRI showing DIL(s)

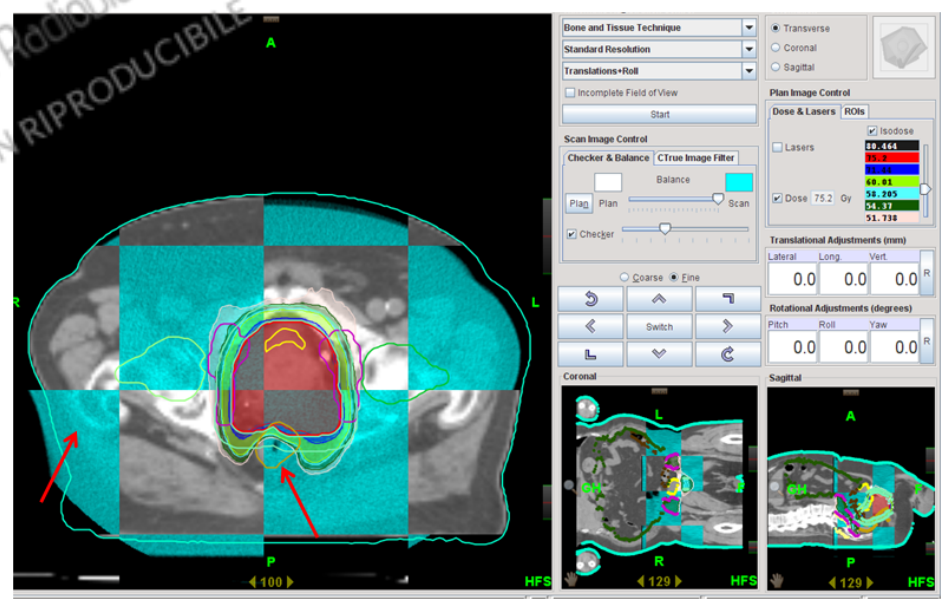
Patient characteristics	D-arm	ND-arm
Patient n°	18	20
Median age	70 (range 56-77)	71,8 (range 67-80)
Median iPSA (ng/ml)	7,05 (range 4.12-18.5; mean 8.45)	7,09 (range 3,7-15; mean 7,4)
Gleason Score	Patient number	Patient number
5	1	0
6	9	10
7	8	8
8	0	1
ADT	13	17

Material and methods

- All DIL contoured on MRI fusion (with Radiologist)
- Helical SIB-IMRT delivered using Tomotherapy
- Daily IGRT by integrated MV-CT.







- **Acute and late toxicities were evaluated according to RTOG-EORTC scale.**
- **Outcome evaluated as biochemical control (according to Phoenix criteria).**

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Results

Mean FU: 25 months (range 6-40)

DIL irradiation NOT feasible in 3 patients (2 due to DIL volume/Prostate volume ratio > 20%; 1 due to rectum-DIL distance < 3mm)

ACUTE TOXICITY	G2		> G3	
	Gastrointestinal	Genitourinary	Gastrointestinal	Genitourinary
D-arm	6%	12%	0%	0%
ND-arm	5%	5%	0%%	5%

LATE TOXICITY	≥ G2	
	Gastrointestinal	Genitourinary
D-arm	0%	0%
ND-arm	0%	0%

At last FU overall bDFS was 100%. Only 1 patient in each group was again in ADT.

Updated September 2016

Conclusion

Our results show ultraboost on the DIL, up to an EQD2 of 93,2 Gy, is feasible and safe by Tomotherapy, without increasing acute or late toxicities. However, in order to assess late toxicity and biochemical response, a longer follow-up is needed.