DICHIARAZIONE

Relatore: Giuditta Chiloiro

Come da nuova regolamentazione della Commissione Nazionale per la Formazione Continua del Ministero della Salute, è richiesta la trasparenza delle fonti di finanziamento e dei rapporti con soggetti portatori di interessi commerciali in campo sanitario.

- Posizione di dipendente in aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Consulenza ad aziende con interessi commerciali in campo sanitario **(Varian Medical Systems)**
- Fondi per la ricerca da aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Partecipazione ad Advisory Board **(NIENTE DA DICHIARARE / NOME AZIENDA)**
- Titolarietà di brevetti in compartecipazione ad aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Partecipazioni azionarie in aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Altro

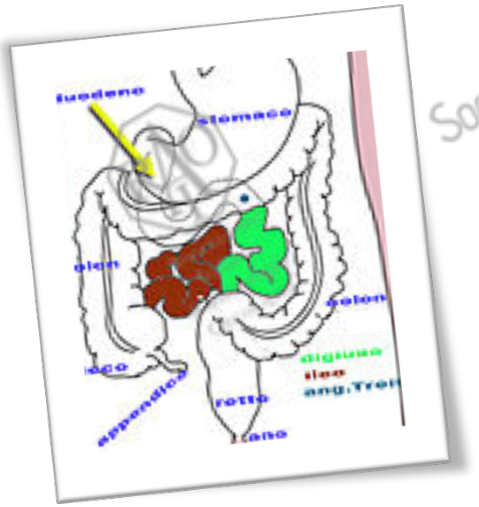
Ipofrazionamento: standard terapeutico e ricerca

Giuditta Chiloiro

Gemelli ART Advanced Radiation Therapy

IPOFRAZIONAMENTO

Trattamento radioterapico che prevede l'utilizzo di dosi per frazione maggiori di 2 Gy con una riduzione del numero di applicazioni



- **Ipofrazionato 3D/ IMRT**
- **SIB/IMRT**
- **SBRT**
- **IORT**
- **BRT**

Scoring Criteria

Therapy/Prevention/Etiology/Harm:

1a:	Systematic reviews (with homogeneity) of randomized controlled trials
1b:	Individual randomized controlled trials (with narrow confidence interval)
1c:	All or none randomized controlled trials
2a:	Systematic reviews (with homogeneity) of cohort studies
2b:	Individual cohort study or low quality randomized controlled trials (e.g. <80% follow-up)
2c:	"Outcomes" Research; ecological studies
3a:	Systematic review (with homogeneity) of case-control studies
3b:	Individual case-control study
4:	Case-series (and poor quality cohort and case-control studies)
5:	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"

Scoring Criteria

- 

- IF (cut off 5)

Hypofractionated 3D RT/IMRT

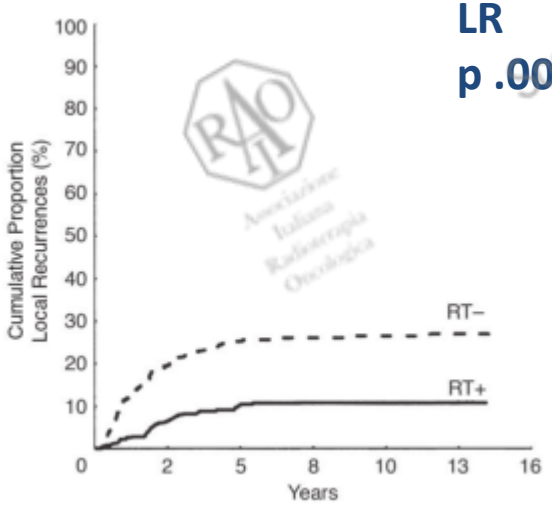
Short course RT: pre TME

Ipofrazionato 3D/IMRT:
Level 1b
IF: 20.982

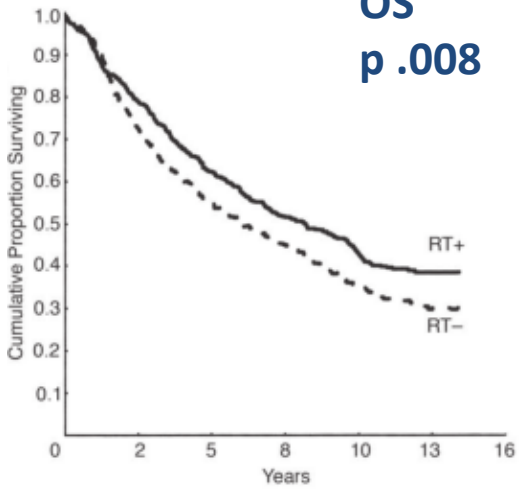
Short ERT (Pre TME era)

Swedish trial | **Short RT+ no TME sugery vs no TME surgery** | **SCRT**

LR
p .0003



OS
p .008



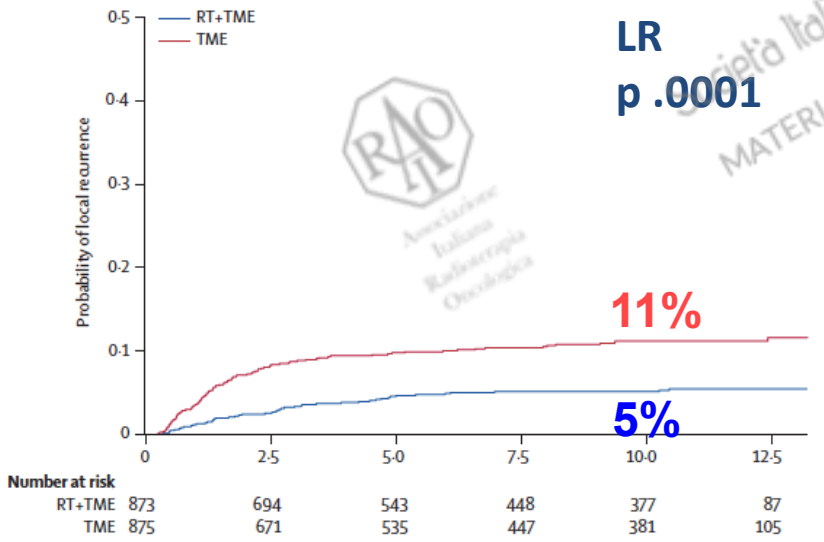
Folkesson J, JCO 2005

Retto

Ipofrazionato 3D/IMRT:
Level 1b
IF: 44

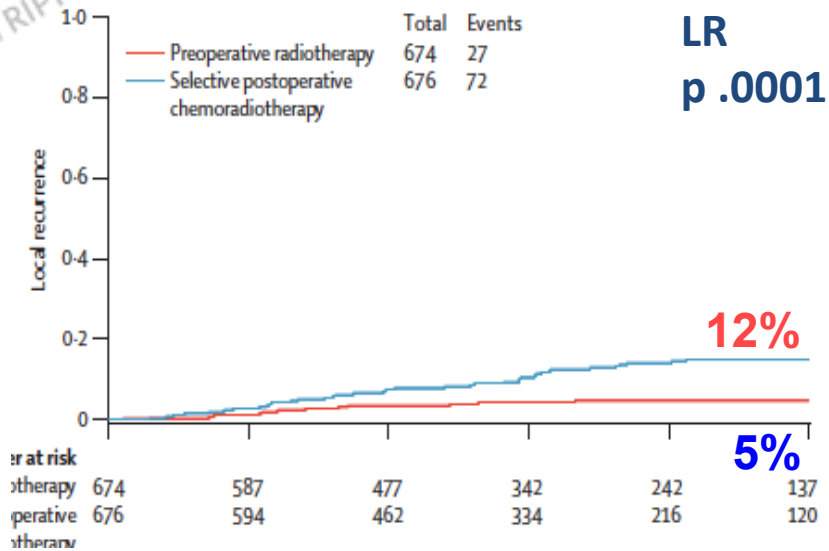
Short course RT: TME era

Short ERT		
Dutch Trial	Short RT+ TME vs TME	SCRT
MRC C07	Short RT+ TME vs TME	SCRT



LR
p .0001

Lancet Oncol 2011; 12: 575–82



LR
p .0001

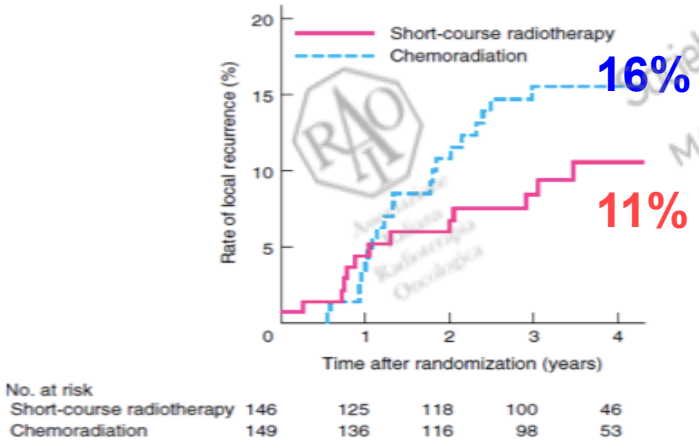
Lancet 2009; 373: 811–20

Ipofrazionato 3D/IMRT:
Level 2b
IF: 5.596
IF: 20.982

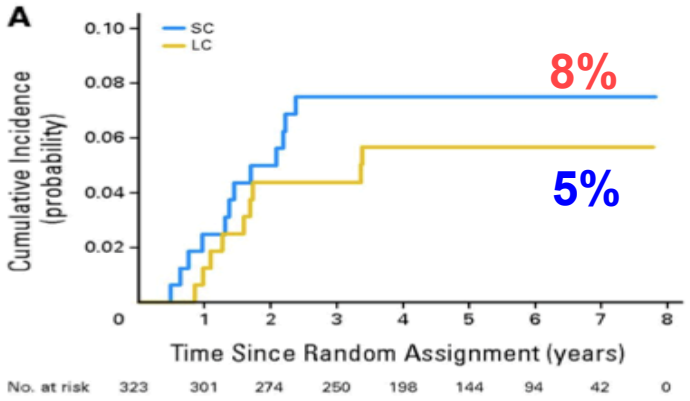
Short course RT: SC vs LC RT

Short vs Long ERT

Polish Trial	Short RT vs Chemo RT
TROG Trial	Short RT vs Chemo RT



Polish Trial (Bujko 2006)
Rate of Local Recurrence (LR)
14.4% vs 18.6%
P= 0.17



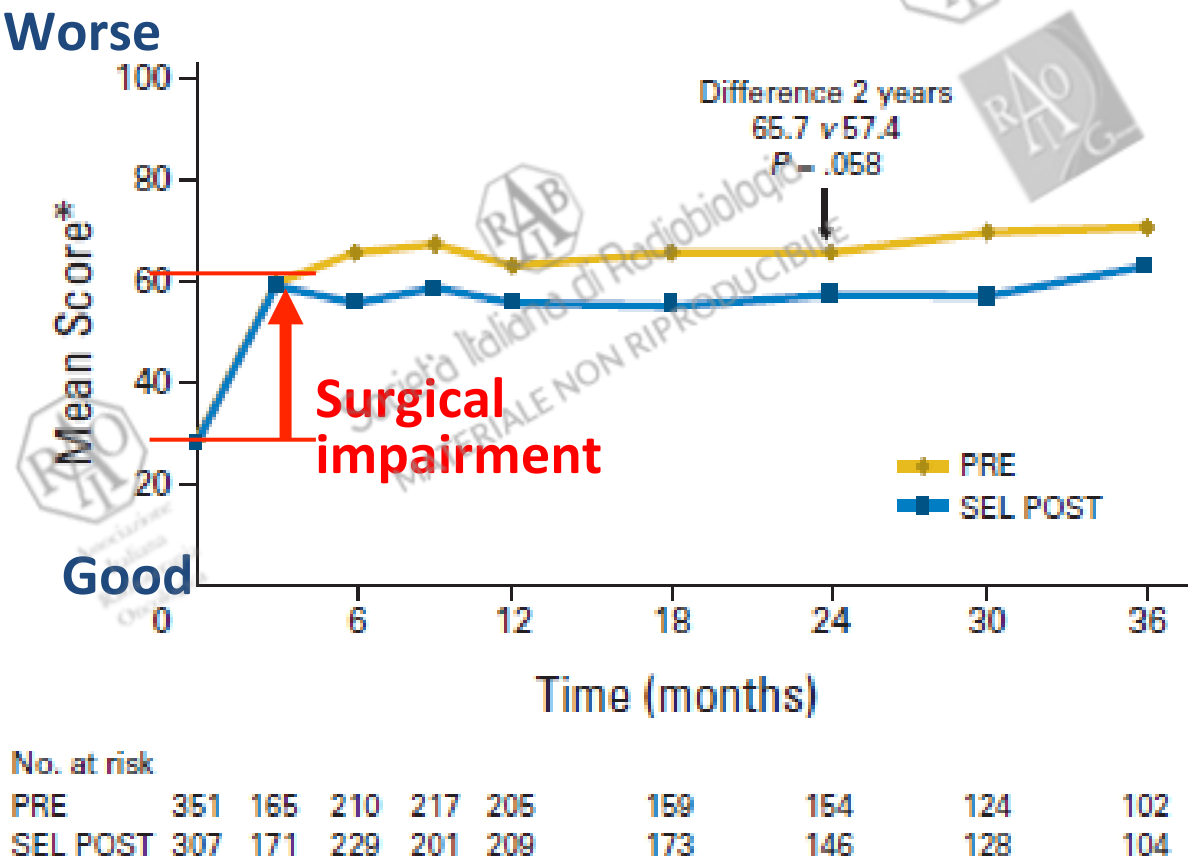
TROG-01 Trial (Ngan 2012)
Cumulative Incidence of LR
7.5% vs 4.4%
P = 0.24

Bujko, BJS 2006, Ngan, JCO 2012

Ipofrazionato 3D/IMRT:
Level 1b
IF: 20.982

Short course RT: toxicity

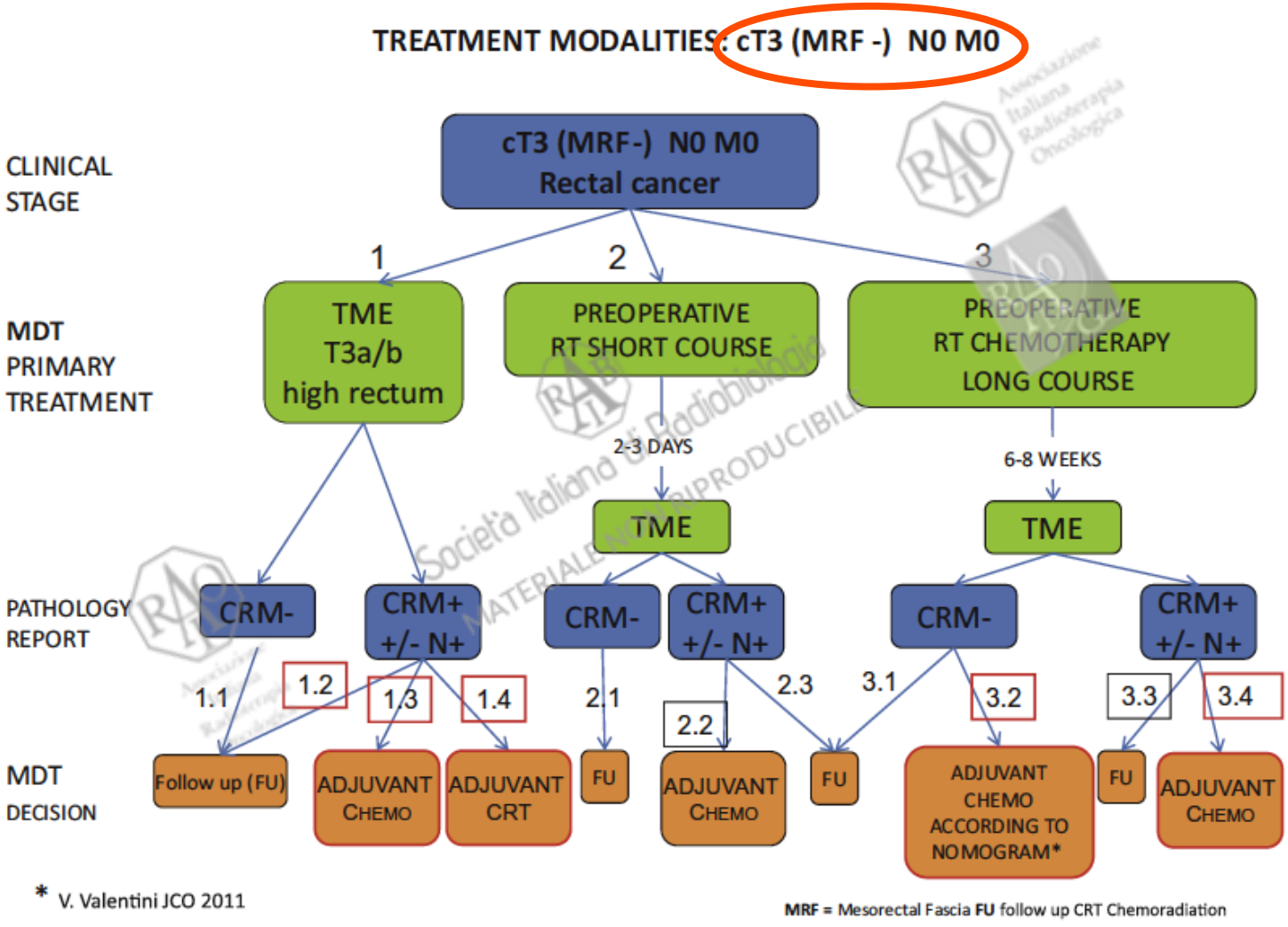
Male Sessual Disfunction



Stephens RJ et Al JCO 2010

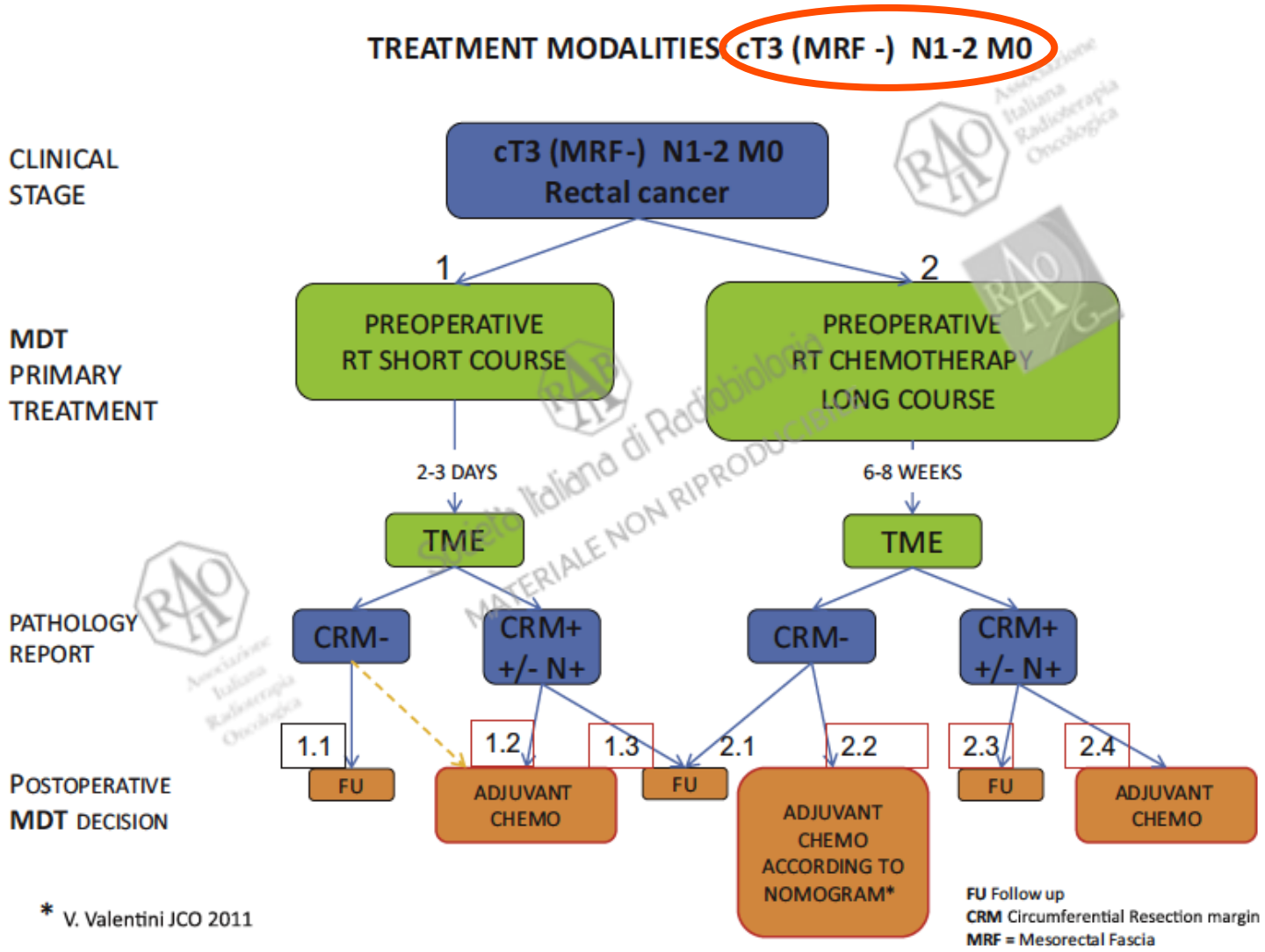
Retto

Ipofrazionato 3D/IMRT



Van de Velde G et Al, EJC,2013

Ipofrazionato 3D/IMRT:



Van de Velde G et Al, EJC,2013

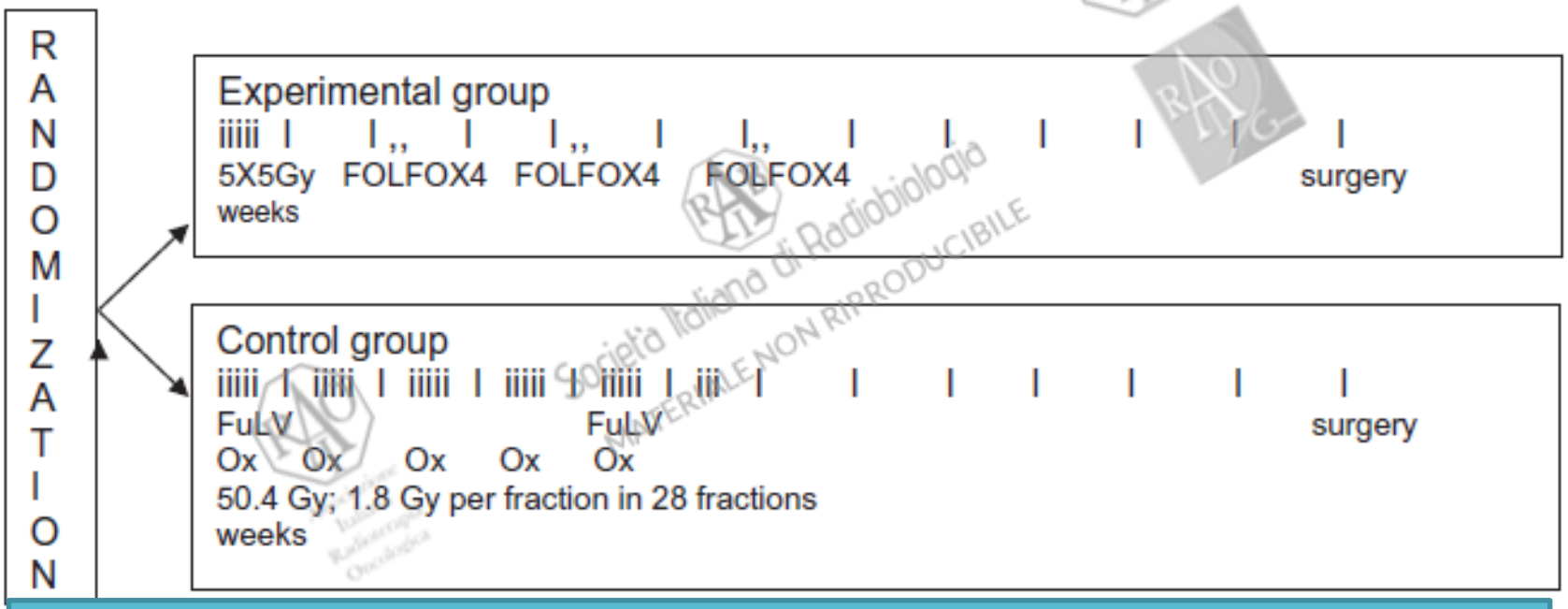
Ipofrazionato 3D/IMRT:
Level 2b
IF: 5.596

SCRT: delayed surgery

- **Stockholm III phase III trial (interim analysis):**
  - same surgery complication than CRT, less than SCRT immediate surgery
- **SCRT phase II trial (112 pts):**
  - ypT0-2: 29.4% vs 11.9% at diagnosis
  - ypN0: 63.6% vs 45.8% at diagnosis
  - ypCR: 8%

SCRT and CT in the pause: unresectable tumor

Ipofrazionato 3D/IMRT:
Level 1b
IF: 9.269



515 pz→
-R0: 71% (CRT) to 77%(SC RT)
-pCR: 12% (CRT) to 16% (SC RT)
-3yrs OS: 65% (CRT) to 73% (SC RT)

SCRT and CT: ongoing trial

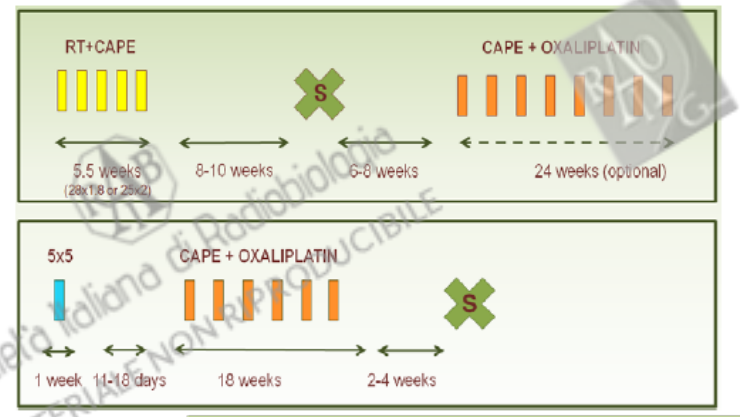
RAPIDO

Trial Design

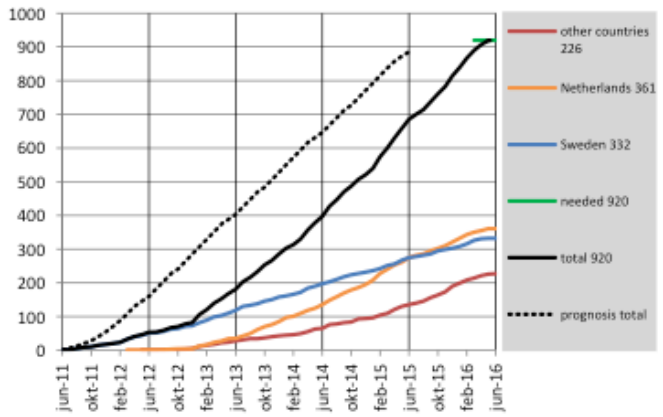
Inclusion criteria:
Locally advanced primary rectal cancer with pelvic MRI indicating at least criterion: cT4a, cT4b, EMVI+, N2, positive MRF or lateral LN+

Primary endpoint:
3-year disease-free survival

Stratification:
- Institution
- PS 0 vs 1
- cT3 vs cT4
- cN- vs cN+



Inclusion

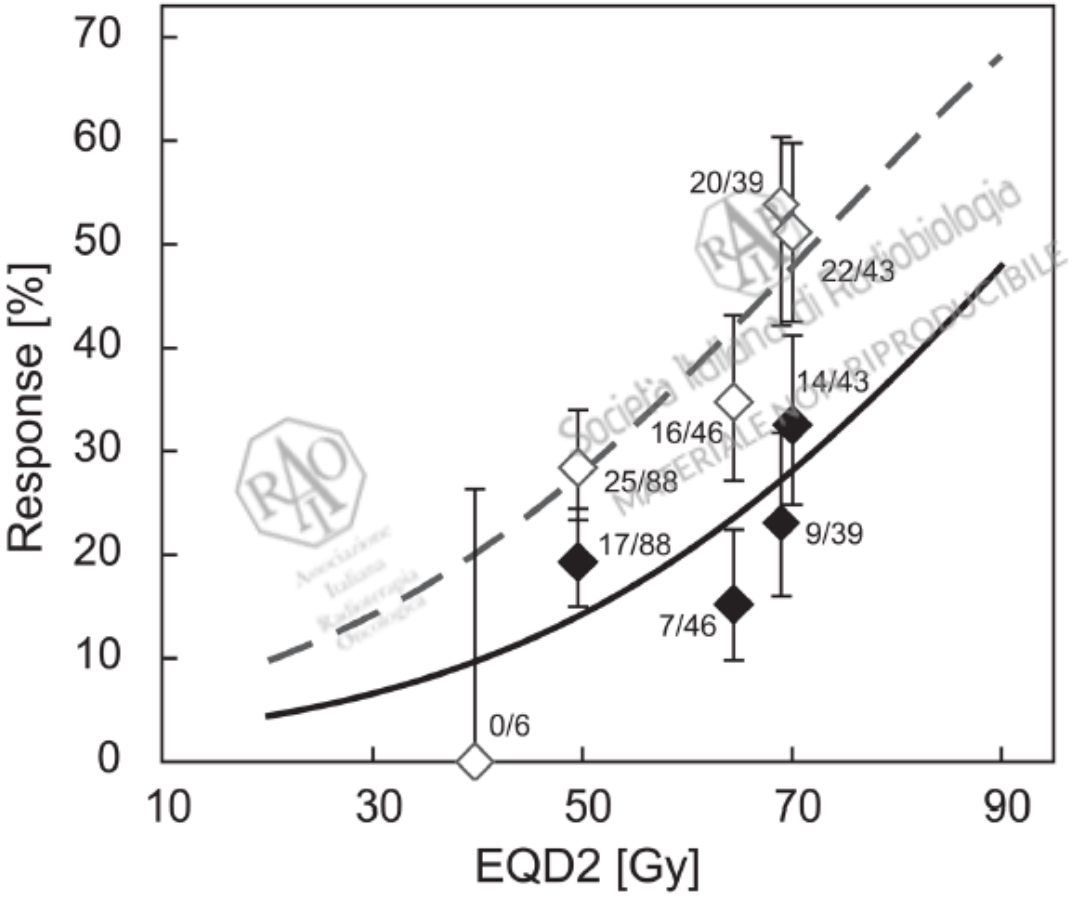


INCLUSION CLOSED!

The last patient was included on 2 June 2016, so within 5 years **920 patients** were included! After a slow start, the inclusion rate was according to plan. **54 centers** from **7 countries** are participating, which makes the RAPIDO a very successful international, multicenter and multi-disciplinary trial. THANK YOU! The intention is to present the first outcomes in spring 2017.

SIB/VMAT

RT dose-response model T3/T4 RC



After preoperative RT

TRG 1-2:
D50 = 72 Gy

TRG 1:
D50 = 92 Gy

Appelt AL et Al, IJROBP 2013

Retto

3D- BOOST:
Level 2b
IF 4.258

Int. J. Radiation Oncology Biol. Phys., Vol. 50, No. 5, pp. 1299–
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0360-3016/01/$–see f

ELSEVIER

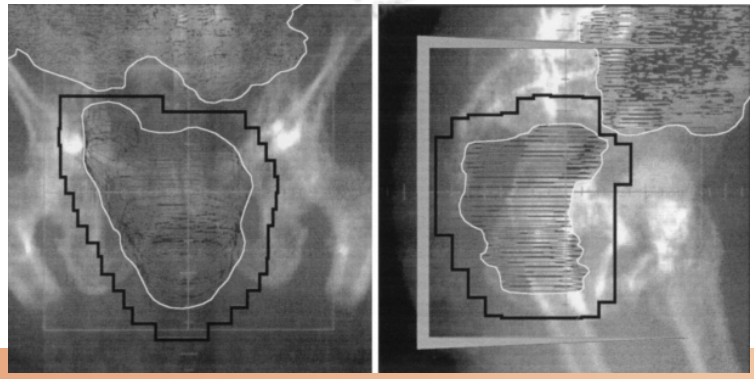
PII S0360-3016(01)01540-1

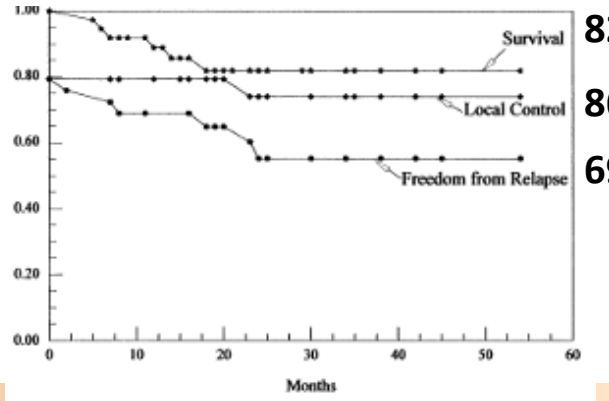
CLINICAL INVESTIGATION **Rectum**

A PHASE I/II TRIAL OF THREE-DIMENSIONALLY PLANNED CONCURRENT BOOST RADIOTHERAPY AND PROTRACTED VENOUS INFUSION OF 5-FU CHEMOTHERAPY FOR LOCALLY ADVANCED RECTAL CARCINOMA

Robert J. Myerson, M.D.,* Vincenzo Valentini, M.D.,† Elisa H. Birnbaum, M.D.,‡
Numa Cellini, M.D.,† Claudio Coco, M.D.,§ James W. Fleshman, M.D.,‡
Maria Antonietta Gambacorta, M.D.,† Domenico Genovesi, M.D.,† Ira J. Kodner, M.D.,‡
Joel Picus, M.D.,‖ Gary A. Ratkin, M.D.,‡ and Thomas E. Read, M.D.‡

Methods and Materials: Thirty-seven patients were enrolled on a prospective Phase I/II protocol conducted jointly at Washington University, St. Louis and the Catholic University of the Sacred Heart, Rome evaluating a three-dimensionally (3D) planned boost as part of the preoperative treatment of patients with unresectable or recurrent rectal cancer. Preoperative treatment consisted of 4500 cGy in 25 fractions over 5 weeks to the pelvis, with a 3D planned 90 cGy per fraction boost delivered once or twice a week concurrently (no time delay) with the pelvic radiation. Thus, on days when the boost was treated, the tumor received a dose of 270 cGy in one fraction while the remainder of the pelvis received 180 cGy. When indicated, nonaxial beams were used for the boost. The boost treatment was twice a week (total boost dose 900 cGy) if small bowel could be excluded from the boost volume, otherwise the boost was delivered once a week (total boost dose 450 cGy). Patients also received continuous infusion of 5-fluorouracil (1500 mg/m²-week) concurrently with the radiation as well as postoperative 5-FU/leucovorin.



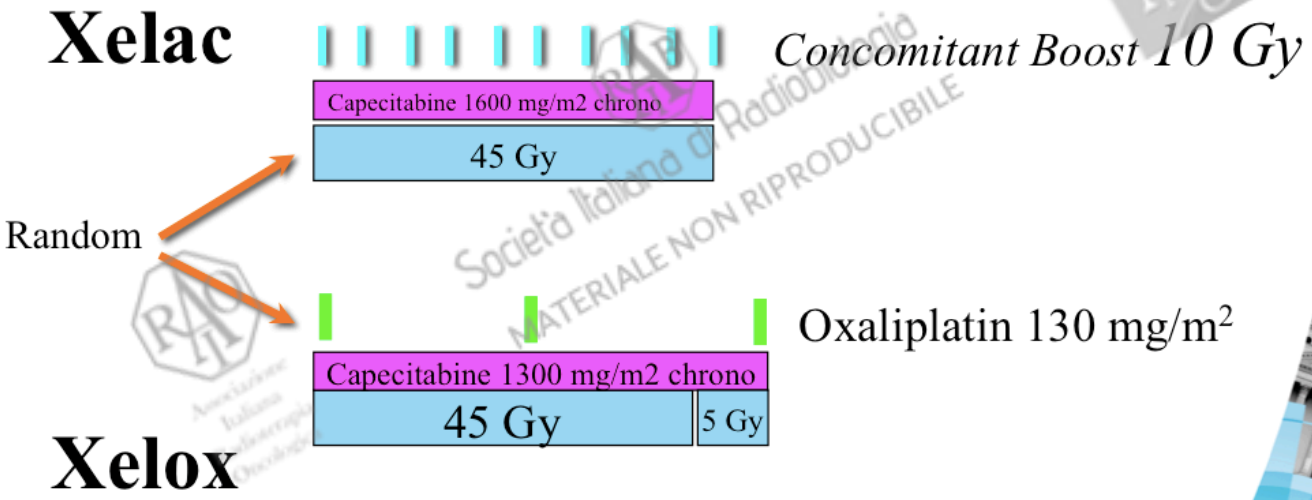


3 yrs:
82%
86%
69%

Sequential boost RT: 1.8Gy/ fr RT for pelvic followed by 1.8 Gy/ fr RT for boost volume .			
Authors	**Nr pts**	**TD (Gy)**	**RT Scheduling**
Chen, 1994	31	55.8	25x1.8 Gy + 6x1.8Gy boost
Mohiuddin, 2000	15 vs 18	45-50.4 vs 55.8-59.4	25x1.8 Gy + 0 to 3x1.8 Gy boost 25x1.8 Gy + 6 to 8x1.8 Gy boost
Standard fractionated RT for pelvic field followed by hyperfractionated RT for boost volume (twice daily)			
Movsas, 1998	11vs 9 vs 7	54.6 vs 57 vs 61.8	25x1.8 Gy + 8/10/14x1.2Gy boost (twice daily)
Movas 2006	22	61.8	25x1.8 Gy + 14x1.2 Gy boost (twice daily)
Hyperfractionated RT for pelvic field followed by hyperfractionated RT for boost volume (twice daily)			
Allal, 2002	50	50	36x1.25 Gy (2 daily) + 4x1.25 Gy boost (twice daily)
Mohiuddin, 2006	50	55.2-60	38x1.2Gy (twice daily) + 8 to 12x1.2 Gy boost (twice daily)
Simultaneous integrated boost delivered to boost volume during RT pelvic field			
Myerson, 2001	37	49.5-55	25x1.8 Gy + simultaneous boost: 5 to 10x0.9 Gy (once or twice a week)
De Ridder, 2007	13	55.2	23x2Gy + simultaneous boost: 23x0.4Gy (once daily)
Standard fractionated RT for pelvic with conc boost delivered during last week(s) RT pelvic field			
Janjan, 2000	45	52.5	25x1.8 Gy + 5x1.5 Gy conc boost to last week pelvic RT
Krishnan, 2006	54	52.5	25x1.8 Gy + 5x1.5 Gy conc boosto last week pelvic RT

Concomitant boost dose intensification

Interact Trial



Interact Trial: analysis 01/14

Preliminary results

TRG

	Xelac (%)	Xelox (%)	p
TRG1	31.4	30.8	ns
TRG 1-2	60.2	51.0	ns

TOX

Interact Trial: analysis 01/14

Retto

Phase II studies

SIB-IMRT:
Level 2b
IF 3.090

CLINICAL Colorectal Cancer and Other Gastrointestinal Malignancies

Article in Press

Preoperative Chemoradiation With VMAT-SIB in Rectal Cancer: A Phase II Study

Vincenzo Picardi, Gabriella Macchia, Alessandra Guido, Lucia Giaccherini, Francesco Deodato, Andrea Farioli, Savino Cilla, Gaetano Compagnone, Andrea Ardizzoni, Dajana Cuicchi, Maria Antonietta Gambacorta, Francesco Cellini, Giovanni Frezza, Gilberto Poggioli, Vincenzo Valentini, Lorenzo Fuccio, Alessio Giuseppe Morganti

Dose: CTV2 (mesorectum and pelvic lymph nodes) = 45 Gy /1.8 Gy
CTV1 (concomitant boost) on GTV + 2-cm margin= 57.5 Gy/2.3 Gy

Concomitant CT: XELOX

Primary outcome: pCR→ 4/18
pT0-Tmic: 11/18 = 61.1%

CTCAE 3.0 Tox: ≥G3→44.4%

ONGOING Phase II study

Recruiting Trial of Using SIB-IMRT in Preoperative Radiotherapy for Locally Advanced Rectum Cancer
Condition: Rectal Cancer
Interventions: Radiation: conventional fraction; Radiation: SIB

Recruiting IMRT-SIB and Capecitabine in Preoperative Rectal Cancer Treatment
Condition: Rectal Carcinoma
Interventions: Radiation: IMRT-SIB; Drug: Capecitabine; Procedure: Surgery

Picardi V, Clin Colorectal Cancer 2016

Stereotactic Radiotherapy

Fegato: M+

SBRT:
Level 3a
IF: 6.163

EJC
EUROPEAN JOURNAL OF CANCER

Abstract

Although resection is the standard of care for liver metastasis, 80–90% of patients are not resectable at diagnosis. Advances in combination chemotherapy, particularly with targeted agents, have increased tumour response and survival in patients with unresectable metastatic colorectal cancer, but these techniques have limitations and may be associated with high recurrence rates. Some autopsy series have shown that as many as 40% of patients with metastatic colorectal cancer have disease confined to the liver; aggressive local therapy may improve overall survival in such patients. Local control of liver metastases can also ease hepatic capsular pain to improve quality of life. Stereotactic body radiation therapy (SBRT) offers an alternative, non-invasive approach to the treatment of liver metastasis through precisely targeted delivery of radiation to the tumours while minimising normal tissue toxicity. Early applications of SBRT to liver metastases have been promising with the reports of 2-year local control rates of 71–86% and other studies reporting 18-month local control rates of 71–93%. While these data establish the safety of SBRT for liver metastases, more rigorous phase II clinical studies are needed to fully evaluate long-term efficacy and toxicity results. In the interim, this review stresses that SBRT of liver must be performed cautiously given the challenges of organ motion and the low toxicity tolerance of the surrounding hepatic parenchyma.

Dawood O et al. Eur J Cancer 2009

Fegato: M+

SBRT: Level 2b

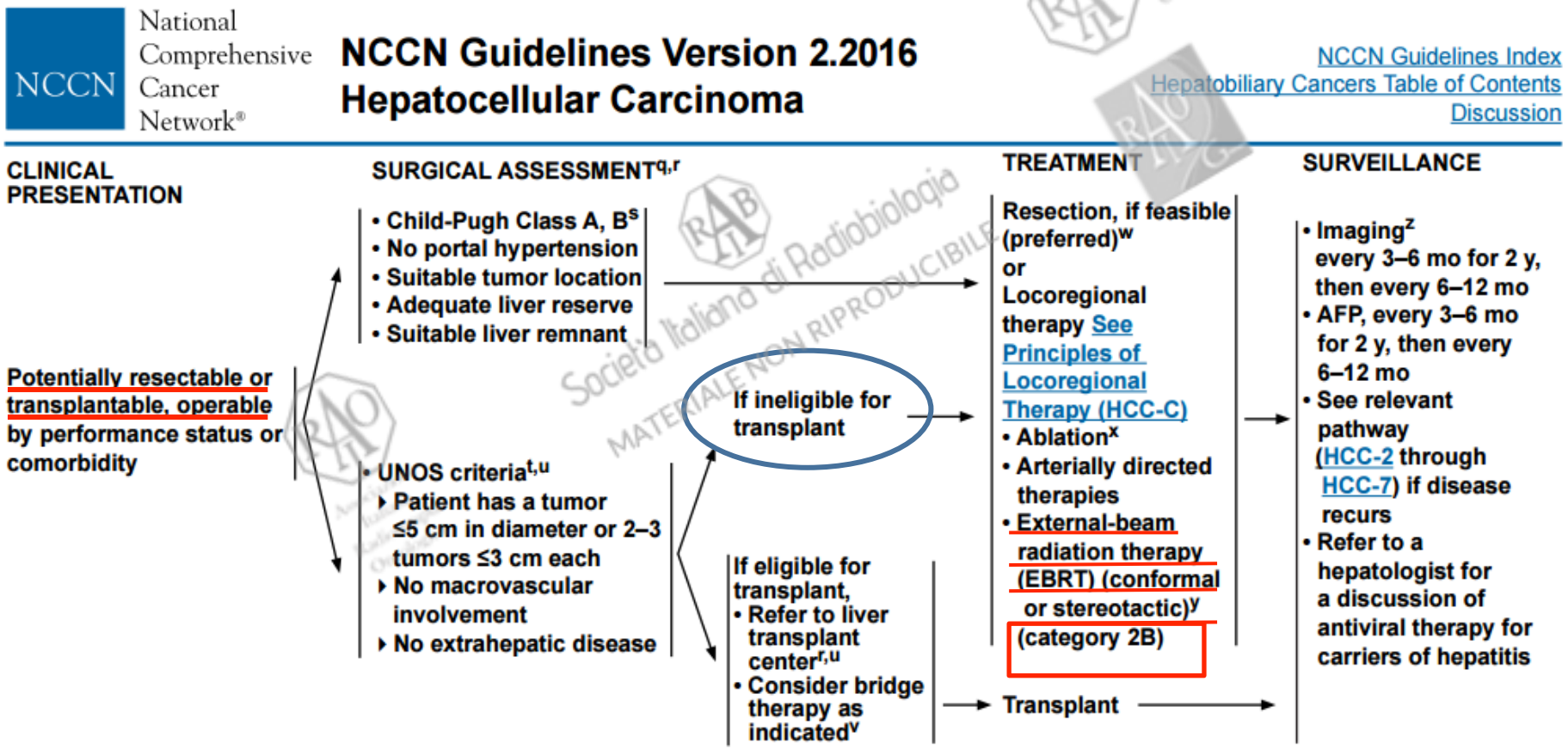
Author	Nr pts	SBRT schedule
Blomgren 1998	21	30 Gy/10fr
Herfarth 2001	56	14-26 Gy/1 fr
Fuss 2004	17	36 Gy/3-6 fr
Schefter 2005	18	36-66Gy/ 3 fr
Wulf 2006	34	21-36 Gy/1-3 fr
Mendez-Romero 2006	25	25-37.5Gy/3-5 fr
Hoyer 2006	64	45Gy/3fr
Lee 2009	68	27-60Gy/6fr
Ambrosino 2009	27	25-60Gy/ 3fr
Goodman 2009	19	18-30Gy/ 1fr
Van der Pool 2010	20	37.5Gy/ 3fr
Dewas 2012	99	36-48Gy/ 3fr
Fumagalli 2012	113	45Gy/3fr

SBRT in HCC

Author	Nr pts	SBRT schedule
Blomgren 1998	20	30 Gy/10fr
Herfarth 2001	4	14-26 Gy/1 fr
Fuss 2004	1	36 Gy/3-6 fr
Wulf 2006	5	21-36 Gy/1-3 fr
Mendez-Romero 2006	11	25-37.5Gy/3-5 fr
Tse 2008	31	24-54Gy/6fr
Goodman 2009	7	18-30Gy/ 1fr
Cardenas 2010	17	36- 48Gy/ 3fr
Dewas 2012	48	36-48Gy/ 3fr
Mancuso 2012	11	75Gy/3fr
Bujold 2013	102	24-54Gy/6fr
Sanuki 2014	221	35-40Gy/5fr

SBRT: STANDARD

SBRT in HCC



Fegato: HCC

SBRT: STANDARD

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2016
Hepatocellular Carcinoma

NCCN Guidelines Index
Hepatobiliary Cancers Table of Contents
Discussion

CLINICAL PRESENTATION

Unresectable
- Inadequate hepatic reserve[aa]
- Tumor location

→ Evaluate whether patient is a candidate for transplant (See UNOS criteria under Surgical Assessment HCC-5)[u]

Transplant candidate →
- Refer to liver transplant center
- Consider bridge therapy as indicated[v]

TREATMENT

SURVEILLANCE
- Imaging[z] every 3–6 mo for 2 y, then every 6–12 mo
- AFP, every 3–6 mo for 2 y, then every 6–12 mo
- See relevant pathway (HCC-2 through HCC-7) if disease recurs

Not a transplant candidate →

Options:[bb]
- Locoregional therapy preferred[cc, dd]
  - Ablation
  - Arterially directed therapies
  - EBRT (conformal or stereotactic)[y] (category 2B)
- Systemic therapy
  - Sorafenib (Child-Pugh Class A [category 1] or B)[aa,ee,ff]
  - Chemotherapy[gg]
    - Systemic
    - Intra-arterial
- Clinical trial
- Best supportive care

Inoperable by performance status or comorbidity, local disease or local disease with minimal extrahepatic disease only →

Options:[bb]
- Locoregional therapy preferred[cc]
  - Ablation
  - Arterially directed therapies
  - EBRT (conformal or stereotactic)[y] (category 2B)
- Sorafenib (Child-Pugh Class A [category 1] or B)[aa,ee,ff]
- Clinical trial
- Best supportive care

Dose intensification

- Advanced/ unresectable lesions:
  - Dose > 54 Gy should be consider

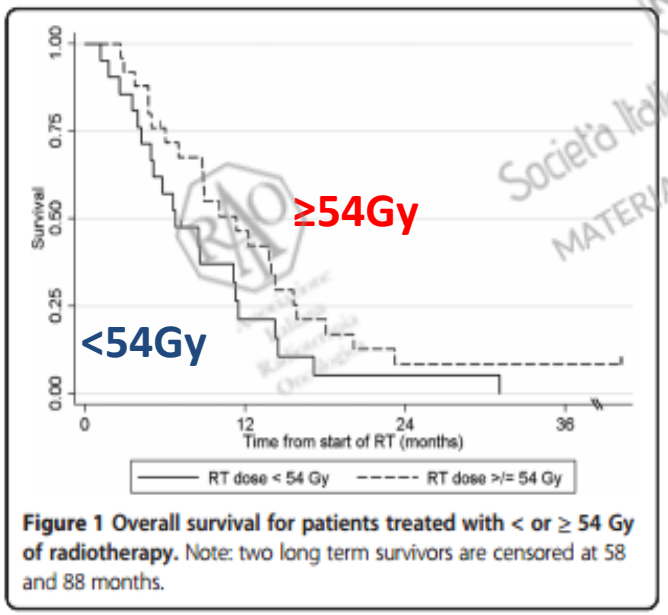
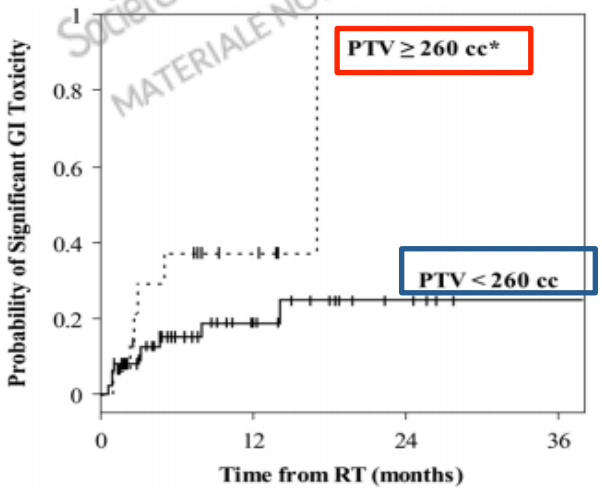


Figure 1 Overall survival for patients treated with < or ≥ 54 Gy of radiotherapy. Note: two long term survivors are censored at 58 and 88 months.

CTV definition

- Advanced/ unresectable lesions:
  - Elective Nodal Irradiation (ENI)→NO OS benefit
  - Involved GTV → reduction of volume→ reduction toxicities



Murphy JD, *IJROBP* 2007

Pancreas

SBRT:
Level 2a IF: 5.98

Author	Nr pts	SBRT Schedule	EQD2	LC
Tozzi et al. 2013	30	7.5Gyx6	70Gy	2 yrs: 75%
Rwingema et al 2011	71	18-25Gyx1 8Gyx3	46.8/82.5Gy 38.4Gy	1yrs: 38%
Chang et al 2009	77	25Gyx1	82.5 Gy	1yrs: 84%
Gurka et al 2013	11	25Gyx5	32.5Gy	81%
Rajagopalon et al 2013	12	24Gyx1 12Gyx3	76.8Gy 72Gy	NR
Scorsetti et al 2011	37	45Gy/6fr	69.75Gy	6 mts: 79,2%
Lominska et al 2012	28	Various schemes	NA	1 yrs: 70%
Schellenberg et al 2012	16	25Gy x 1	82.5Gy	81%
Goyal et al 2010	19	20-25Gy x 1 24-30Gy/8-10Gy	56-82.5Gy 38.4-54Gy	81%
Koong et al 2005	16	25Gy x 1	82.5Gy	94%

De Bari B, Critical Reviews in Oncology/Hematology 2016

Pancreas

SBRT:
Level 2a IF: 5.98

Author	Nr pts	SBRT Schedule	EQD2	LC
Tozzi et al. 2013	30	7.5Gyx6	70Gy	2 yrs: 75%
Rwingema et al 2011	71	18-25Gyx1 8Gyx3	46.8/82.5Gy 38.4Gy	1yrs: 38%
Chang et al 2009	77	25Gyx1	82.5 Gy	1yrs: 84%
Gurka et al 2013	11	25Gyx5	32.5Gy	81%
Rajagopalon et al 2013	12	24Gyx1 12Gyx3	76.8Gy 72Gy	NR
Scorsetti et al 2011	37	45Gy/6fr	69.75Gy	6 mts: 79,2%
Lominska et al 2012	28	Various schemes	NA	1 yrs: 70%
Schellenberg et al 2012	16	25Gy x 1	82.5Gy	81%
Goyal et al 2010	19	20-25Gy x 1 24-30Gy/8-10Gy	56-82.5Gy 38.4-54Gy	81%
Koong et al 2005	16	25Gy x 1	82.5Gy	94%

LC:
1 year 59% to 94%

De Bari B, Critical Reviews in Oncology/Hematology 2016

Pancreas

SBRT:
Level 2a IF: 5.98

Author	Nr pts	SBRT Schedule	EQD2	Toxicity G3
Tozzi et al. 2013	30	7.5Gyx6	70Gy	NR
Rwingema et al 2011	71	18-25Gyx1 8Gyx3	46.8/82.5Gy 38.4Gy	**G3 nausea 1pt** **G3 GI 1pt** **G5 GIparesis 1 pt**
Chang et al 2009	77	25Gyx1	82.5 Gy	NR
Gurka et al 2013	11	25Gyx5	32.5Gy	NR
Rajagopalon et al 2013	12	24Gyx1/ 12Gyx3	76.8Gy/72Gy	NR
Scorsetti et al 2011	37	45Gy/6fr	69.75Gy	**Late G3GI 4,2%**
Lominska et al 2012	28	Various schemes	NA	**Late G3GI 7.14%**
Schellenberg et al 2012	16	25Gy x 1	82.5Gy	**Acute≥ G2GI 19%** **Late≥ G2GI 47%**
Goyal et al 2010	19	20-25Gy x 1 24-30Gy/8-10Gy	56-82.5Gy 38.4-54Gy	**G3 GI > 16%**
Koong et al 2005	16	25Gy x 1	82.5Gy	**Acute G3GI 12.5%**

Acute G3 GI tox: 0- 12.5%
Late G3 GI tox: 0- 22.3%

De Bari B, Critical Reviews in Oncology/Hematology 2016

Pancreas

SBRT:
Level 2b
IF 4.258

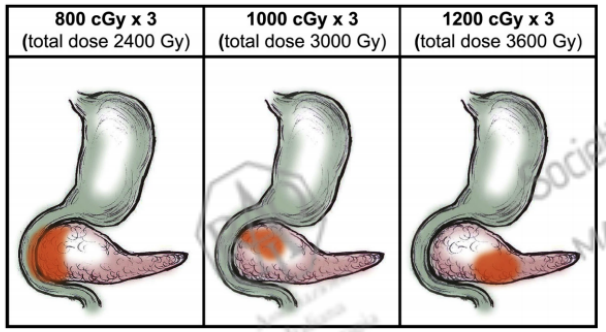
National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2016
Pancreatic Adenocarcinoma

NCCN Guidelines Index
Pancreatic Table of Contents
Discussion

Unresectable/Locally Advanced (non-metastatic):

- **No standard total dose or dose per fraction has been established for SBRT; therefore, it should preferably be utilized as part of a clinical trial.**[12]



Hypofractionated SBRT dose according to the relationship among the tumor, duodenum and stomach.

α/β duodenum: 3
Dmax (BED) duodenum: 130 Gy

Study	Fractionation	Conventional radiation $Eq_{1.8}$ (Gy)	Tumor control BED_{10} (Gy)	Long-term toxicity equivalent dose (Gy) BED_3	Median follow-up (mo)	Local control (%)	Grade ≥3 toxicity (%)	
							Acute	Long term
Hoyer *et al.* (27)	15 Gy × 3	95	112.5	270	6	57	78	33
Chang *et al.* (26)	25 Gy × 1	74	87.4	233	12	84	1	9
Present Study	8–12 Gy × 3	51–76	43–54	88–180	24	78	8	6

A. MAHADEVAN et al. IJROBP 2010

Ongoing trials

Phase III FOLFIRINOX (mFFX) +/- SBRT in Locally Advanced Pancreatic Cancer

This study is currently recruiting participants. (see Contacts and Locations)

Verified September 2016 by Stanford University

Sponsor:
Stanford University

Information provided by (Responsible Party):
Stanford University

ClinicalTrials.gov Identifier:
NCT01926197

First received: August 15, 2013
Last updated: September 19, 2016
Last verified: September 2016
History of Changes

Phase II Neoadjuvant Chemotheraphy (Gemcitabine and Nab-Paclitaxel vs. mFOLFIRINOX) and Sterotatic Body Radiation Therapy for Borderline Resectable Pancreatic Cancer

This study is currently recruiting participants. (see Contacts and Locations)

Verified December 2015 by University of Pittsburgh

Sponsor:
University of Pittsburgh

Information provided by (Responsible Party):
Nathan Bahary, MD, University of Pittsburgh

ClinicalTrials.gov Identifier:
NCT02241551

First received: August 29, 2014
Last updated: December 1, 2015
Last verified: December 2015
History of Changes

Immunotherapy and SBRT Study in Borderline Resectable Pancreatic Cancer

This study has been terminated.

Sponsor:
NewLink Genetics Corporation

Information provided by (Responsible Party):
NewLink Genetics Corporation

ClinicalTrials.gov Identifier:
NCT02405585

First received: March 25, 2015
Last updated: June 30, 2016
Last verified: June 2016
History of Changes

Società Italiana di Radiobiologia
XXVI CONGRESSO NAZIONALE AIRO
XXX CONGRESSO NAZIONALE AIRB
IX CONGRESSO NAZIONALE AIRO GIOVANI

Intra-Operative Radiation Therapy

IORT:
Level 2b
IF 2.403

Role of the IORT in gastric cancer

IORT tested in several small trials:

Randomized trial (S + RT vs S+ **IORT**+ RT)	✓ LC **NO OS**
Randomized trial (S vs S+ **IORT**)	**NO OS**
Randomized trial (subgroup 78pts) (RT+ S vs RT+ S+ **IORT**)	**NO OS**

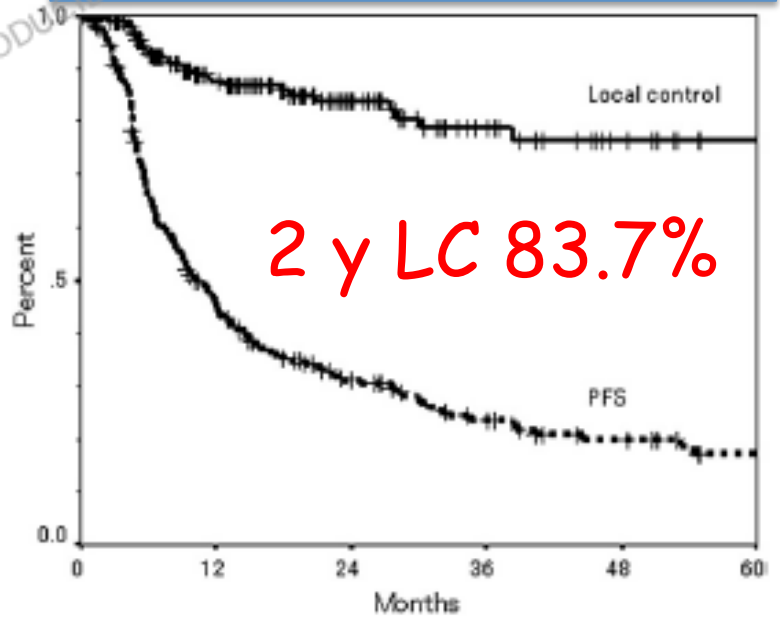
Sinderal el al. 1993; Kramling et al. 1996; Skoropad et al. 2000

IORT:
Level 2b
IF 4.258

IORT in pancreatic cancer: resectable?

	Median (%)	Range
LR (2 years) Alexakis N Br J Surg 2004	**13**	**34-87**
Hepatic	5-11	38- 73
Extra –abdominal	8-29	

Multi-istitutional retrospective analysis

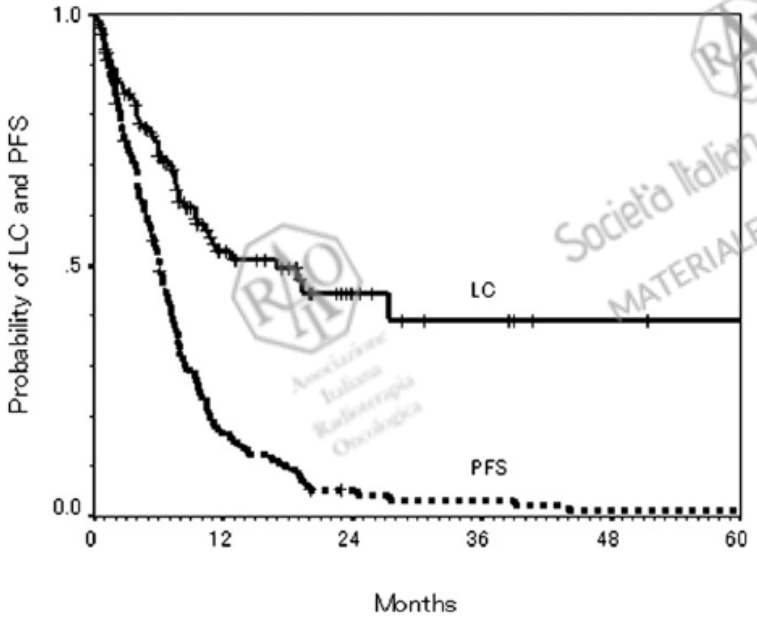


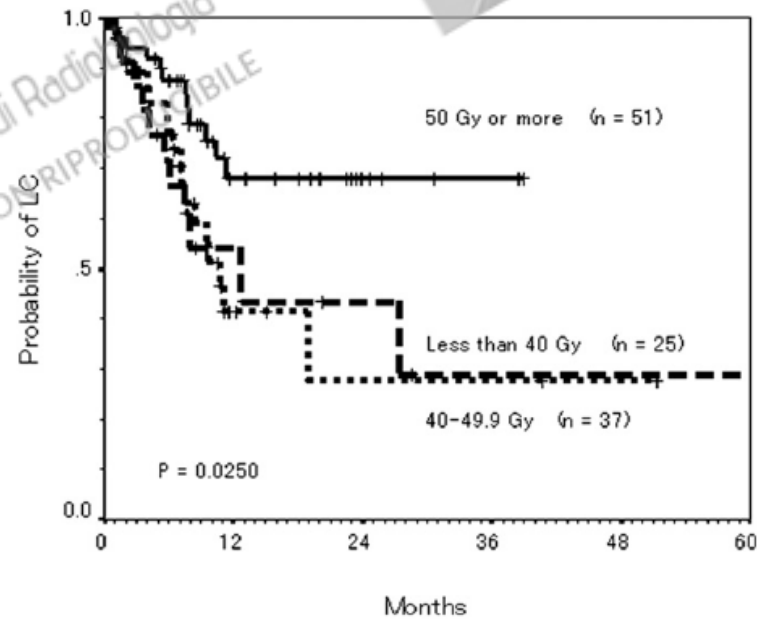
Ogawa K et al. IJROBP 2010

IORT:
Level 2b
IF 4.258

IORT in pancreatic cancer: unresectable?

Multi-istitutional retrospective analysis





Ogawa K et al. IJROBP 2010

Retto

IORT: Level 2b

Author	Nr pts	LC	In field LC	Adverse factor for LR
Dubois 2011	72	91%	NA	NA
Roeder 2007	243	93%	7 (2.8%) presacral	N+ (4/7) Adjuvant RT-CT
Kusters 2009	290	86%	5.9% 64% (lateral/ventral)	Positive margin
Calvo 2011	241	92%	3% presacral	N+
Kusters 2010	605	88%	12% 5 yrs	No downstaging N+ Positive margin No adjuvant CT
Haddock 2011 Recurrence	607	77% 3yrs	12%	
Kusters 2009 Recurrence	170	54%	14.9% (57% presacral)	

IORT:
Level 2b
IF 4.258

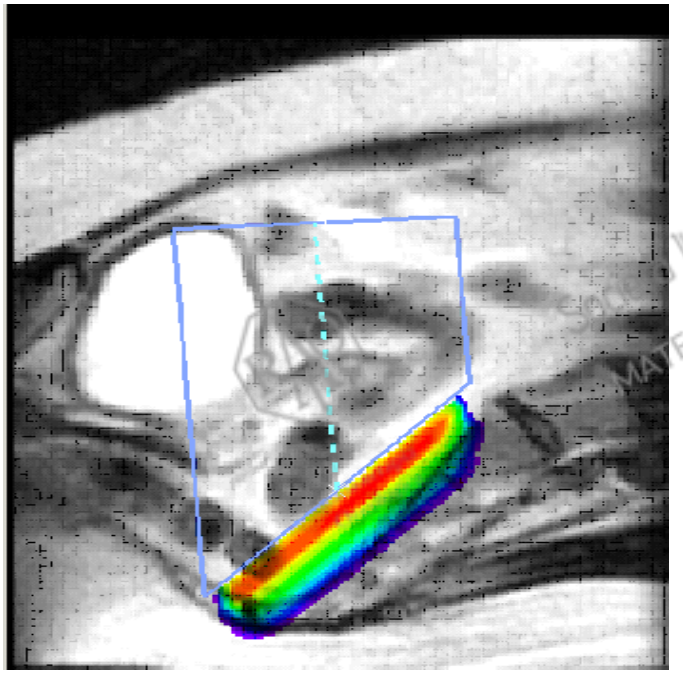
Clinical Investigation: Gastrointestinal Cancer

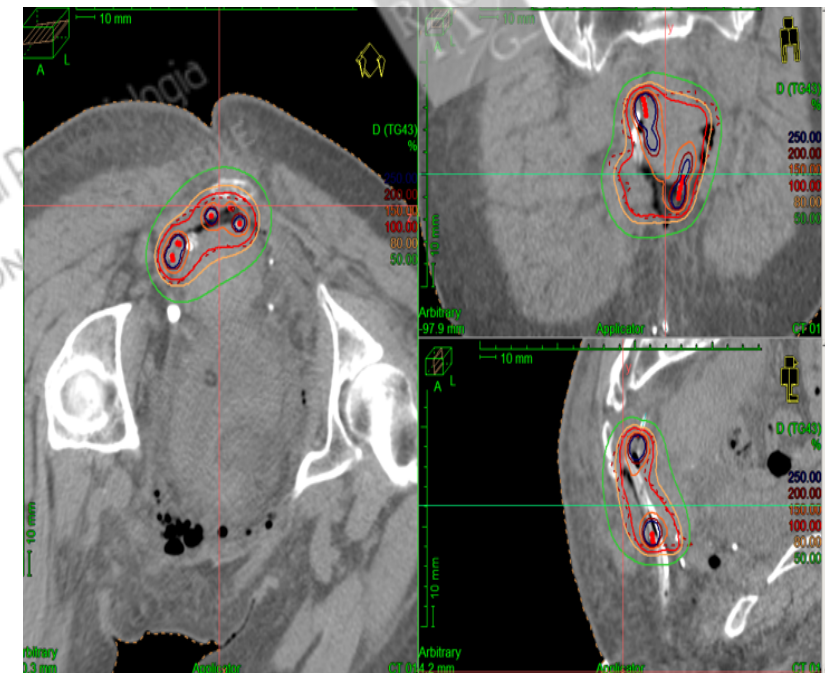
Intraoperative Radiation Therapy Reduces Local Recurrence Rates in Patients With Microscopically Involved Circumferential Resection Margins After Resection of Locally Advanced Rectal Cancer

CRM state	5 x 5Gy/45-50Gy +/- Cape	5 x 5Gy/45-50Gy +/- Cape HDRBT 10 Gy	p
CRM (≤ 2mm)	22	21	
5yrs- DFS	79%	70%	n.s.
CRM+ (23%)	17	31	
5yrs- DFS	41%	84%	.01

Alberda W et al, IJROBP 2014

From IOeRT to HDRBT

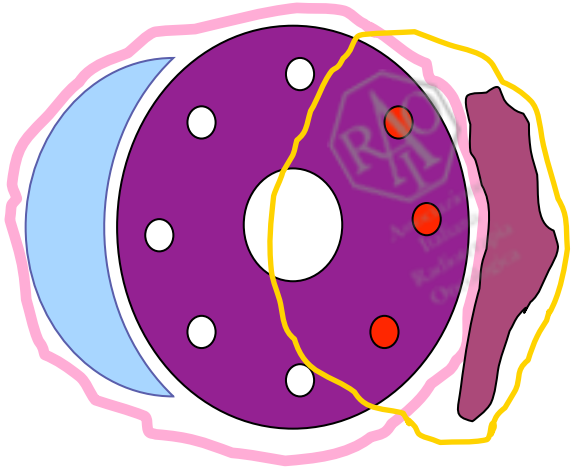


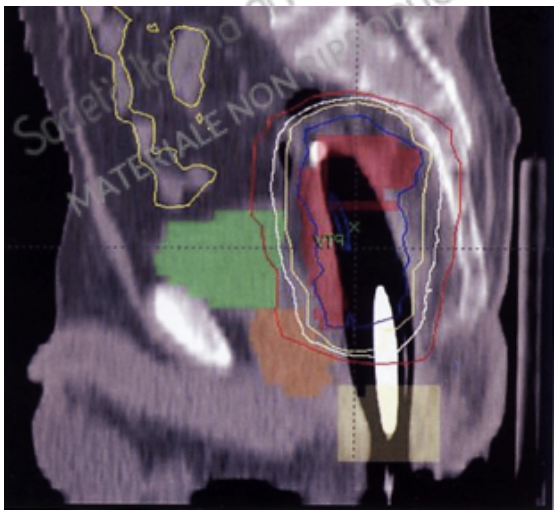


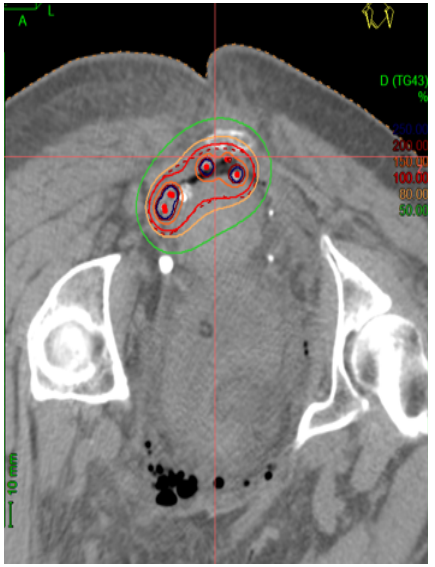
HDR
Brachytherapy

Brachytherapy: Level 2b

- Neoadjuvant treatment in T2,T3 and early T4N0 rectal cancer
- Post surgical (as IORT)







By the courtesy of C.Marijnen and T.Vuong

Brachytherapy:
Level 4
IF: 2.088

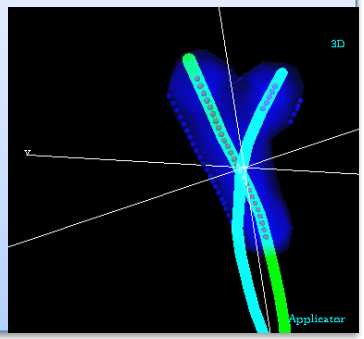
BRACHYTHERAPY
An International Multidisciplinary Journal

Brachytherapy. 2015 May-Jun;14(3):401-4. doi: 10.1016/j.brachy.2014.12.002. Epub 2015 Jan 13.

A Phase I study of high-dose-rate intraluminal brachytherapy as palliative treatment in extrahepatic biliary tract cancer.

Mattiucci GC[1], Autorino R[2], Tringali A[3], Perri V[3], Balducci M[1], Deodato F[4], Gambacorta MA[1], Mantini G[1], Tagliaferri L[1], Mutignani M[3], Morganti AG[4].

- **18** patients with non-metastatic extrahepatic biliary cancer **unsuitable for surgical resection or radiochemotherapy**
- metal stents followed by HDR-192Ir-ILBT
- **Dose escalation** → safe dose of 25Gy/5fr

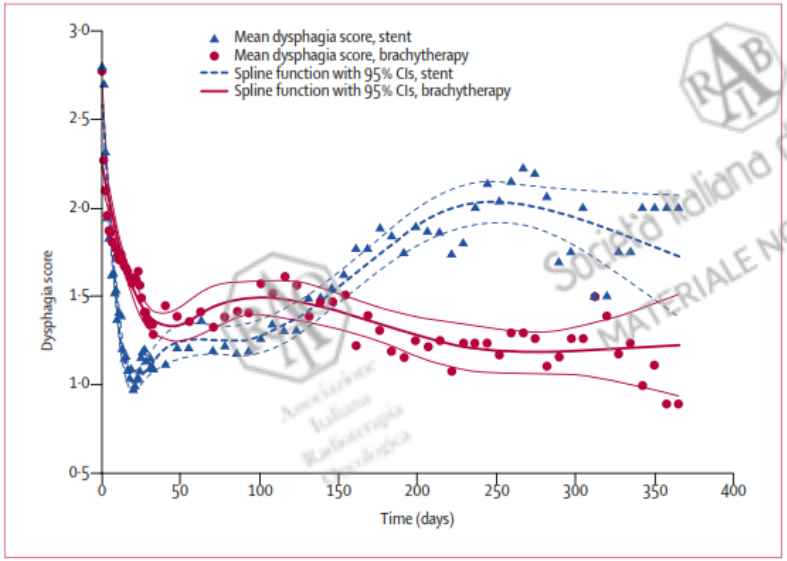


15Gy/ 3 fr	20Gy/ 4fr	25Gy/5 fr
3 pts	9 pts	6 pts
	1 acute toxicity (cholangitis)	

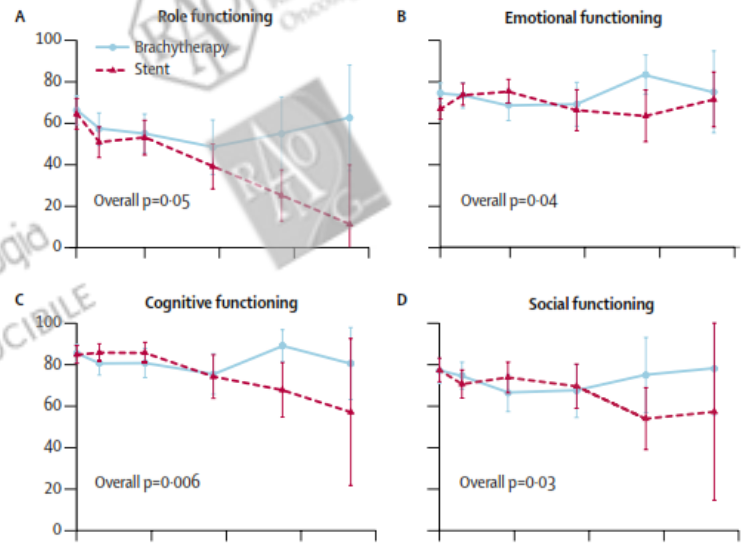
Brachytherapy:
Level 1b
IF: 2.67 IF: 44

Stent vs BRT

Dysphagia control



Quality of life



Medical costs p= 0.87

Average cost per patient (€)	Brachytherapy (n=101)	Stent placement (n=108)	p*
Total treatment†	1415	1945	0·001
Total intramural care‡	6085	5675	0·85
Medical procedures§	170	250	0·01
Extramural care¶	465	345	0·81
Total	8135	8215	0·87

H. Bergquist, *Diseases of the Esophagus 2005*

Homs M, Lancet 2004

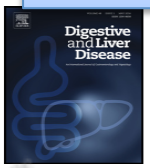
Esofago

Brachytherapy

Contents lists available at ScienceDirect

Digestive and Liver Disease

journal homepage: www.elsevier.com/locate/dld



Oncology

Underuse of brachytherapy for the treatment of dysphagia owing to esophageal cancer. An Italian survey

Lorenzo Fuccio[a,*], Alessandra Guido[b], Cesare Hassan[c], Leonardo Frazzoni[a], Alessandra Arcelli[b], Andrea Farioli[a], Lucia Giaccherini[b], Andrea Galuppi[b], Daniele Mandolesi[a], Francesco Cellini[d], Giovanna Mantello[e], Gabriella Macchia[f], Nicola de Bortoli[g], Alessandro Repici[h], Vincenzo Valentini[d], Franco Bazzoli[a], Alessio Giuseppe Morganti[b]

40 RT center:

Responses to the survey.

Questions of the survey	Answer	No [%]	95%CI
Centres performing brachytherapy of the oesophagus for dysphagia (last 3 years)	Yes	7 [17.5]	7.3–32.9
	No	33 [82.5]	67.2–92.7
No of cases per centre performing brachytherapy of the oesophagus (last 3 years)	<5	3 [7.5]	1.6–20.4
	5–10	3 [7.5]	1.6–20.4
	>10	1 [2.5]	0.06–13.2
	Not performed	33 [82.5]	67.2–92.7
Centres using brachytherapy for treatment of dysphagia due to esophageal cancer as	First line	3 [7.5]	1.6–20.4
	Second line	4 [10]	2.8–23.7
	Not performed	33 [82.5]	67.2–92.7
Limitations to the diffusion and use of brachytherapy main reasons	Lack of experience	10 [25]	22.4–27.8
	Complexity	2 [5]	3.8–6.6
	Logistical problems	1 [2.5]	1.7–3.7
	Lack of effective response	1 [2.5]	1.7–3.7
	Not otherwise specified	26 [65]	61.9–67.9
Centres performing esophageal stenting as first line treatment for dysphagia due to esophageal cancer	Yes	37 [92.5]	79.6–98.4
	No	3 [7.5]	1.6–20.4

7/40

Only 1 > 10 cases

First line 3/40

Lack of experience 10/40

Conclusion

- **Hypofractionated 3D RT/IMRT:**
  - ✓ Rectal cancer — SC RT + TME → **Level 1b**; SC delay TME → Level 2b
- **SIB/VMAT:**
  - ✓ Rectal cancer — CONC BOOST → **Level 1b**; SIB/VMAT → Level 2b
- **SBRT:**
  - ✓ Hepatic metastases → Level 2b
  - ✓ HCC → Level 2b
  - ✓ Pancreatic cancer → Level 2b
- **IORT:**
  - ✓ stomach, pancreas and rectal — LC → Level 2b
- **Brachytherapy:**
  - ✓ Esophagus — Dyspagia control → **Level 1b**
  - ✓ Rectal, extrahepatic biliary — LC → Level 2b/4