Ospedale di Circolo
Fondazione Macchi

Gruppo Regionale AIRO Lombardia

Associazione Italiana Radioterapia Oncologica

Gruppo Interregionale Piemonte, Liguria e Valle d'Aosta

SBRT nel distretto addome-pelvi:

- Tumori del fegato:
  - Metastasi epatiche
  - HCC
- Tumore del pancreas
- Tumore della prostata

HUMANITAS
CANCER CENTER

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Liver metastases: background

- Early diagnosis of metastatic disease is improved and prevalence of oligometastatic patients is increasing

- The liver is a common site of metastases for gastrointestinal, lung and breast cancers

- In colorectal cancer 30% to 70% of patients will develop liver metastases, often isolated or associated with limited metastatic foci of disease.

Hoyer, I. J. Rad Onc Biol Phys, 2012
Comito T et al, I. BMC Cancer. 2014

Surgery

- The introduction of modern chemotherapy regimens has improved the PFS and only minimally the OS, with a limited local control of disease

- Surgical resection of CRC liver metastases improves overall survival

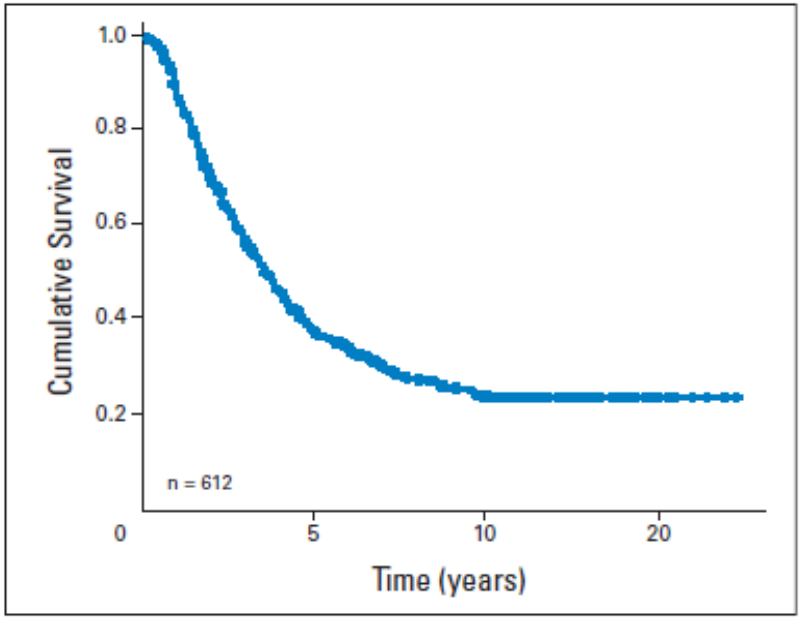


Fig 1. Kaplan-Meier plot of disease-specific survival for 612 patients with potential 10-year follow-up who underwent resection of colorectal liver metastases from 1985 to 1994 at Memorial Sloan-Kettering Cancer Center.

- 1 year rates of 90-95%
- 5-year rates of 30-60%
- median OS of 40-53 months

Fong Y. et al. (1995) CA Cancer J.Clin.
Tomlison JS et al. (2007) JCO
Simmonds P.C. et al. (2006) Br.J.Cancer
Lam VW et al., (2013) J Gastrointest Surg.

Clinical Score for Predicting Recurrence After Hepatic Resection for Metastatic Colorectal Cancer Analysis of 1001 Consecutive Cases

Table 4. MULTIVARIATE PREDICTORS OF RECURRENCE

	Hazard	Coefficient	p
Positive margin	1.7	0.5	0.004
Extrahepatic disease	1.7	0.5	0.003
>1 tumor	1.5	0.4	0.0004
Carcinoembryonic antigen >200 ng/ml	1.5	0.4	0.01
Size >5 cm	1.4	0.3	0.01
Node-positive primary	1.3	0.28	0.02
Disease-free interval <12 months	1.3	0.25	0.03
Bilateral tumor	0.9	−0.1	0.4

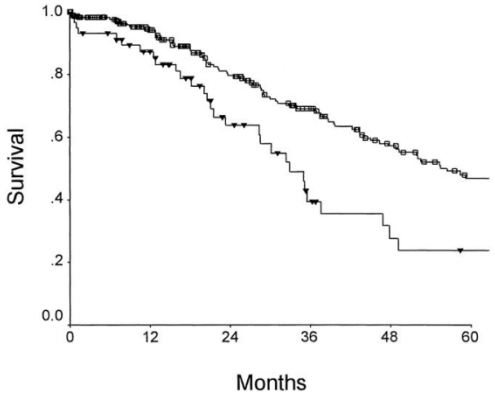
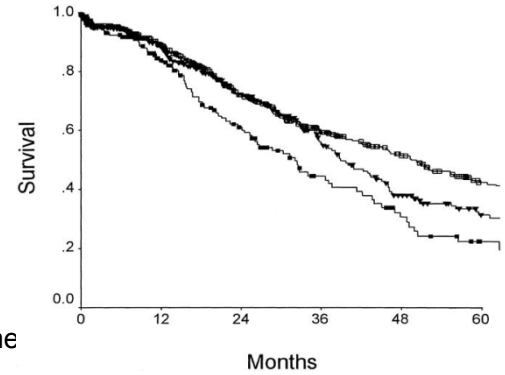


Figure 6. Prediction of long-term outcome for small (<3 cm) metastases.



Survival after hepatic resection for colorectal metastases as related to number of liver tumors.

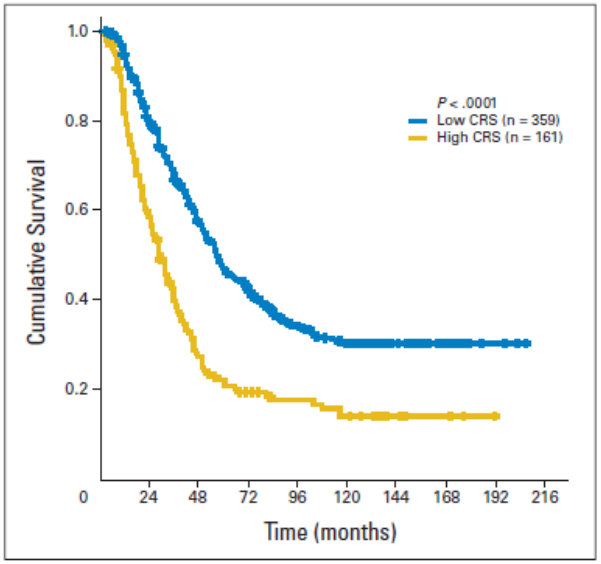


Fig 2. Kaplan-Meier plots of disease-specific survival stratified by low-risk clinical risk score (CRS; top curve) and high-risk CRS (bottom curve).

Actual 10-Year Survival After Resection of Colorectal Liver Metastases Defines Cure

James S. Tomlinson, William R. Jarnagin, Ronald P. DeMatteo, Yuman Fong, Peter Kornprat, Mithat Gonen, Nancy Kemeny, Murray F. Brennan, Leslie H. Blumgart, and Michael D'Angelica

Patients selection

HUMANITAS

Fong Y. et al. Ann Surg. 1999

Surgery for non-CRC Liver metastases

The role of non-CRC liver metastases ablation was often controversial

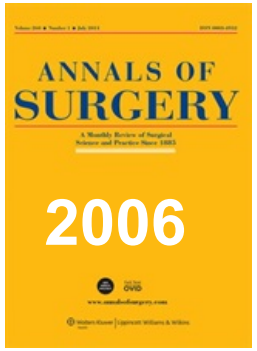
Hepatic Resection for Noncolorectal Nonendocrine Liver Metastases

Analysis of 1452 Patients and Development of a Prognostic Model

René Adam, MD, PhD, Laurence Chiche, MD, Thomas Aloia, MD, Dominique Elias, MD, PhD, Rémy Salmon, MD, Michel Rivoire, MD, Daniel Jaeck, MD, Jean Saric, MD, Yves Patrice Le Treut, MD, Jacques Belghiti, MD, Georges Mantion, MD, Gilles Mentha, MD, and the Association Française de Chirurgie

All patients	1452	36	35
Group 1: 5-yr survival >30%			
Adrenal	28	66	63
Testicular	78	51	82
Ovarian	65	50	98
Small bowel	28	49	58
Ampullary	15	46	38
Breast	454	41	45
Unknown	28	38	30
Renal	85	38	36
Uterine	43	35	32
Group 2: 5-yr survival 15%–30%			
Gastric adenocarcinoma	64	27	15
Exocrine pancreatic	40	25	20
Cutaneous melanoma	44	22	27
Choroid melanoma	104	21	19
Duodenal	12	21	34
Group 3: 5-yr survival <15%			
Gastroesophageal junction	25	12	14
Pulmonary	32	8	16
Esophageal	20	32*	16
Head and neck	15	24*	18

Benevento et al (2000) J Surg Oncol
Van Ruth (2001) Eur J Surg Oncol



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treatments. In current practice, liver surgery for noncolorectal nonendocrine metastases should be considered only when the metastatic disease is well controlled or responding to systemic therapy. When applied in these situations, surgery may be able to offer selected patients a real benefit in long-term survival.

- Only 10-60% of patients were suitable to surgical resection because of

  - technical difficulties
  - unfavourable tumour factors
  - patients co-morbiditities

Table 2. Contraindications to hepatic resection in patients with colorectal cancer liver metastases

Category	Contraindication
Technical (A)	
1. Absolute	Impossibility of R0 resection with ≥25%–30% liver remnant
	Presence of unresectable extrahepatic disease
2. Relative	R0 resection possible only with complex procedure (portal vein embolization, two-stage hepatectomy, hepatectomy combined with ablation[a])
	R1 resection
Oncological (B)	
1.	Concomitant extrahepatic disease (resectable)
2.	Number of lesions ≥5
3.	Tumor progression

Any patient should be categorized as A1 or A2/B1, B2, or B3. This classification may help to clearly define the type of unresectable patients included in all clinical trials.
[a]Includes all methods, including radiofrequency ablation.

Adam, de Gramont (2012) The Oncologist.
Fong Y. et al. (1995) CA Cancer J.Clin.
Simmonds P.C. et al. (2006) Br.J.Cancer
Lam VW et al., (2013) J Gastrointest Surg.

RFA

- **Radiofrequency ablation (RFA) is the most valid alternative to surgery:**
  - local control rates of 90-98%
  - 1, 2 and 5-year survival rates of 87%-70% and 34%,
  - median overall survival of 25 months

- **Limits:**
  - lesions higher than 3 cm of diameter
  - lesions located in proximity of major blood vessels, main biliary tract, gallbladder or just beneath the diaphragm

liver metastases treatment:
is there an alternative?

Kemeny N. et al, Oncology 2006
Shen A et al, J Gastroenterol Hepatol. 2013

Liver metastases treatment: RT could be an alternative?

The **liver tissue low tolerance to irradiation** involves the risk of the radiation-induced liver disease

RILD (2 weeks to 4 months after RT)
- anicteric ascites
- elevation of alkaline phosphatase and liver transaminases
- liver failure
- death

According to the radiobiological model and the liver **parallel architecture….**

… The risk of RILD is proportional to the **mean radiation dose** delivered to normal liver tissue

…It should be possible the safely liver irradiation with adequate dose constraints for normal liver (**minimum volume of 700mL should receive a total dose less than 15 Gy**)

Song, Choi et al, IJROBP 2010
Tai et al, IJROBP 2009 - Sawrie et al, Cancer Control 2010
Pan CC, Kavanagh BD, Dawson LA, IJROBP, 2010 (suppl)

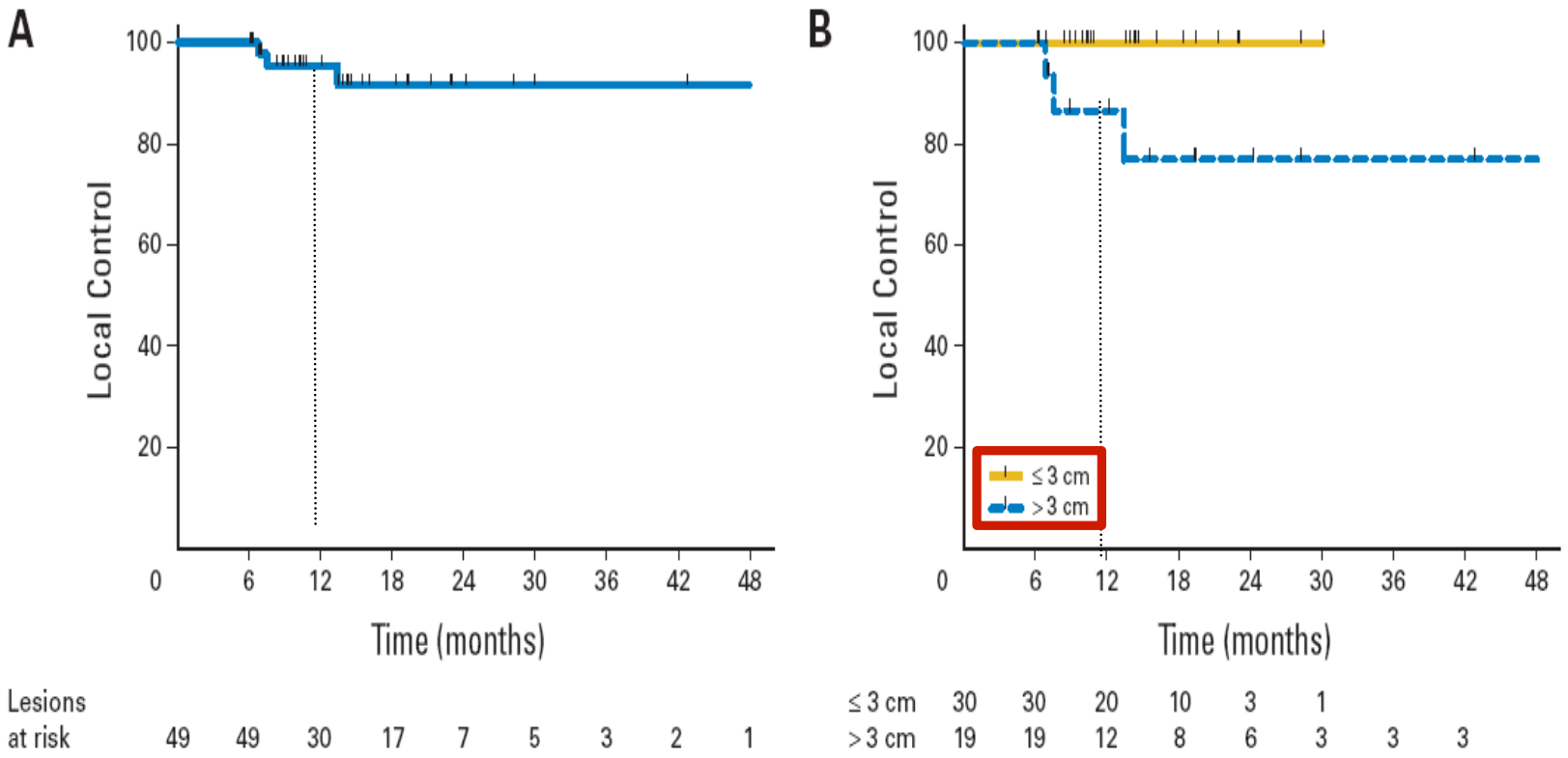
Liver metastases treatment: SBRT could be an alternative?

Table 1 Prospective clinical trials in the literature studying stereotactic ablative radiotherapy in liver metastases and their results

Ref.	Design	No of patients	Tumor size	SABR dose	Toxicity	Outcomes
Scorsetti *et al*[15]	Phase II (preliminary report)	61 (76 tumors)	1.8-134.3 cm^3 (mean 18.6 cm^3)	75 Gy in 3 fractions	No case of RILD. Twenty-six percent had grade 2 transaminase increase (normalised in 3 mo). Grade 2 fatigue in 65% patients, one grade 3 chest wall pain which regressed within 1 year.	1-yr LC94, 22-mo LC 90.6%
Goodman *et al*[16]	Phase I (HCC and liver mets)	26 (19 liver mets)	0.8-146.6 mL (median, 32.6 mL)	Dose escalation, 18-30 Gy (1 fr)	No dose-limiting toxicity 4 cases of Grade 2 late toxicity (2 GI, 2 soft tissue/rib)	1-yr local failure, 3% 2-yr OS, 49% (mets only)
Ambrosino *et al*[17]	Prospective cohort	27	20-165 mL (median, 69 mL)	25-60 Gy (3 fr)	No serious toxicity	Crude LC rate 74%
Lee *et al*[18]	Phase I - II	68	1.2-3090 mL (median, 75.9 mL)	Individualized dose, 27.7-60 Gy (6 fr)	No RILD, 10% Grade 3/4 acute toxicity No Grade 3/4 late toxicity	1-yr LC, 71% Median survival, 17.6 mo
Rusthoven *et al*[19]	Phase I - II	47	0.75-97.98 mL (median, 14.93 mL)	Dose escalation, 36-60 Gy (3 fr)	No RILD, Late Grade ¾ < 2%	1-yr LC, 95% 2-yr LC, 92% Median survival, 20.5 mo
Høyer *et al*[10]	Phase II (CRC oligomets)	64 (44 liver mets)	1-8.8 cm (median, 3.5 cm)	45 Gy (3 fr)	One liver failure, two severe late GI Toxicities	2-yr LC, 79% (by tumor) and 64% (by patient)
Méndez Romero *et al*[20]	Phase I - II (HCC and mets)	25 (17 liver mets)	1.1-322 mL (median, 22.2 mL)	30-37.5 Gy (3 fr)	Two Grade 3 liver toxicities	2-yr LC, 86% 2-yr OS, 62%
Herfarth *et al*[21]	Phase I - II	35	1-132 mL (median, 10 mL)	Dose escalation, 14-26 Gy (1 fr)	No significant toxicity reported	1-yr LC, 71% 18-mo LC, 67% 1-yr OS, 72%

Correlation between dose prescription and tumor size

60 Gy /3 fr



For lesion diameter > 3cm, a prescription dose of >60 Gy should be considered.

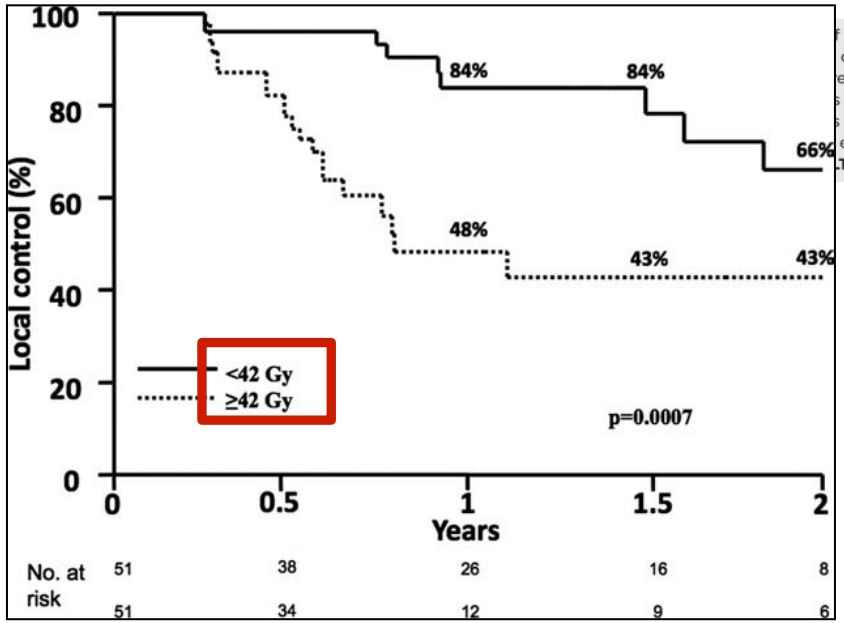
Rusthoven et al. (2009) JCO

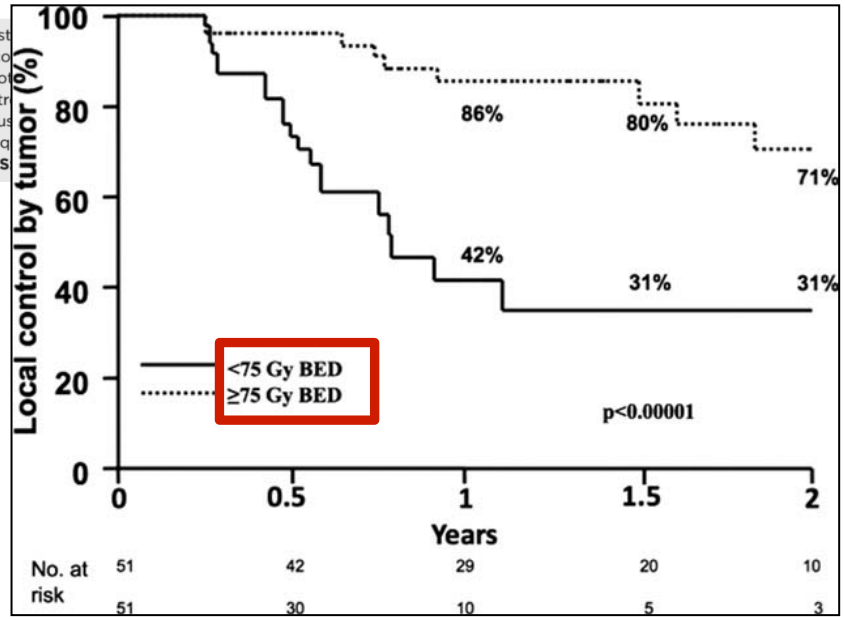
Original Article

Stereotactic Body Radiotherapy for Colorectal Liver Metastases

A Pooled Analysis

Correlation between dose prescription and local control





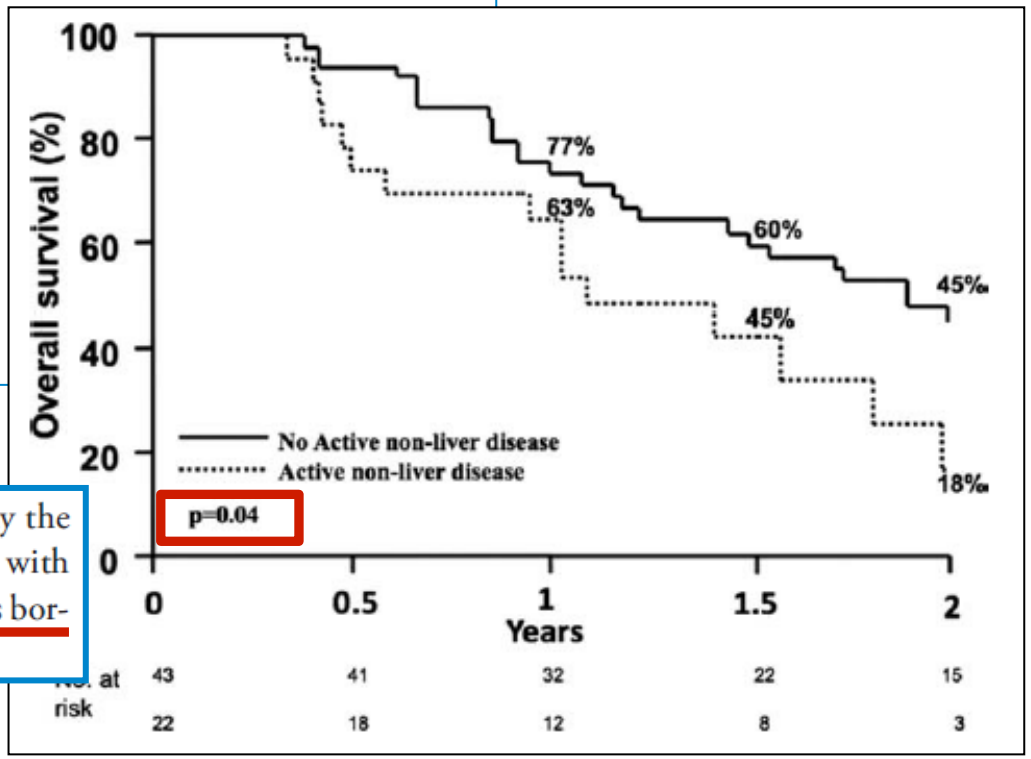
for 1-year local control >90% is 46 to 52 Gy in 3 fractions. **CONCLUSIONS:** Liver stereotactic body radiotherapy is well tolerated and effective for colorectal liver metastases. The strong correlation between local control and OS supports controlling hepatic disease even for heavily pretreated patients. For a 3-fraction regimen of stereotactic body radiotherapy, a prescription dose of ≥48 Gy should be considered, if normal tissue constraints allow. *Cancer*

Chang et al.Cancer, 2011

Correlation between dose prescription and OS

Factor	Local Control		Factor	Overall Survival
	By Lesion	By Patient		
Total dose	.0015	.034	Active nonliver disease	.046
No. of prior chemotherapy regimens	.63	.84	Local failure	.06
Age	.13	.42	Total No. of chemotherapy regimens	.64
No. of days of SBRT	.75	.88	No. of lesions (1 vs 2-4)	.5
GTV	.94	.42[a]	GTV	.14[a]
Dose per fraction	.003	.18		
No. of prior chemotherapy regimens	.6	.81		
Age	.28	.42		
No. of days of SBRT	.11	.37		
GTV	.74	.68		
BED	.004	.09		
No. of prior chemotherapy regimens	.42	.58		
Age	.35	.71		
No. of days of SBRT	.2	.5		
GTV	.86	.53		

OS ($P = .09$). On multivariate analysis for OS, only the absence of active extrahepatic disease was associated with improved OS ($P = .046$). However, local control was borderline significant for OS ($P = .06$).



Chang et al.Cancer, 2011

Liver SBRT: our phase II study

Is Stereotactic Body Radiation Therapy an Attractive Option for Unresectable Liver Metastases? A Preliminary Report From a Phase 2 Trial

Marta Scorsetti, MD,* Stefano Arcangeli, MD,* Angelo Tozzi, MD,* Tiziana Comito, MD,* Filippo Alongi, MD,* Pierina Navarria, MD,* Pietro Mancosu, MSc,* Giacomo Reggiori, MSc,* Antonella Fogliata, MSc,‡ Guido Torzilli, MD,† Stefano Tomatis, MSc,* and Luca Cozzi, PhD‡

INCLUSION CRITERIA:

- Unresectable liver metastases
- Maximum tumor diameter < 6cm
- ≤ 3 discrete lesions
- Performance status 0-2
- Good compliance to treatment

END POINTS:

Primary: in-field local control

Secondary: toxicity and overall survival

Table 1 Baseline patient and treatment characteristics

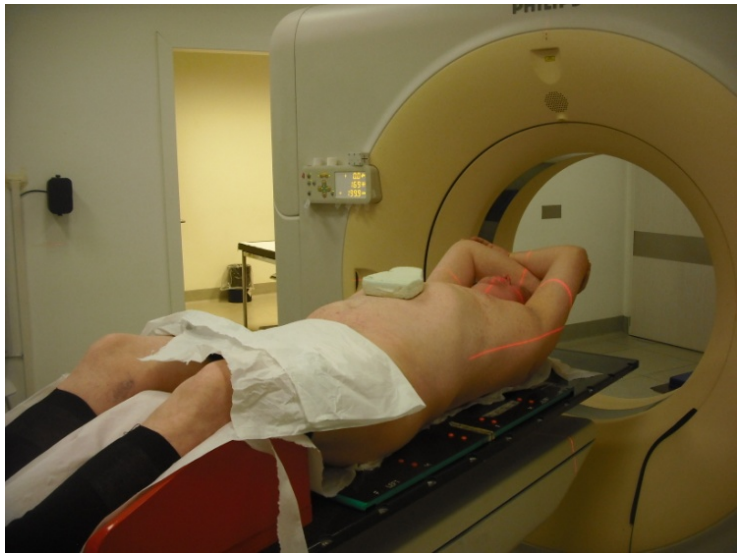
Characteristic	n	%
No. of patients	61	
Male	26	42.6
Female	35	57.4
Median age, y	65	-
Range	39-87	
No. of liver lesions		
1	48	78.7
2	11	18.0
3	2	3.3
Primary		
Colorectal	29	47.5
Breast	11	18.0
Gynecological	7	11.5
Other	14	22.9
Time since diagnosis, mo		
≤12	35	57.4
>12	26	42.6
No. of prior systemic treatment regimens		
0	10	16.4
1	15	24.6
2	13	21.3
3	14	22.9
≥4	9	14.7
Presence of stable extrahepatic disease		
Yes	21	34.4
No	40	65.6
Prior liver-directed therapy		
Yes	28	45.9
Surgery	21	75
RFA	2	7
Both	5	19
No	33	54.1

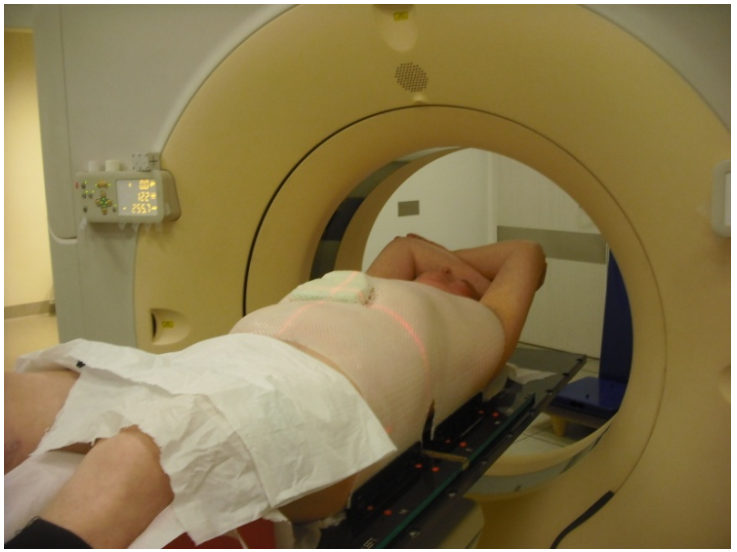
February 2010- September 2011

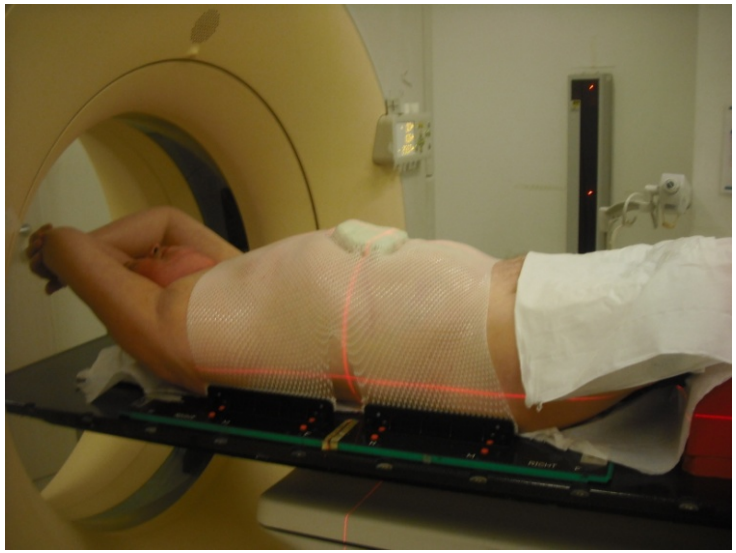
Median FU 12 months

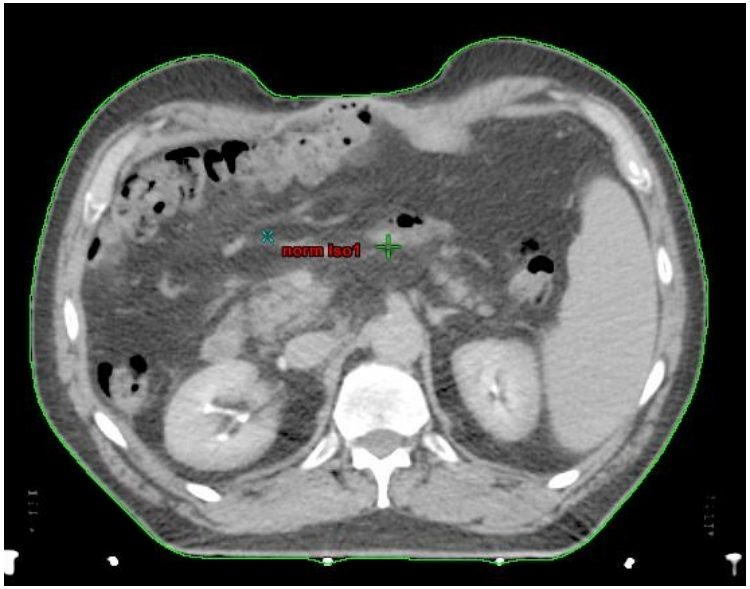
Treatment	No. of lesions	%
Lesion diameter (mm)		
≤30 mm	45	59.2
>30 mm	31	40.8
CTV volume (cm^3)		
Mean ± SD	18.6 ± 22.7	
Range	1.8-134.3	
PTV volume (cm^3)		
Mean	54.9 ± 41.998	
Range	7.7-209.4	
Dose prescription (per lesion)		
Full dose (75 Gy)	62	82
90% (67.5 Gy)	6	8
80% (60 Gy)	4	5
70% (52.5 Gy)	4	5

Abbreviations: CTV = clinical target volume; PTV = planning target volume; RFA = radiofrequency ablation.





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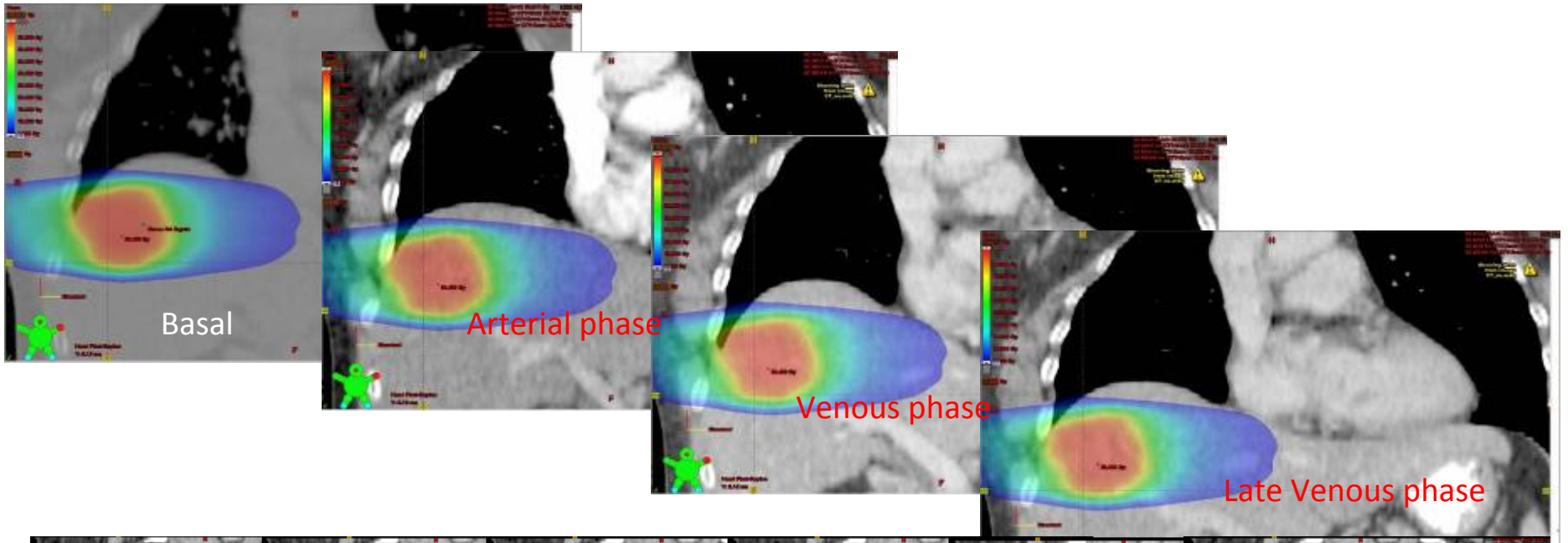
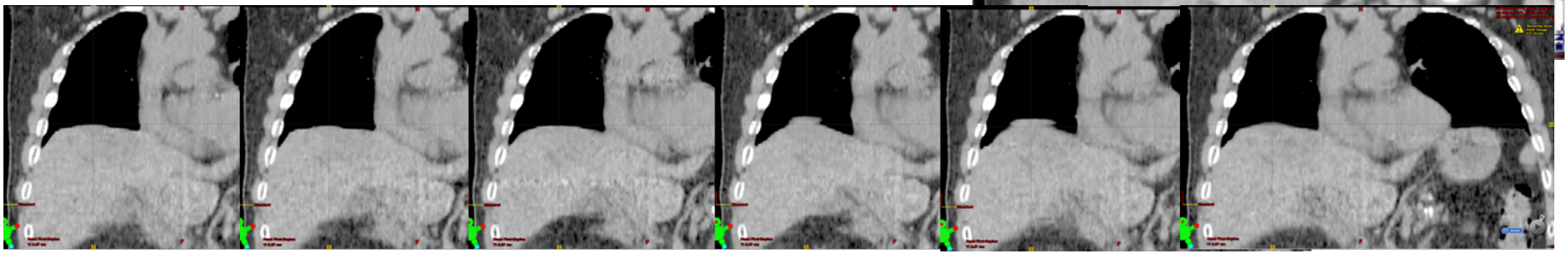
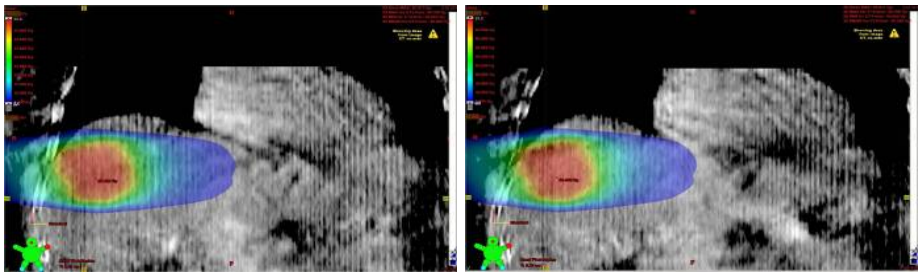


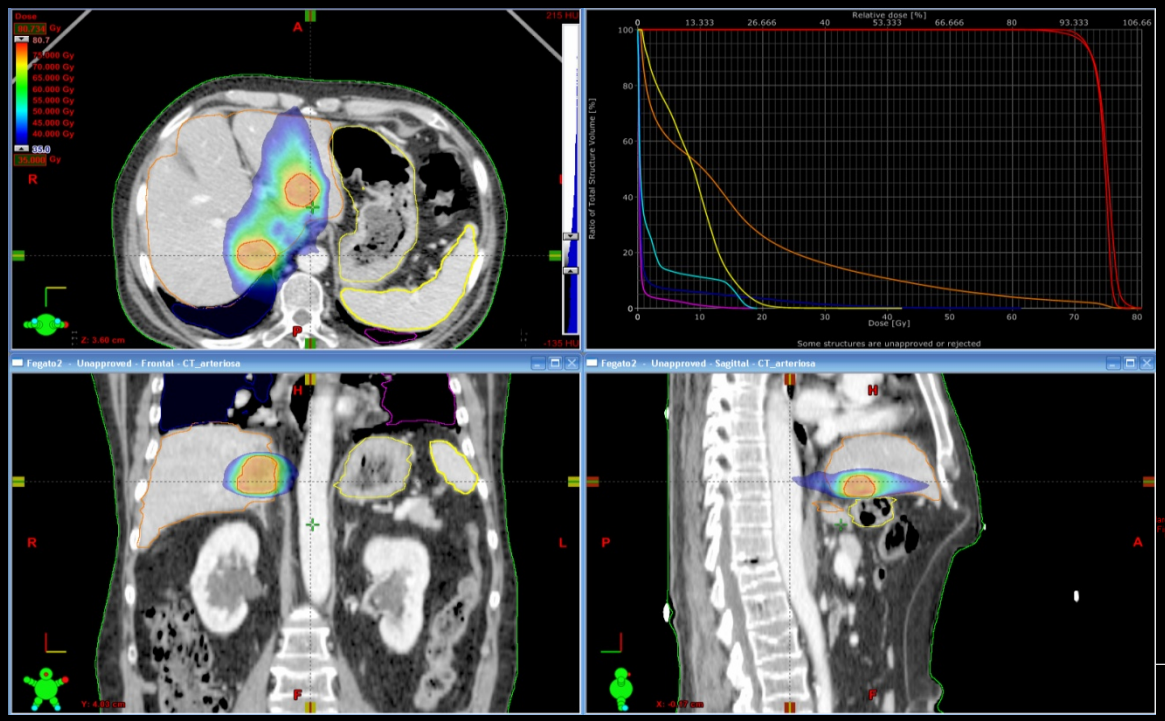


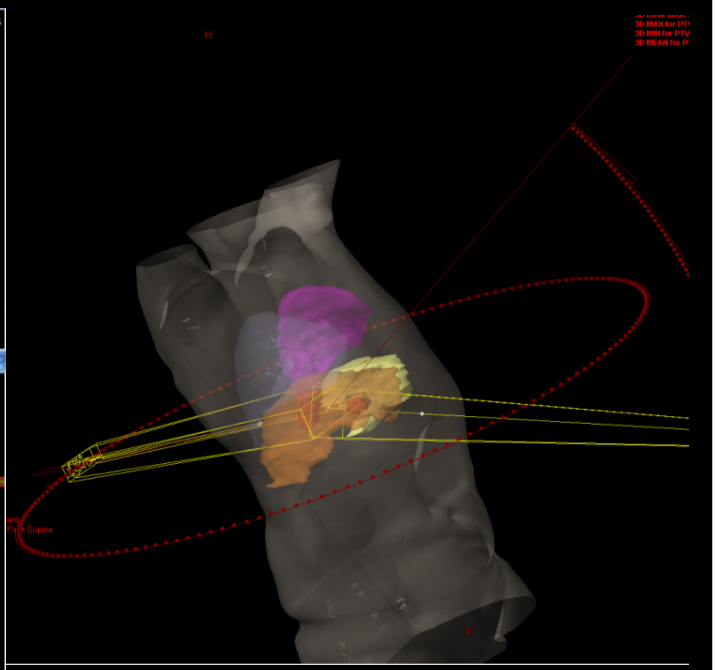
CB_CT Day I

CB_CT Day III



SBRT liver: 25Gy x 3; 10FFF; DR 2400



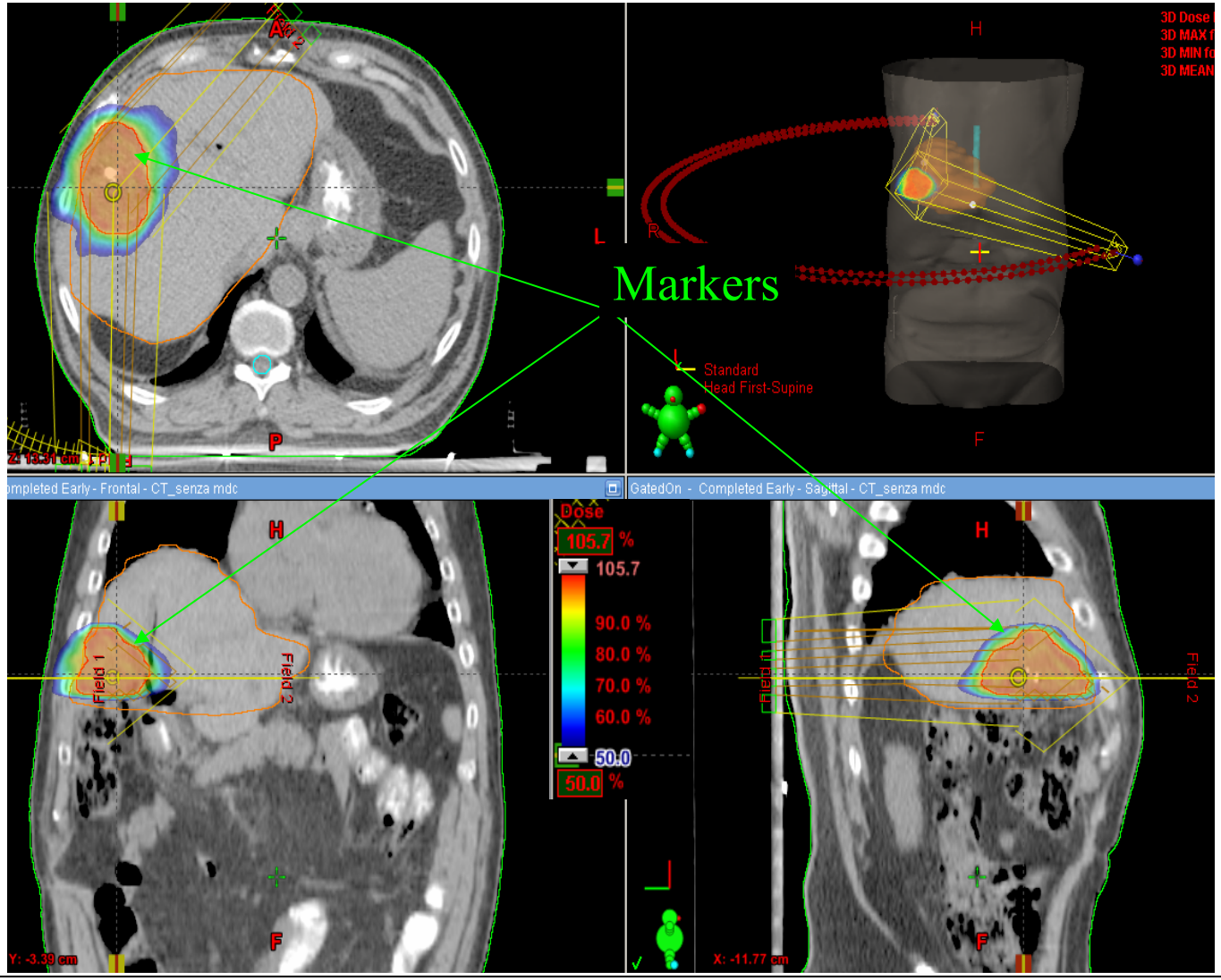


1 isocentre, 3 arcs
Jaw tracking

PTV1&PTV2: V95%=99.5%
Spinal cord: Max dose=17.3 Gy
Stomach: Max=21.0Gy, Mean=9.5 Gy
Liver: Mean=15.5 Gy, D15Gyfree=2811cc

MU:3216+3527+563
BOT: 174s(80+82+14s)

CLIPS AS FIDUCIAL MARKERS



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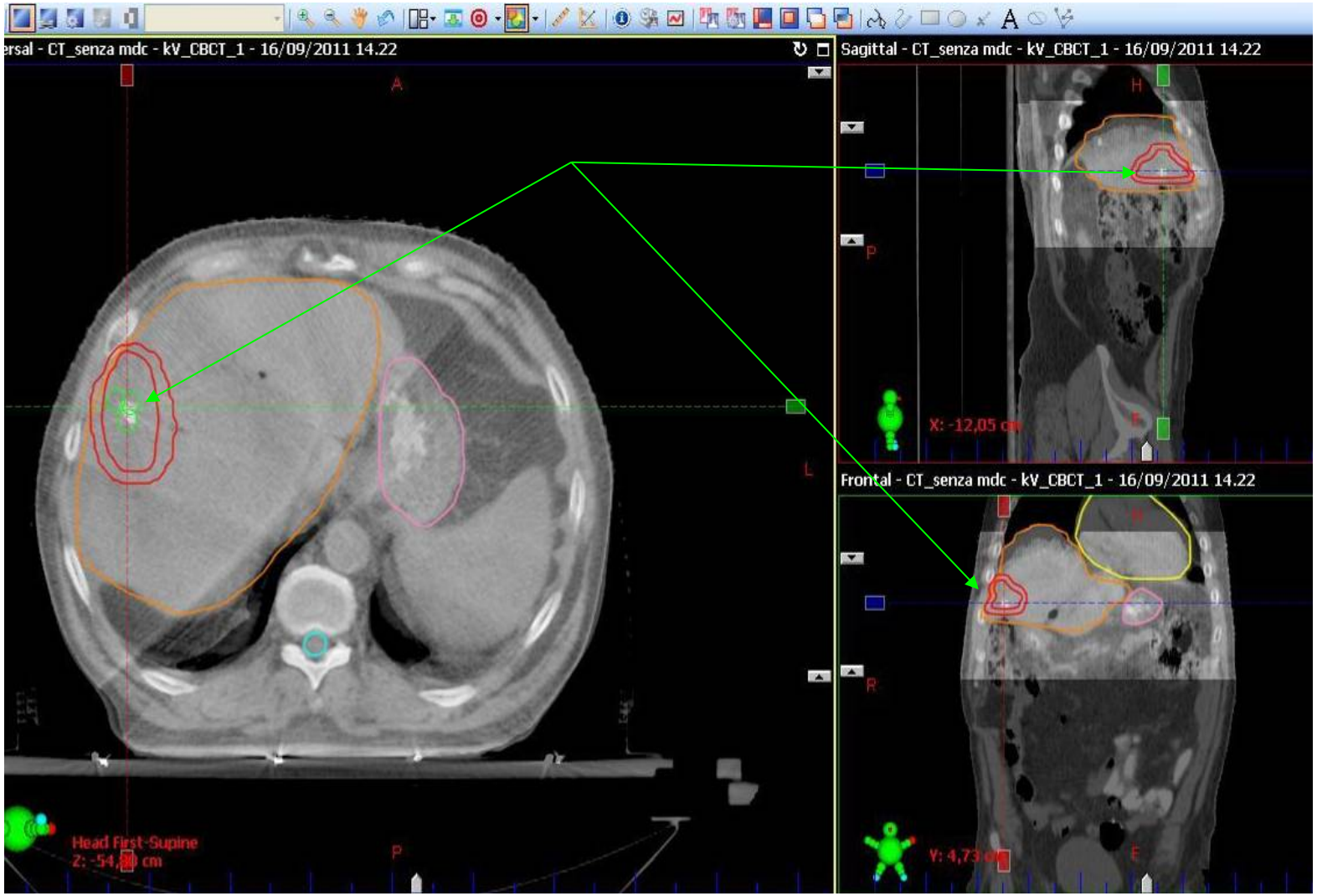
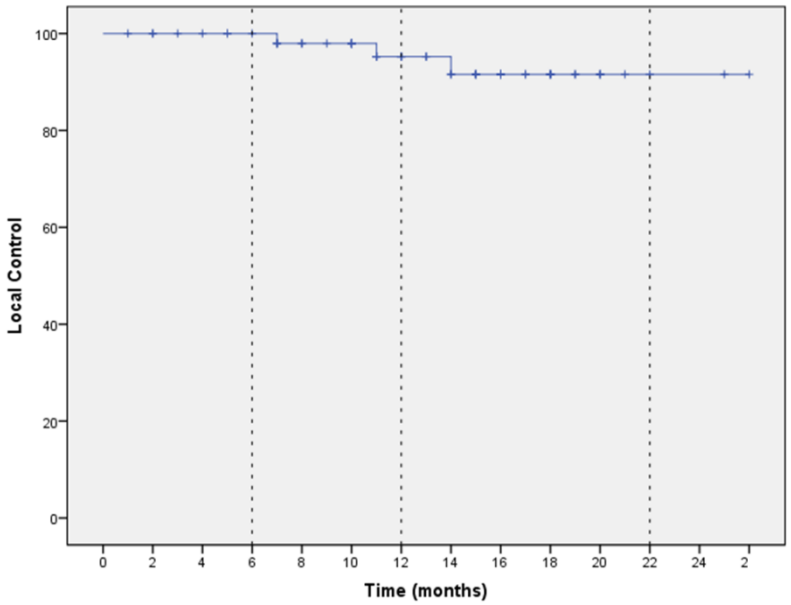
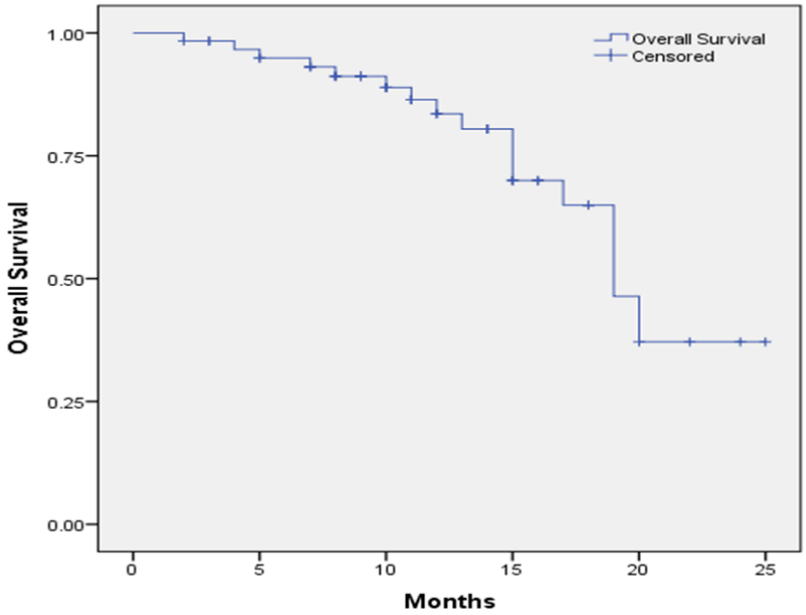




1 year Local Control: 94%

A subgroup analysis for lesions with diameter < 3 cm compared with those > 3 cm revealed no statistical differences in local control rates (p=0.90)

1 year OS = 84%
median OS =19 months



ACUTE TOXICITY:

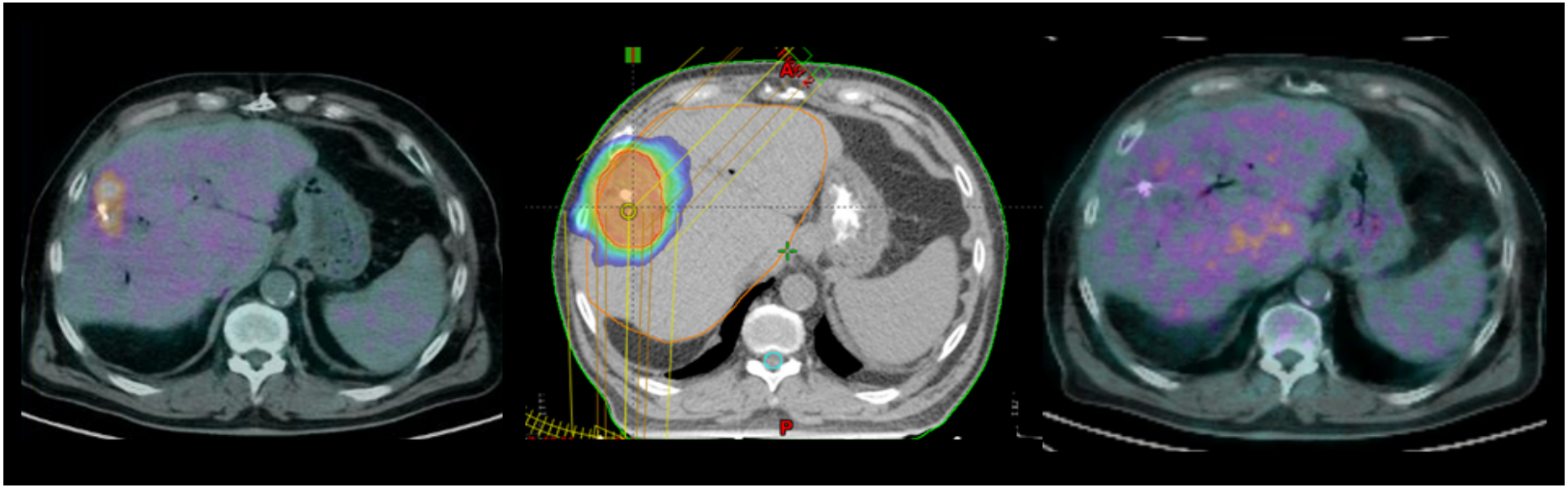
- **G2 toxicity (vomiting, skin erythema and pain) 4%**
- **G2 transient transaminase increase 26%**
- **No G3-G4 or G5 toxicity observed**

LATE TOXICITY:

One case of G3 chronic chest wall pain

NO RILD

Patient treated with SBRT for local relapse after hepatic surgery for colorectal metastasis

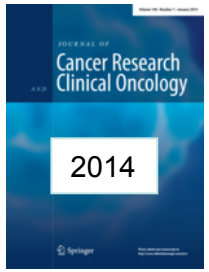


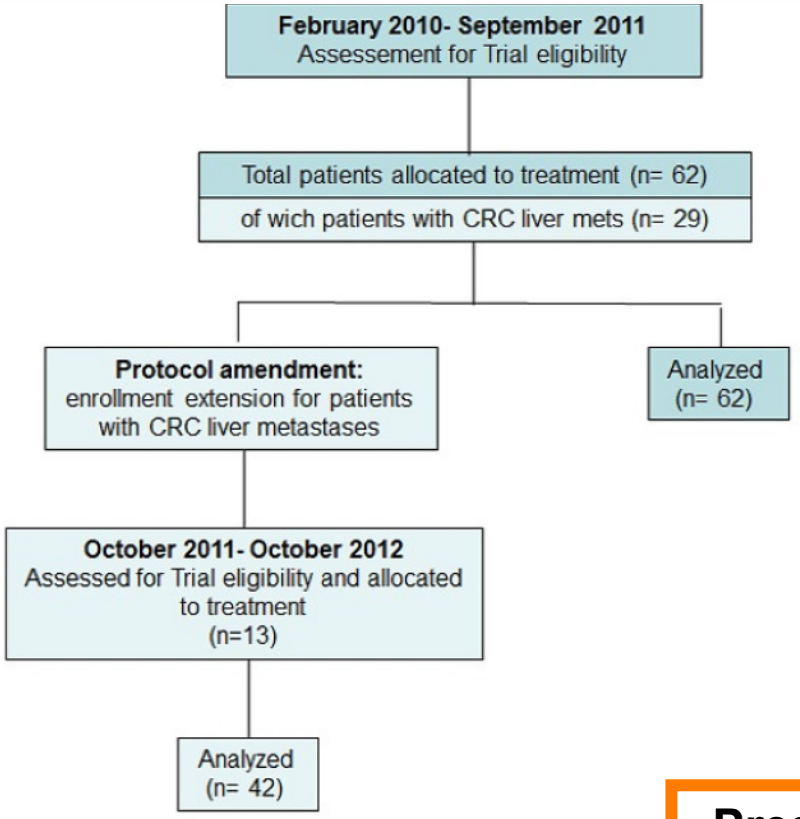
PET –CT pre-treatment, CEA 72

PET –CT post-treatment CEA 2.2

Final results of a phase II trial for stereotactic body radiation therapy for patients with inoperable liver metastases from colorectal cancer

Marta Scorsetti · Tiziana Comito · Angelo Tozzi · Pierina Navarria · Antonella Fogliata · Elena Clerici · Pietro Mancosu · Giacomo Reggiori · Lorenza Rimassa · Guido Torzilli · Stefano Tomatis · Armando Santoro · Luca Cozzi





INCLUSION CRITERIA:

- Unresectable CRC liver metastases
- Maximum tumor diameter < 6cm
- ≤ 3 discrete lesions
- Performance status 0-2
- Good compliance to treatment

END POINTS:

Primary: in-field local control

Secondary: toxicity and overall survival

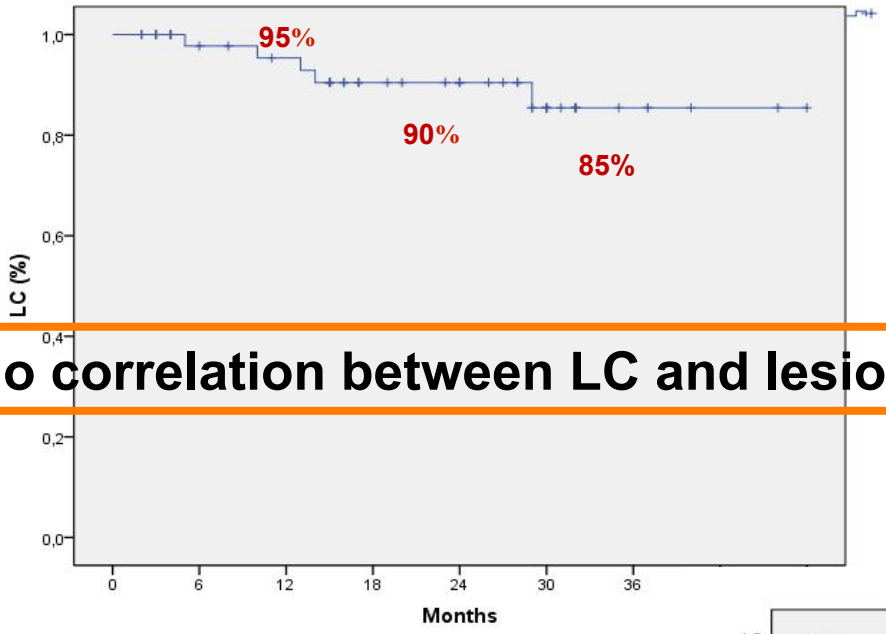
Prescription dose was **75Gy in 3 fractions**

Patients number	42
Mean age (range)y	67 (43–87)
Sex (M:F)	36:6
Primary	
Colon	30 (71%)
Rectum	12 (29%)
TNM Primary Classification	
T1	2 (5%)
T2	9 (21)
T3	28 (67%)
T4	3(7%)
N0	21 (50%)
N1-2	21 (50%)
M1	17 (40%)
Only liver	15 (88%)
Liver and lung	2 (12%)
Timing of liver metastases	
Synchronous (DFI ≤ 12 months)	20 (47.6%)
Metachronous (DFI > 12 months)	22 (52.4%)
Previous local treatments	
Surgery	17 (40%)
RFA or other	4 (9.5%)
Systemic treatments	
Pre-SBRT chemotherapy	42 (100%)
Post-SBRT chemotherapy	6 (14%)
Time of SBRT since diagnosis	
<12 mo	3 (7 %)
>12 mo	39 (93%)

February 2010- October 2012

Median FUP 24 months (4-48 months)

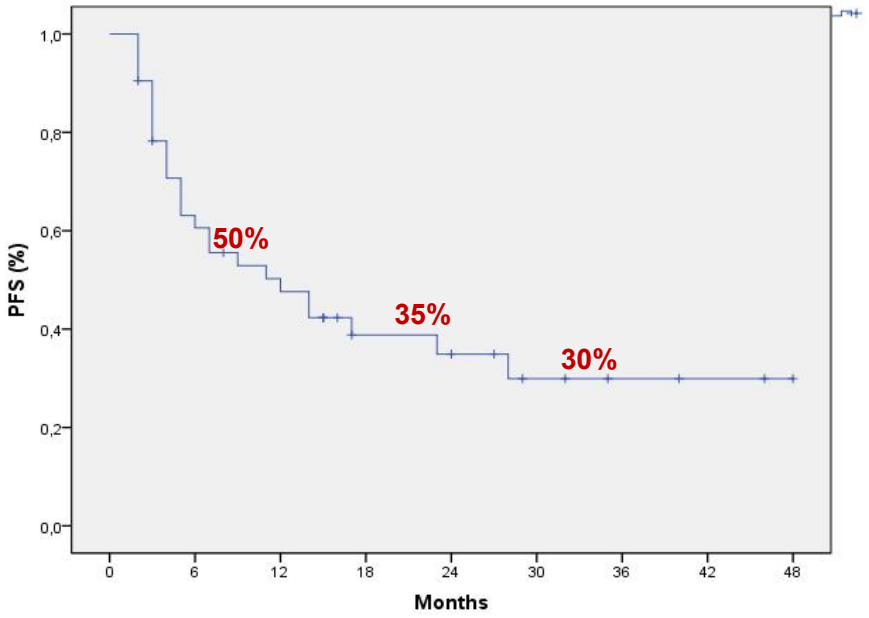
Number of lesions treated	52
Number of lesions for patients	
1	34 (81%)
2	5 (12%)
3	3(7%)
Size of lesions	
< 3 cm	28 (55%)
> 3 cm	24 (45%)
Mean volume (range) [cm^3]	
CTV	18.6 ± 22.03 (1.8-134.3)
PTV	54.90 ± 41.90 (7.7-909.10)



1 - year LC = 95%
2 – years LC = 90%
3 – years LC = 85%

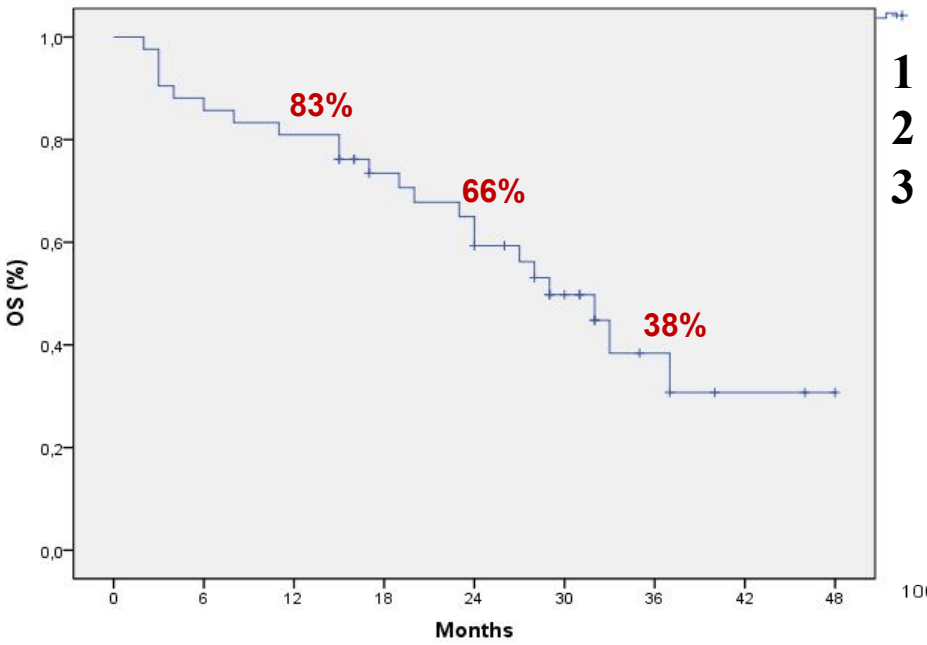
No correlation between LC and lesion size

Median PFS = 12 months

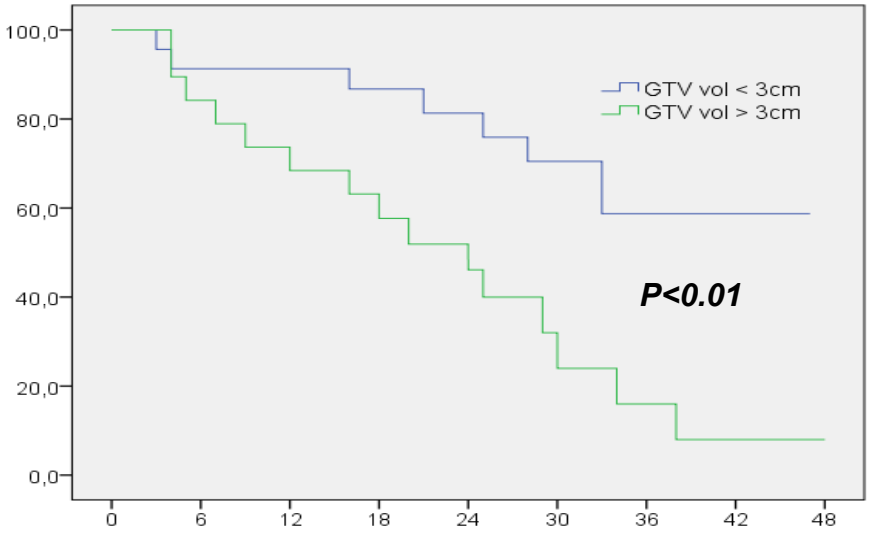


1 - year PFS = 50 %
2 - years PFS = 35%
3 – years PFS = 30%

Median OS = 29 months



1 - year OS = 83%
2 - years OS = 66%
3 - years OS = 38%

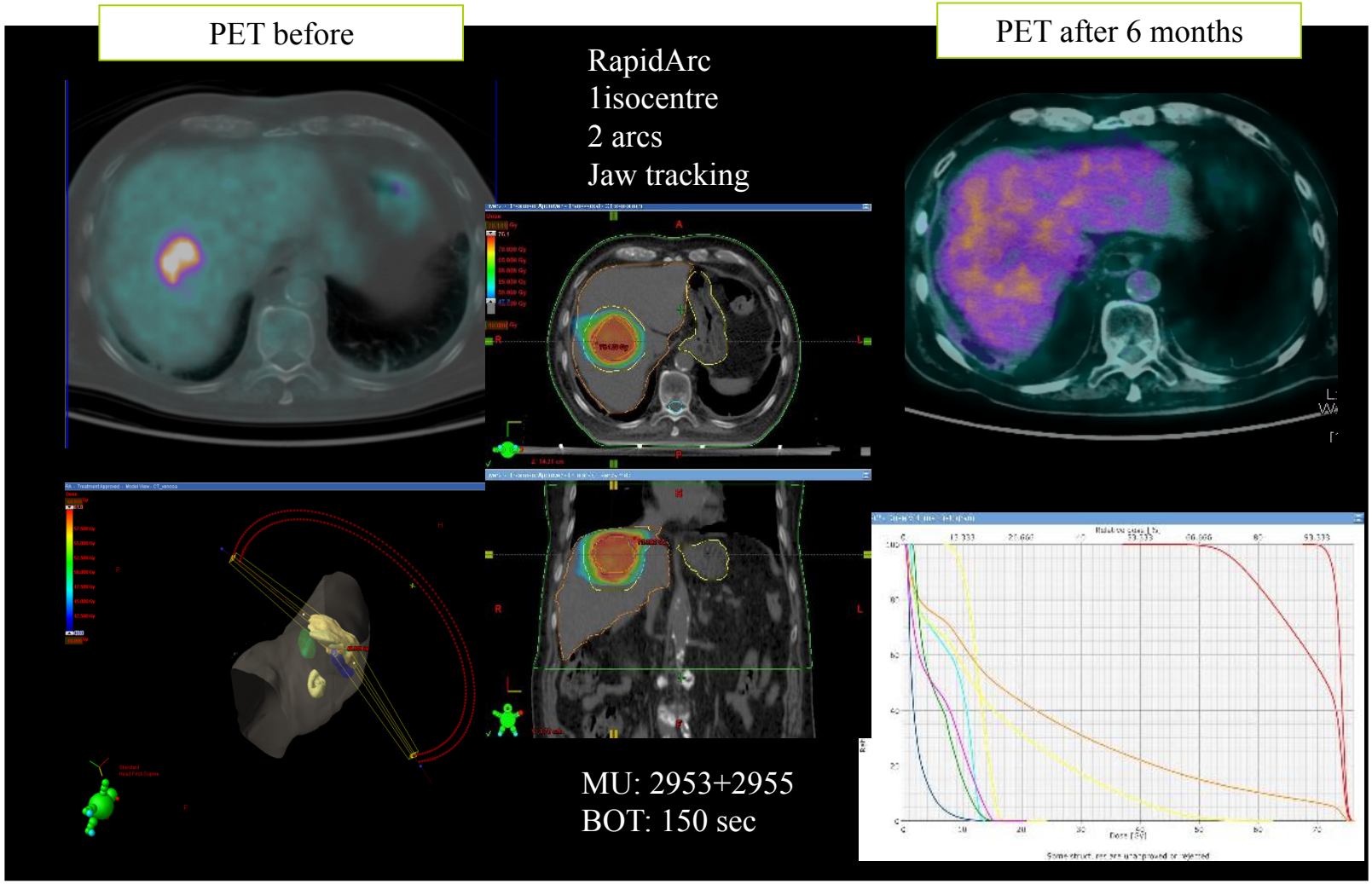


ACUTE and LATE TOXICITY:

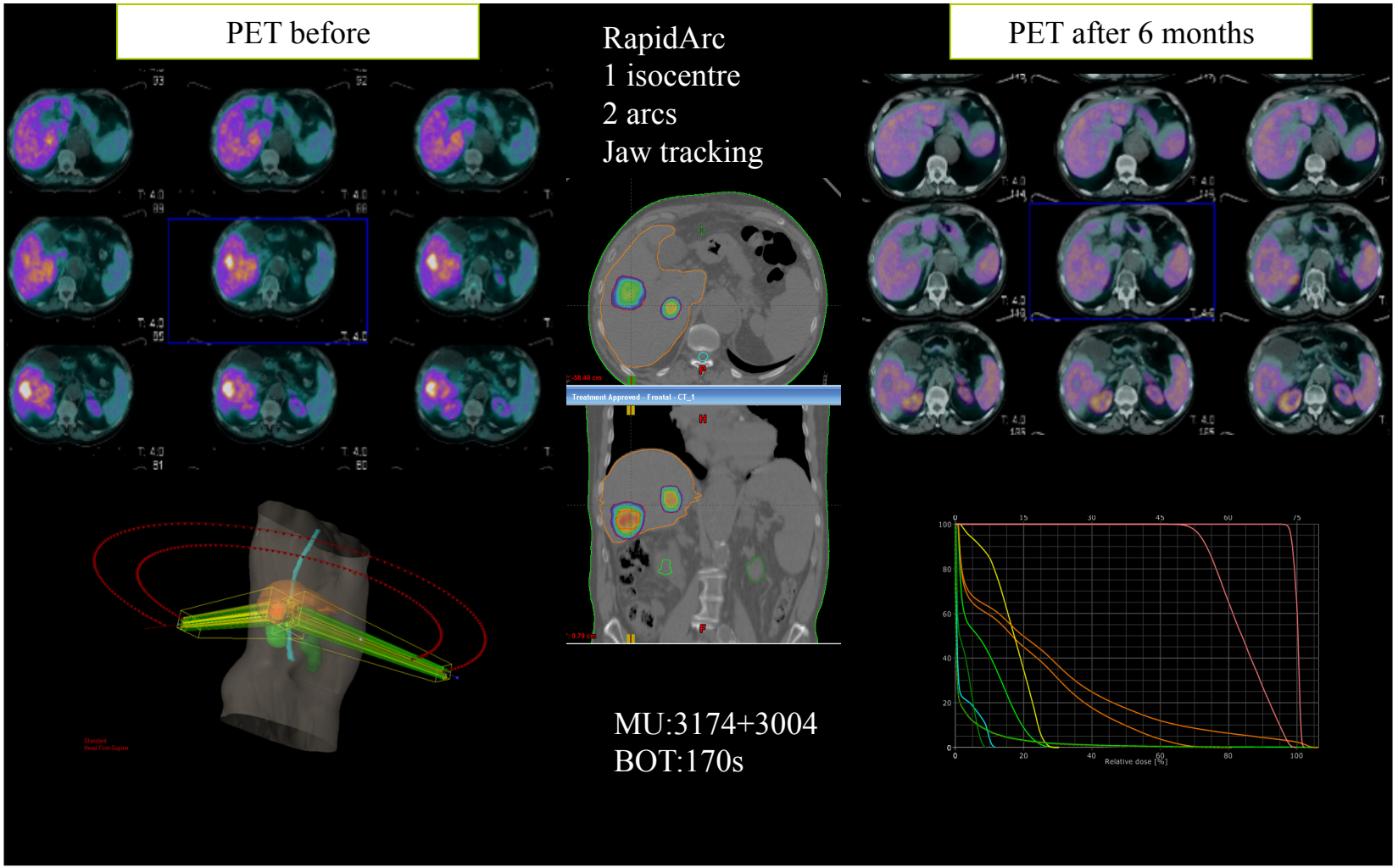
No G3-G4 or G5 toxicity observed

No RILD

Patient treated with SBRT for inoperable colorectal liver metastasis



Patient treated with SBRT for two colorectal liver metastasis



Liver metastases: conclusions

Current evidence of SBRT in liver metastases:

- **Feasibility**: Non invasive and low toxicity
- **Efficacy:** Acceptable local control rate

Stereotactic body radiation therapy for liver metastases

Marta Scorsetti, Elena Clerici and Tiziana Comito

Journal of Gastrointestinal Oncology 2014 ISSN 2078-6891

Table 2

Selection criteria for SBRT

Selection criteria	Patients categories		
	Suitable	Cautionary	Unsuitable
Lesion number	<3	4	>4
Lesion diameter (cm)	1-3	>3 and ≤6	>6
Distance from OARs (mm)	>8	5-8	<5
Liver function	Child A	Child B	Child C
Free liver volume (cc)	>1,000	<1,000 and ≥700	<700

SBRT, stereotactic body radiation therapy; OARs, organs at risk.

Liver metastases: conclusions

Future directions:

1. Selection of patients with favourable prognosis to evaluate the impact on survival
2. Comparative RCTs with other local procedures (SR and RF)

1. Association with chemo\target therapy
2. Multidisciplinary Integration of therapy

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SBRT nel distretto addome-pelvi:

- Tumori del fegato:
  - Metastasi epatiche
  - HCC
- Tumore del pancreas
- Tumore della prostata

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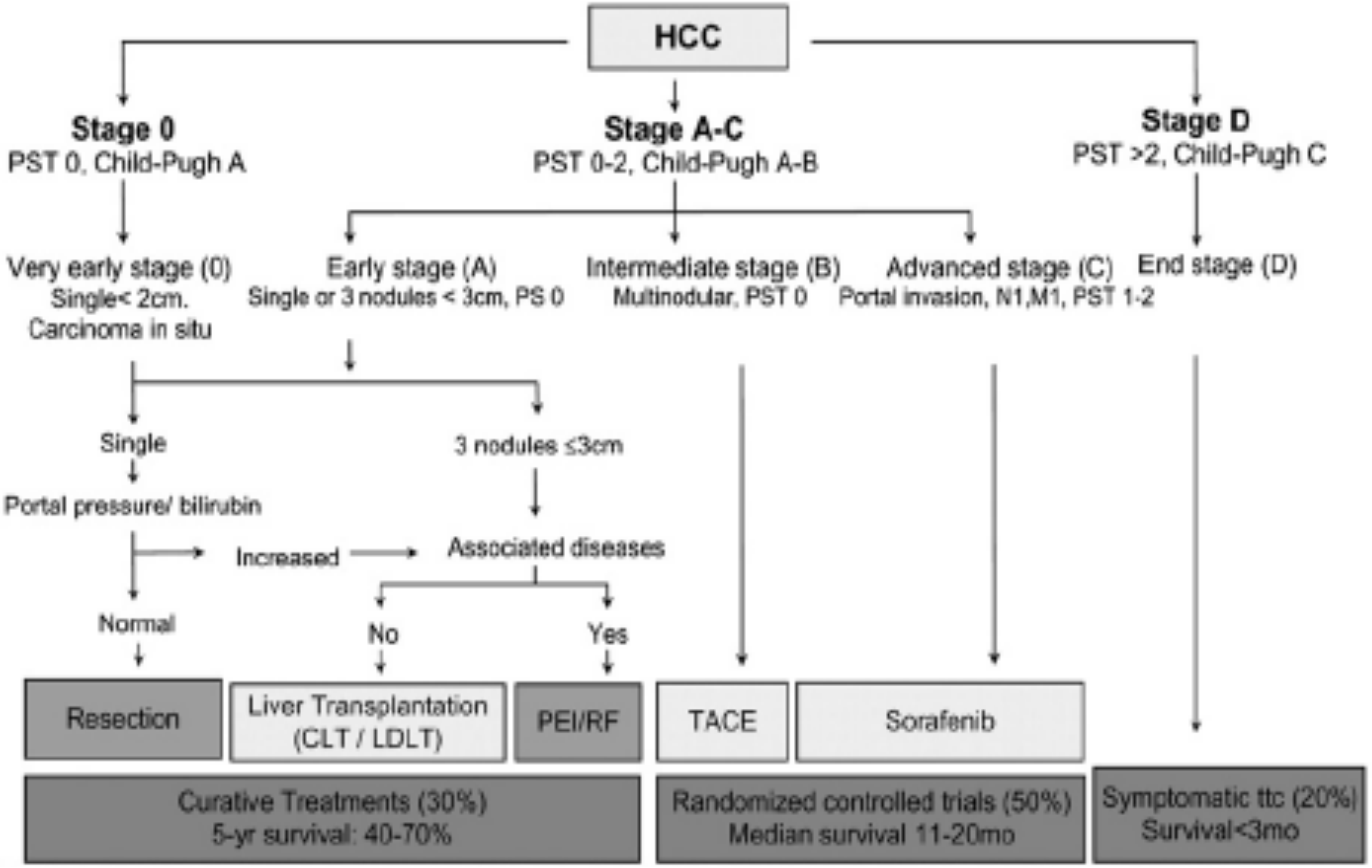
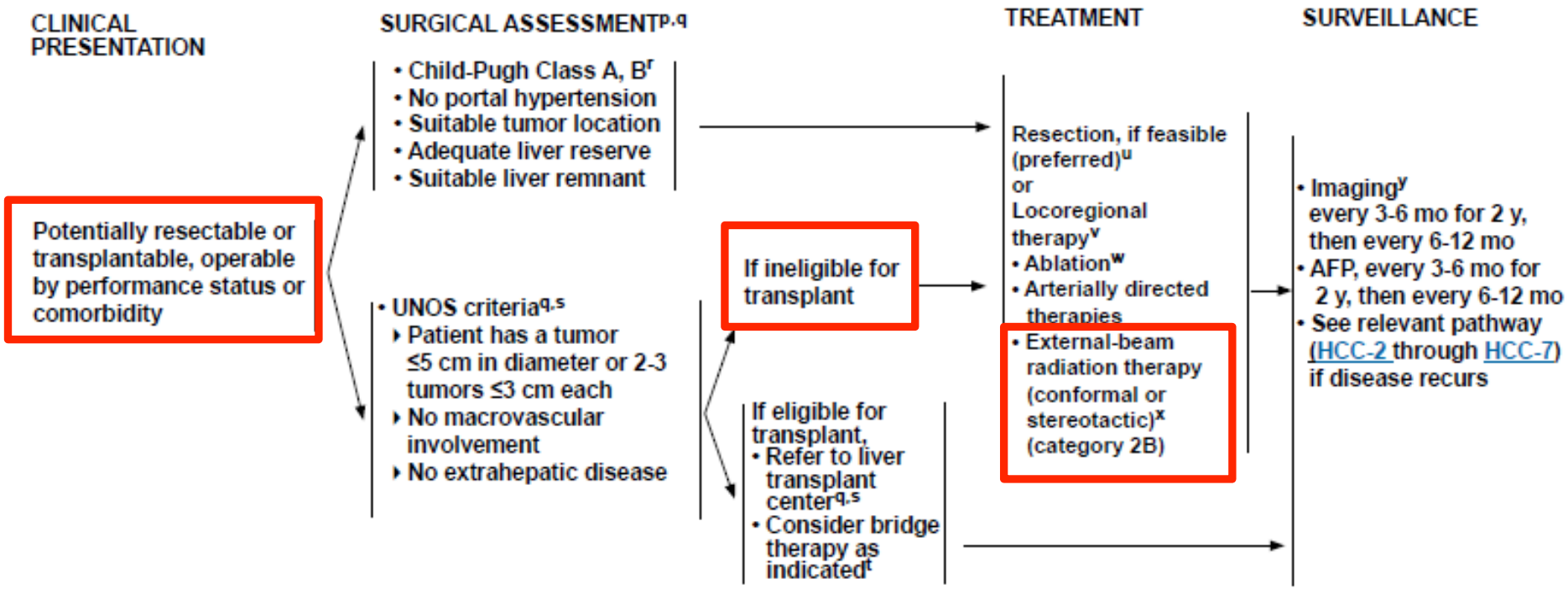
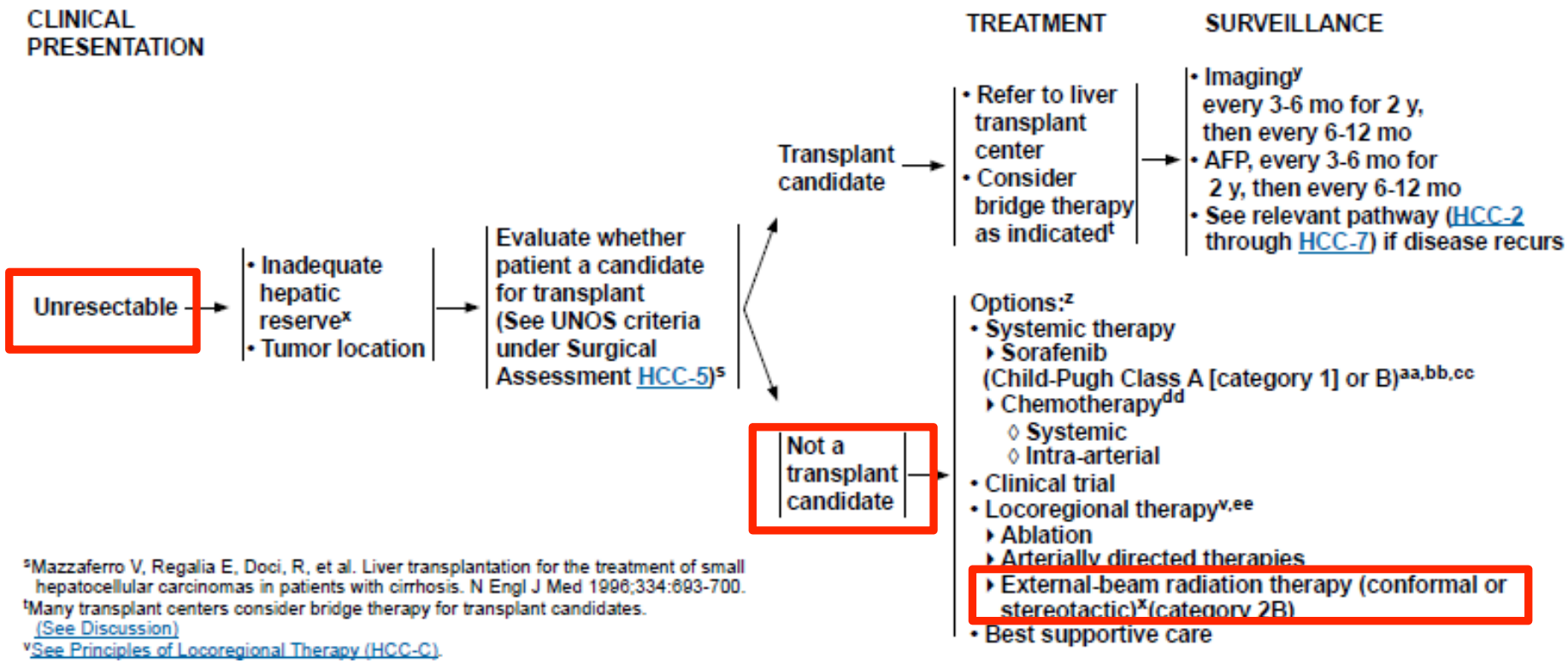
BCLC staging system



Jonathan Klein and Laura A. Dawson, Int J Rad Onc Biol Ph. 2012


CLINICAL PRESENTATION
SURGICAL ASSESSMENT[p,q]
TREATMENT
SURVEILLANCE
Potentially resectable or transplantable, operable by performance status or comorbidity
• Child-Pugh Class A, B[r]
• No portal hypertension
• Suitable tumor location
• Adequate liver reserve
• Suitable liver remnant
• UNOS criteria[q,s]
Patient has a tumor ≤5 cm in diameter or 2-3 tumors ≤3 cm each
No macrovascular involvement
No extrahepatic disease
If ineligible for transplant
If eligible for transplant,
• Refer to liver transplant center[q,s]
• Consider bridge therapy as indicated[t]
Resection, if feasible (preferred)[u]
or
Locoregional therapy[v]
• Ablation[w]
• Arterially directed therapies
• External-beam radiation therapy (conformal or stereotactic)[x] (category 2B)
• Imaging[y] 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



[s]Mazzaferro V, Regalia E, Doci, R, et al. Liver transplantation for the treatment of small hepatocellular carcinomas in patients with cirrhosis. N Engl J Med 1996;334:693-700.
[t]Many transplant centers consider bridge therapy for transplant candidates. (See Discussion)
[v]See Principles of Locoregional Therapy (HCC-C).

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

Options:[z]
- Sorafenib (Child-Pugh Class A [category 1] or B)[aa,bb,cc]
- Clinical trial
- Locoregional therapy[v]
  - Ablation
  - Arterially directed therapies
  - External-beam radiation therapy (conformal or stereotactic)[x] (category 2B)
- Best supportive care

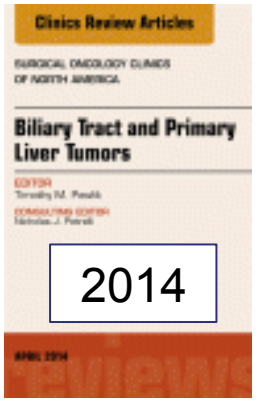
Metastatic disease or Extensive liver tumor burden → Consider biopsy to confirm metastatic disease →

Options:[z]
- Sorafenib (Child-Pugh Class A [category 1] or B)[aa,bb,cc]
- Clinical trial
- Best supportive care

PRINCIPLES OF LOCOREGIONAL THERAPY

External-beam radiation therapy (EBRT)

- All tumors irrespective of the location may be amenable to EBRT (Stereotactic body radiation therapy [SBRT] or 3D-conformal radiation therapy).
- SBRT is an advanced technique of EBRT that delivers large ablative doses of radiation.
- There is growing evidence for the usefulness of SBRT in the management of patients with HCC.[17] SBRT can be considered as alternative to the ablation/embolization techniques mentioned above or when these therapies have failed or are contraindicated.
- SBRT is often used for patients with 1-3 tumors. SBRT could be considered for larger lesions or more extensive disease, if there is sufficient uninvolved liver and liver radiation tolerance can be respected. There should be no extrahepatic disease or it should be minimal and addressed in a comprehensive management plan. The majority of data on radiation for HCC liver tumors arises from patients with Child-Pugh A liver disease; safety data are limited for patients with Child-Pugh B or poorer liver functon. Those with Child-Pugh B cirrhosis can be safely treated, but they may require dose modifications and strict dose constraint adherence.[18] The safety of liver radiation for HCC in patients with Child-Pugh C cirrhosis has not been established, as there are not likely to be clinical trials available for CP-C patients.[19,20]
- Palliative EBRT is appropriate for symptom control and/or prevention of complications from metastatic HCC lesions, such as bone or brain.



An Emerging Role for Radiation Therapy in the Treatment of Hepatocellular Carcinoma and Intrahepatic Cholangiocarcinoma

Jennifer Y. Wo, MD[a,*], Laura A. Dawson, MD[b], Andrew X. Zhu, MD, PhD[c], Theodore S. Hong, MD[a]

Table 1
Summary of SBRT literature for treatment of primary liver tumors

Author, Year	Study Design	Number of Patients	Tumor Size	Portal Vein Thrombus (%)	Dose (Gy	Number of Fractions	1-Y Overall Survival (%)	Grade ≥3 Toxicity (%)
Bujold et al,[5] 2013	Phase 1/2	102	Trial 1: no limits Trial 2: maximum dimension 15 cm	55	24–54	6	55	36
Andolino et al,[16] 2011	Retrospective	60	1–6.5 cm	NA	24–48	3–5	67 at 2 y	37
Cardenes et al,[17] 2010	Phase 1	17	≤6 cm	18	36–48	3–4	75	18
Kwon et al,[18] 2010	Retrospective	42	≤100 mL	0	30–39	3	93	2
Seo et al,[19] 2010	Retrospective	38	<10 cm	NA	33–57	3–4	69	0
Tse et al,[4] 2008	Phase 1	31	9–1913 mL	0	37.5	4	75	29
Méndez Romero et al,[20] 2006	Phase 1/2	8	NA	25	25–30	3–5	75	12.5

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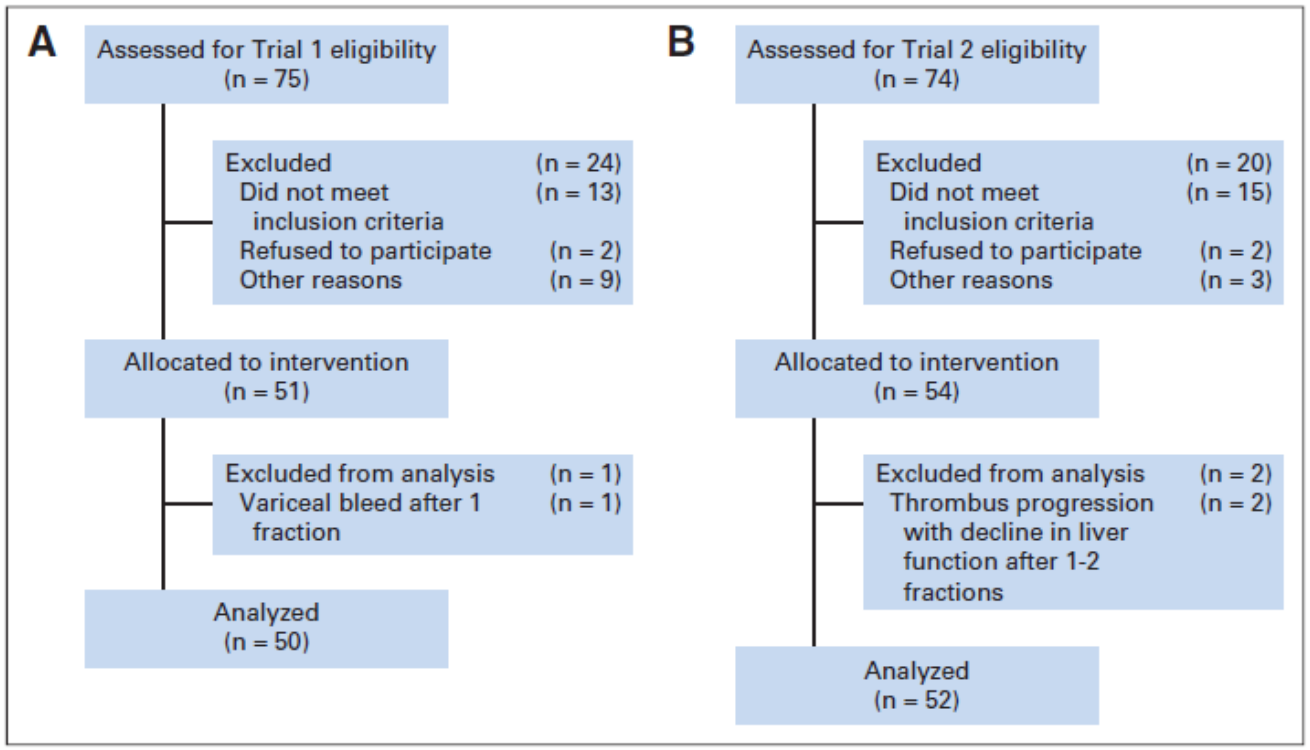
Sequential Phase I and II Trials of Stereotactic Body Radiotherapy for Locally Advanced Hepatocellular Carcinoma

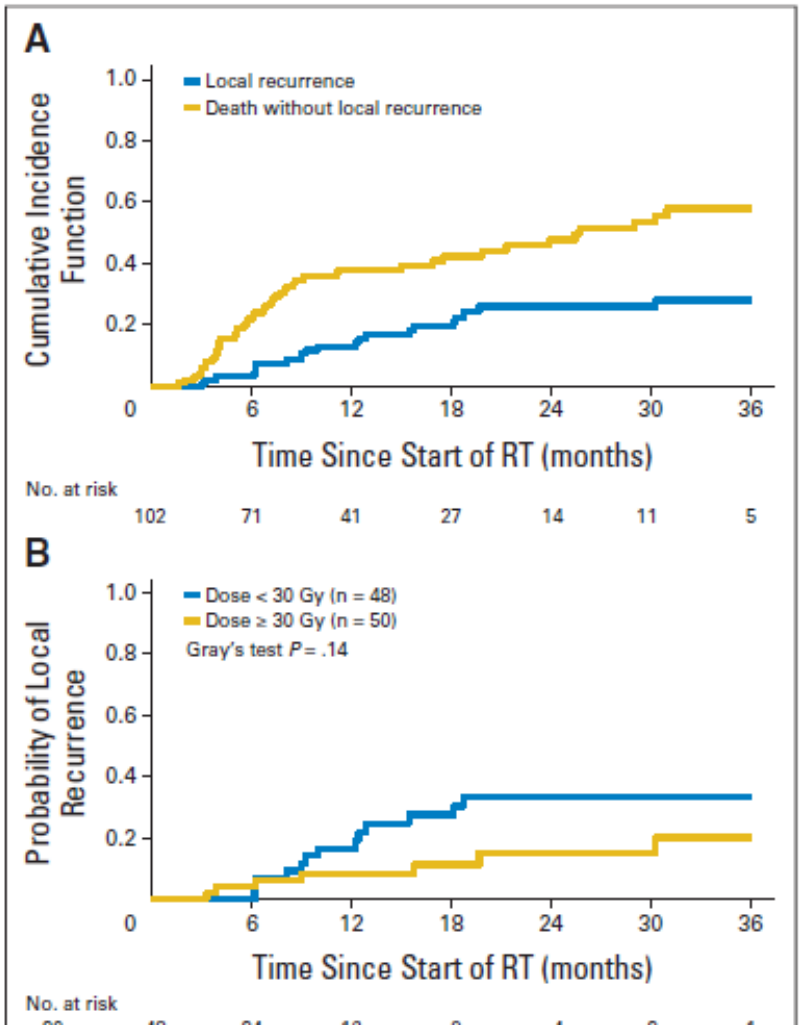
Alexis Bujold, Christine A. Massey, John J. Kim, James Brierley, Charles Cho, Rebecca K.S. Wong, Rob E. Dinniwell, Zahra Kassam, Jolie Ringash, Bernard Cummings, Jenna Sykes, Morris Sherman, Jennifer J. Knox, and Laura A. Dawson



Prescription dose, Gy§	
Median	36.0
Range	24.0-54.0

Table 2. Toxicity, CTCAE ≥ Grade 3

Toxicity	Grade 3		Grade 4		Grade 5	
	No.	%	No.	%	No.	%
All	27	26.5	3	2.9	7*	6.9
Fatigue	1	1.0	0	0.0	—	
Biochemical†						
Albumin	0	0.0	0	0.0	0	0.0
AST/ALT	11	10.9	0	0.0	—	
Bilirubin	3	3.0	2	2.0	—	
Creatinine	1	1.0	0	0.0	0	0.0
INR	0	0.0	—		—	
Hematologic†						
Hemoglobin	2	2.0	0	0.0	0	0.0
Leukocytes	1	1.0	0	0.0	0	0.0
Platelets	9	9.0	0	0.0	0	0.0
GI						
Cholangitis	0	0.0	0	0.0	1	1.0
Gastritis/GI bleed	1	1.0	0	0.0	1	1.0
Liver failure	1	1.0	1	1.0	5*	4.9
Nausea/vomiting	1	1.0	0	0.0	0	0.0
Pain (RUQ/chest wall)	1	1.0	0	0.0	—	
Proportion of patients with CTP deterioration, without progressive disease, %						
3 months						
Score			46			
Class			29			
12 months						
Score			17			
Class			6			



and extrahepatic disease was present in 12%. LC1y was 87% (95% CI, 78% to 93%). SBRT dose (hazard ratio [HR] = 0.96; $P = .02$) and being in Trial 2 (HR = 0.38; $P = .03$) were associated with LC1y on univariate analysis. Toxicity ≥ grade 3 was seen in 30% of patients. In seven patients (two with TVT PD), death was possibly related to treatment (1.1 to 7.7 months after SBRT). Median overall survival was 17.0 months (95% CI, 10.4 to 21.3 months), for which only TVT (HR =

HCC: Humanitas Experience

INCLUSION CRITERIA:

✓ Unsuitable for resection, TACE, RFA or alcohol ablation.

✓ Maximum tumor diameter < 8cm

✓ ≤ 3 discrete lesions

✓ Performance status 0-2

✓ Child-Turgotte-Pugh A or B liver score

✓ Absence of clinical ascites, encephalopathy, active hepatitis or gastric, duodenal or variceal bleed within 2 months of SBRT start.

✓ No concomitant chemotherapy.

Treatment characteristics

February 2011 and April 2014: 54 patients

Treatment charateristics	Value
No. of lesions	**82**
No. of lesions per patient	1 for 31 pts (57%) 2 for 18 pts (34%) 3 for 5 pts (9%)

Dose prescription	Lesions
48-75 Gy/3fr	**30 (37 %)**
36-45 Gy/6fr	**33 (40 %)**
40-50 Gy/10fr	**19 (23 %)**

Dose prescription and fractionation were according to **lesions size** and **liver function**.

SBRT for HCC: Patients characteristics

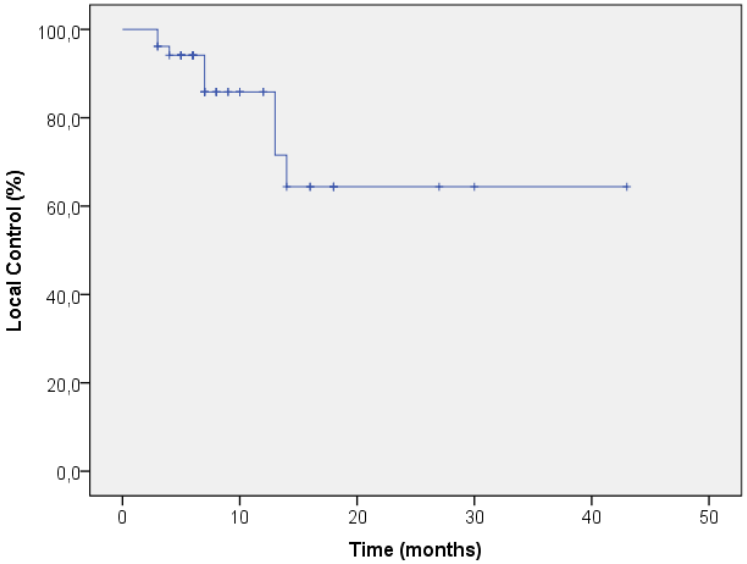
Patients number	43
Mean age (range)y	72 (46–87)
Sex (M:F)	31:12
CTP class	
A	23 (53%)
B	20 (47%)
Hepatitis aetiology	
B	2 (4%)
C	28(64%)
Alcohol related	9 (20%)
No hepatitis	12 (28%)
BCLC stage	
A	10 (44%)
B	15 (36%)
C	9 (20%)
Portal vein thrombosis	
Yes	9 (20%)
No	34 (80%)
Previous local treatments	
Surgery	3 (8%)
RFA	5 (12%)
TACE or TAE	9 (41%)
PEI	2 (4%)
Presence of stable extrahepatic disease at SBRT time	
Yes	2 (4%)
No	41 (96%)
Number of lesions for patients	
1	24 (57%)
2	15 (34%)
3	4 (9%)
Prescription dose	
48-75 Gy /3fr	22 (51%)
36-60 Gy / 6fr	21 (49%)

Median FUP 8 months (range 3-43)

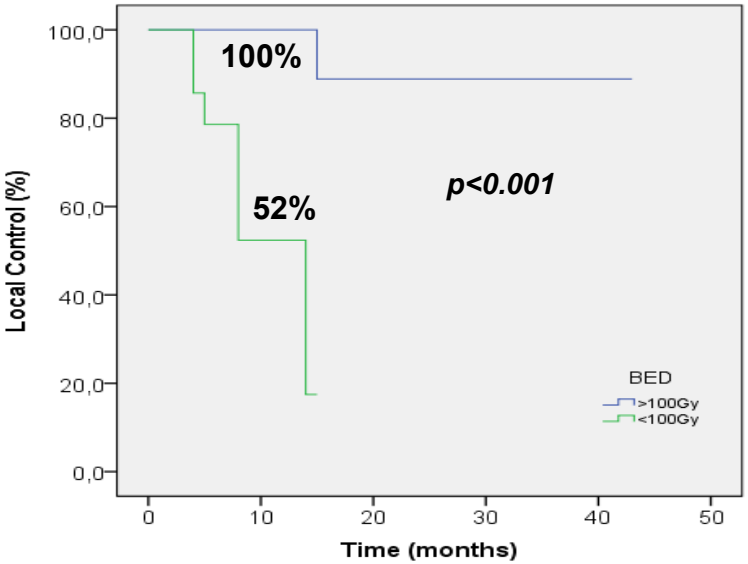
Number of lesions treated	63
Prescription dose	
48-75 Gy /3fr	30 (48 %)
36-60 Gy / 6fr	33 (52 %)
Median tumor size (range)	4.8 cm (1-12.5)

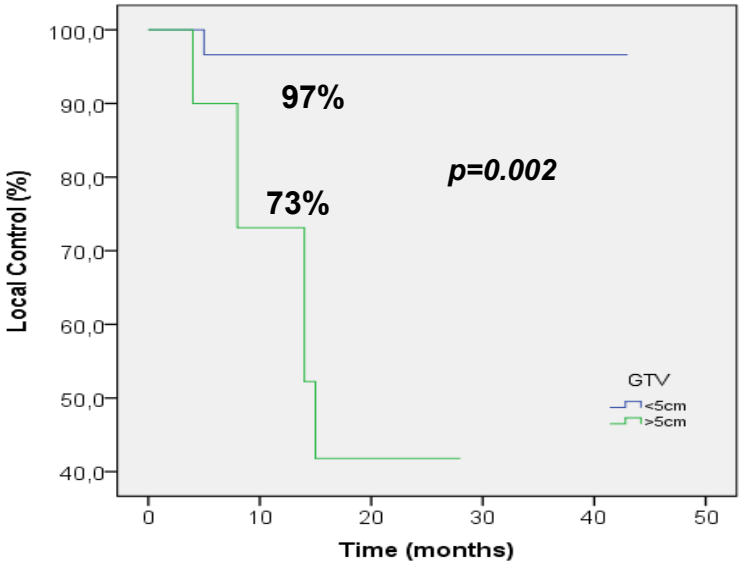
Tumor size **Liver Function**	**(diam < 3cm)** **Child-Pugh A-B**	**(diam 3-6cm)** **Child-Pugh A-B**
Prescription Dose	**48 - 75 Gy (16 - 25Gy / 3 fr)**	**36 – 60 Gy (6 - 10 Gy / 6fr)**

Local control



Actuarial LC
6 months: 94%
12 months: 86%
24 months: 64%.





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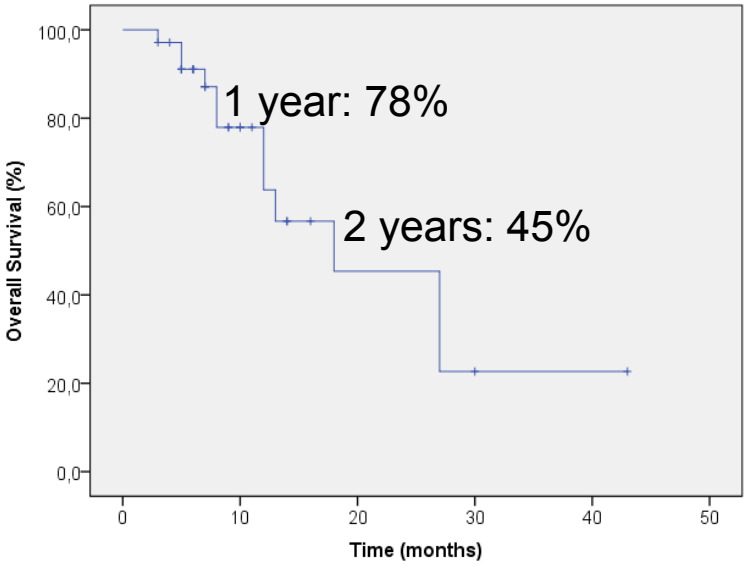
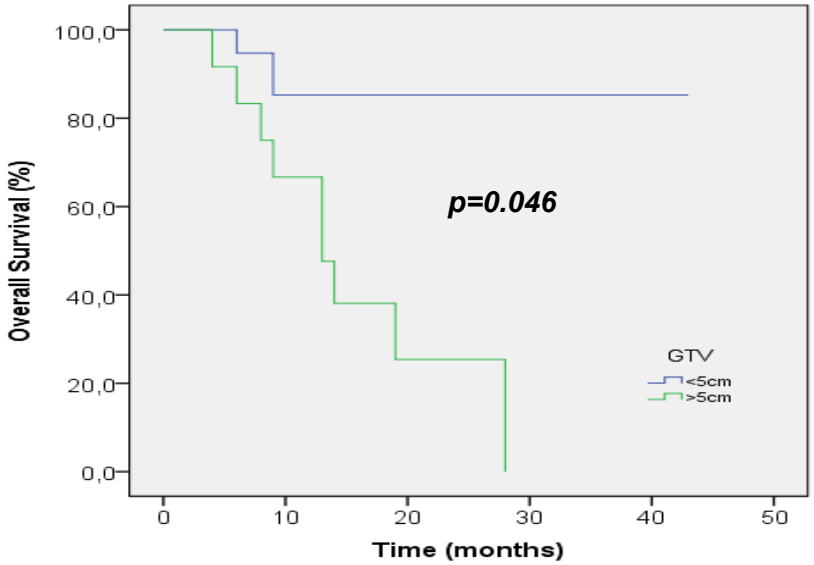
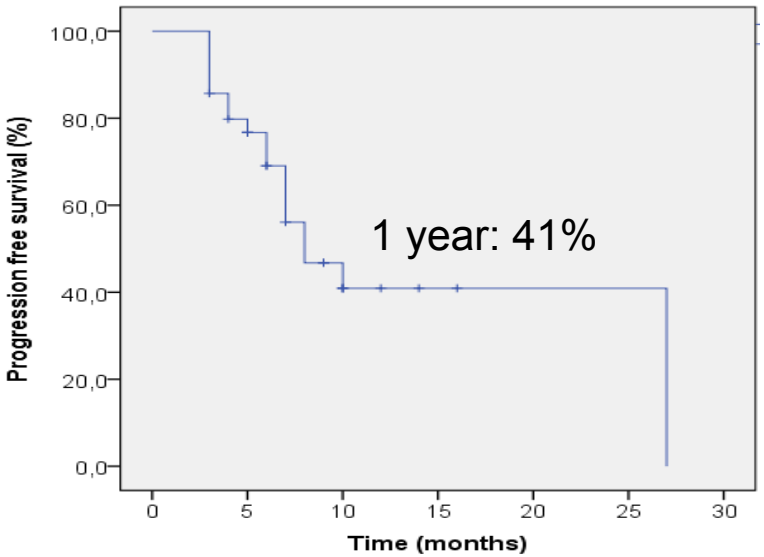
Overall Survival and Progression free survival

Median OS was 18 months.





Median PFS was 8.0 months.



Factors	1 years LC (rates)	*p* value	Median OS (months)	*p* value
Cumulative GTV				
< 5 cm	97%	*0.02*	33.0	*0.04*
> 5 cm	73%		12.8	
Number of fractions				
3	100%	*0.002*	18.9	*0.18*
6	68%		13.2	
BED				
≥ 100 Gy	100%	*0.001*	27.0	*0.05*
< 100 Gy	52%		8.1	
LC				
Local PD	-	-	7.8	*0.04*
No local PD	-		18.8	

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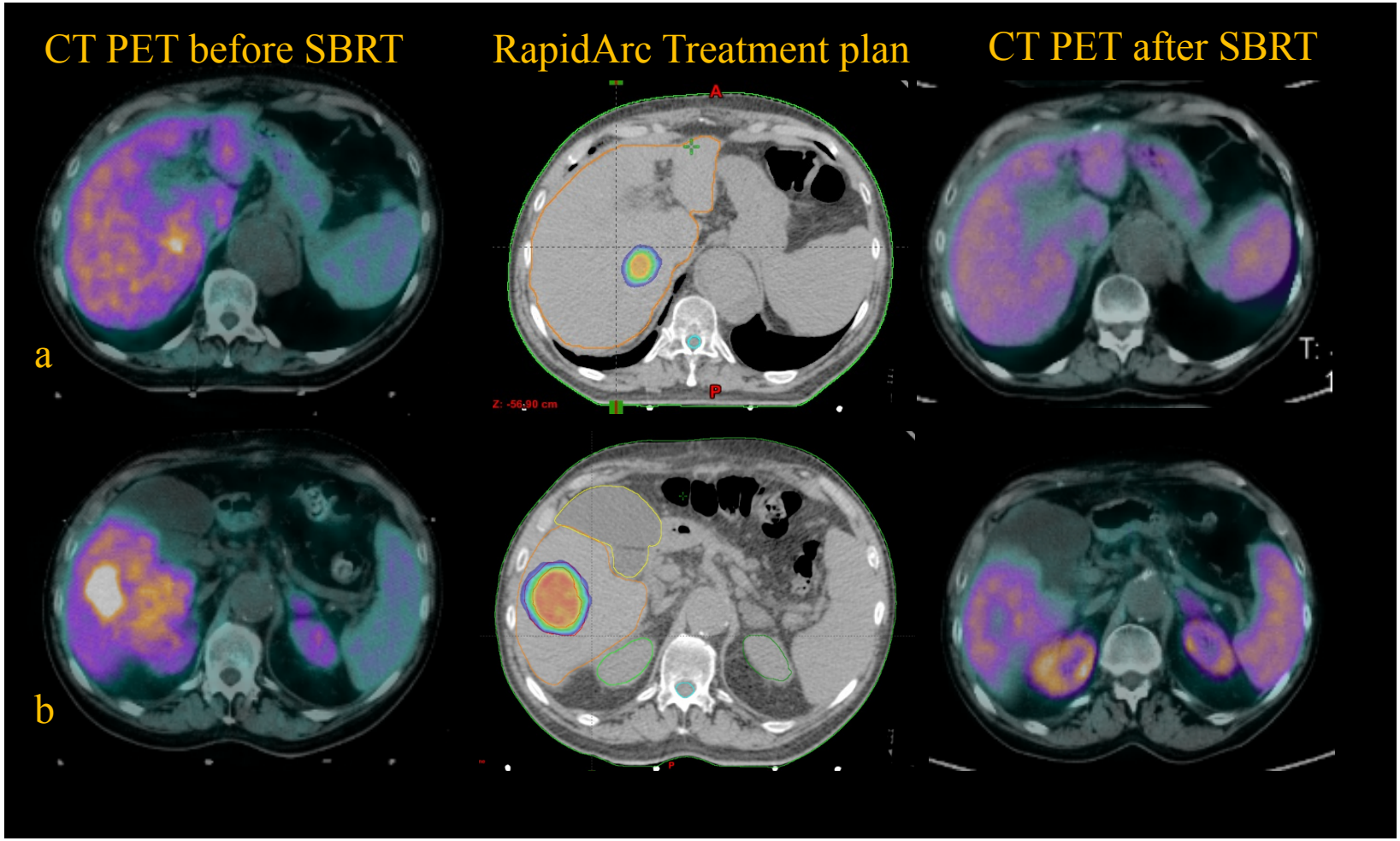
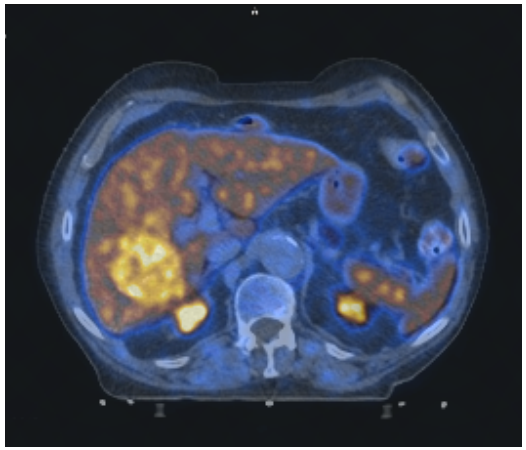
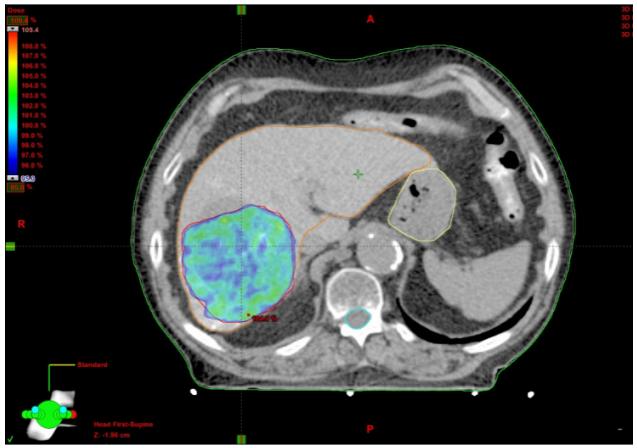


Examples of dose distributions and treatment outcome for two patients in the two fractionation groups (a: 75 Gy in 3 fractions, b: 60 Gy in 6 fractions).

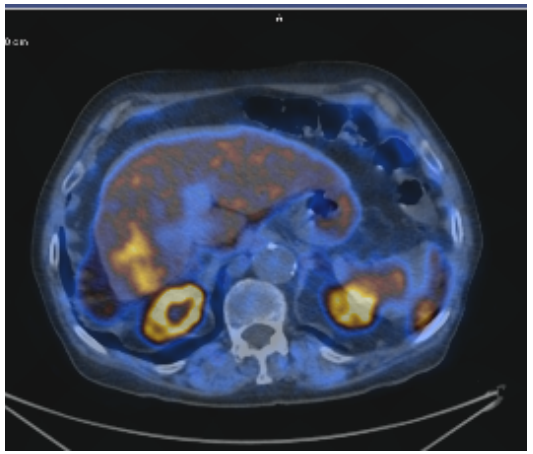
Partial remission after incomplete TACE plus SBRT
CT-PET evaluation



before RT



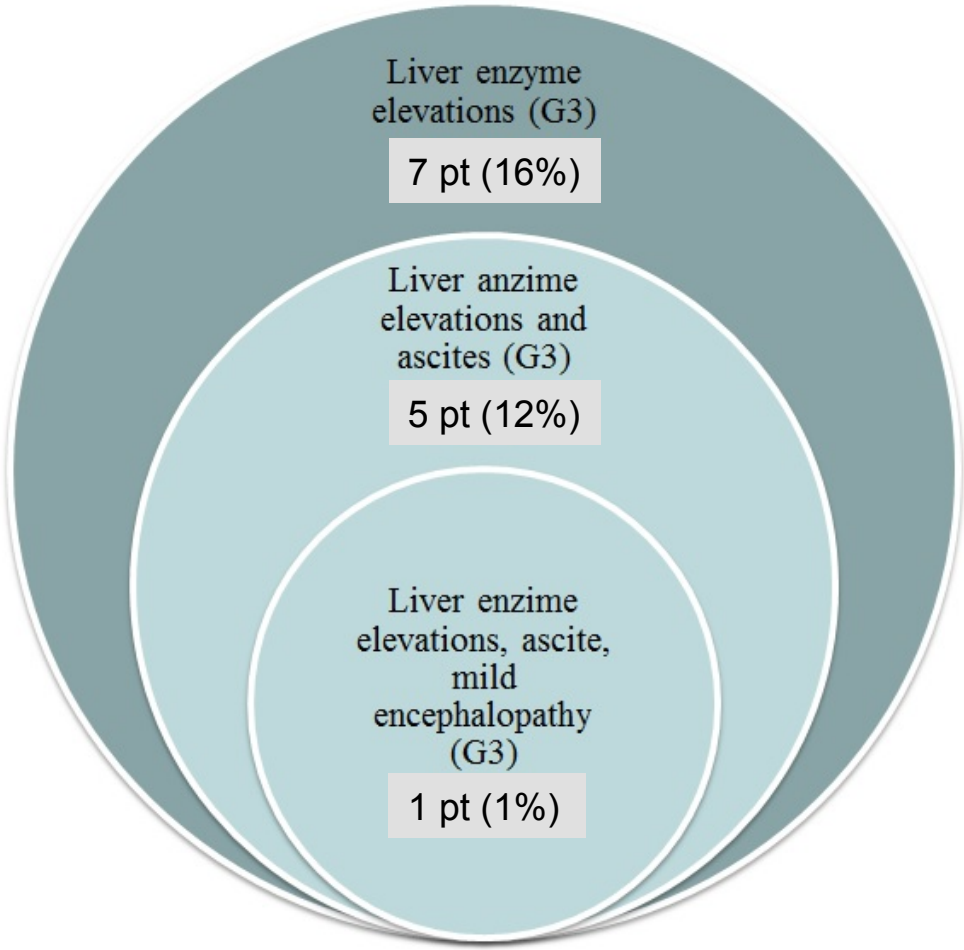
RA Treatment plan



after RT

SBRT HCC dose: 50 Gy /10 fr Beam 10 FFF Two arcs BOT = 01':40'' 1272 MU

Toxicity


Liver enzyme elevations (G3)
7 pt (16%)
Liver anzime elevations and ascites (G3)
5 pt (12%)
Liver enzime elevations, ascite, mild encephalopathy (G3)
1 pt (1%)

HCC: conclusions

Current evidence:

Feasibility: Non invasive and acceptable toxicity

Efficacy: Encouraging local control rate

Future directions:

1. RCTs with other local procedures
2. Integration therapy
3. Escalation RT dose

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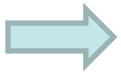
SBRT nel distretto addome-pelvi:

- **Tumori del fegato:**
  - **Metastasi epatiche**
  - **HCC**
- **Tumore del pancreas**
- **Tumore della prostata**

Pancreatic tumors: the challenge of cure

- Second most common gastrointestinal cancer
- High mortality rates

- Decrease of surgical morbidity
- Chemotherapy intensification
- Radiation therapy addition



Only middle OS improved

5-year OS rates < 25%

National Cancer Institute Annual Cancer Statistics Review 1973–1988, Bethesda.

Gudjonsson B: Cancer of the pancreas. 50 years of surgery. Cancer 1987.

Raimondi S, et al Epidemiology of pancreatic cancer: An overview. Nat Rev Gastroenterol Hepatol 2009.

Surgery: the only curative treatment

- median OS 15–22 months and a 5-year survival rate of about 20-25%

Less than 20%-30% of pancreatic tumors are resectable at the time of diagnosis

2. Borderline resectable

3. Unresectable

→ **- CT**
- Chemo- radiation treatment

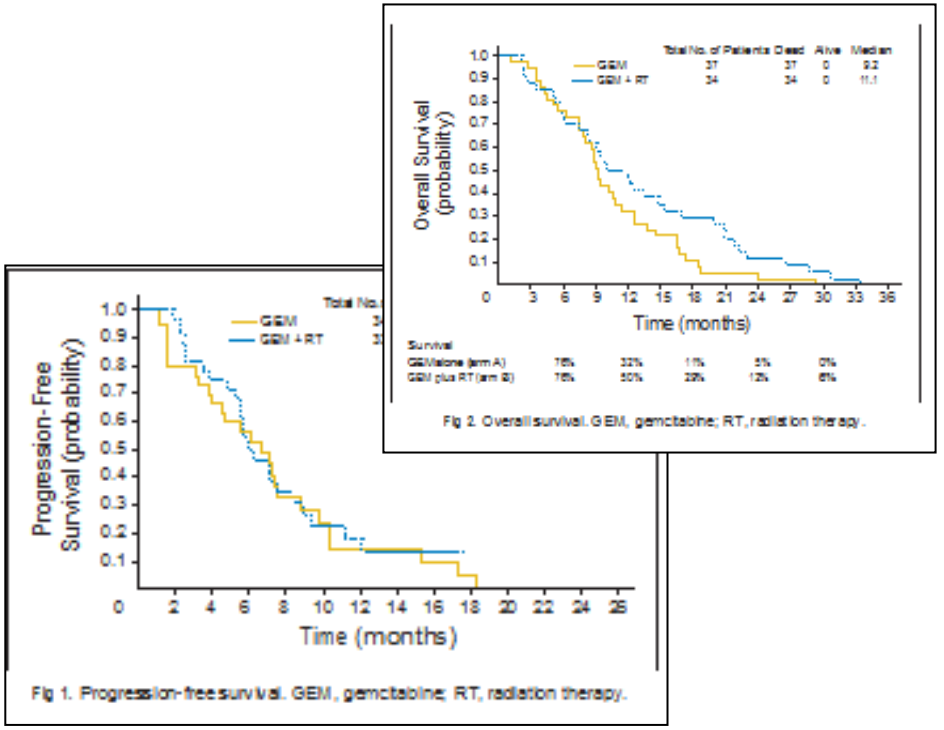
Gemcitabine Alone Versus Gemcitabine Plus Radiotherapy in Patients With Locally Advanced Pancreatic Cancer: An Eastern Cooperative Oncology Group Trial

Patrick J. Loehrer Sr, Yang Feng, Higinia Cardenes, Lynne Wagner, Joanna M. Brell, David Cella, Patrick Flynn, Ramesh K. Ramanathan, Christopher H. Crane, Steven R. Alberts, and Al B. Benson III

- **CRT: 50.4 Gy/ 28 fr Gy + GEM**
- **GEM alone**

CRT:

- Increased toxicity
- Median survival improvement (9.2 to 11.1 months)
- No differences in PFS



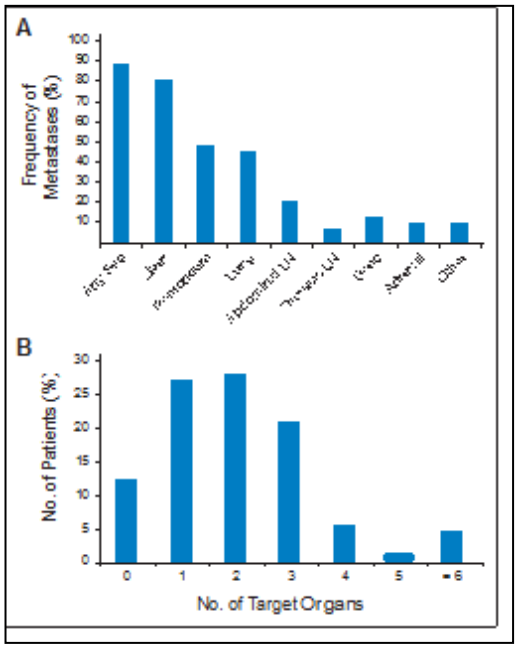
How much is important the local control of this “systemic” disease?

DPC4 Gene Status of the Primary Carcinoma Correlates With Patterns of Failure in Patients With Pancreatic Cancer

Christine A. Iacobuzio-Donahue, Baojin Fu, Shinichi Yachida, Mingde Luo, Hisashi Abe, Clark M. Henderson, Felip Vilardell, Zheng Wang, Jesse W. Keller, Priya Banerjee, Joseph M. Herman, John L. Cameron, Charles *J. Yeo, Marc K. Halushka, James R. Eshleman, Marian Raben, Alison P. Klein, Ralph H. Hruban, Manuel Hidalgo, and Daniel Laheru*

- Up to 30% of patients died for locally destructive disease with few or no distant metastases

- There is a population with genetically determined tendency to local progression



The importance of prognostic factors: Ca 19.9

Prognostic impact of perioperative serum CA 19-9 levels in patients with resectable pancreatic cancer.

Kondo N1, Murakami Y, Uemura K, Hayashidani Y, Sudo T, Hashimoto Y, Nakashima A, Sakabe R, Shigemoto N, Kato Y, Ohge H, Sueda T.

CA 19-9 level as indicator of early distant metastasis and therapeutic selection in resected pancreatic cancer.

Kim TH, Han SS, Park SJ, Lee WJ, Woo SM, Yoo T, Moon SH, Kim SH, Hong EK, Kim DY, Park JW.

Preoperative CA 19-9 level is an important prognostic factor in patients with pancreatic adenocarcinoma treated with surgical resection and adjuvant concurrent chemoradiotherapy.

Hallemeier CL1, Botros M, Corsini MM, Haddock MG, Gunderson LL, Miller RC.

High serum CA 19-9 but not tumor size should select patients for staging laparoscopy in radiological resectable pancreas head and peri-ampullary cancer.

Alexakis N, Gomatos IP, Sbarounis S, Toutouzas K, Katsaragakis S, Zografos G, Konstandoulakis MM.

How is possible to increase the local control?

SBRT →
- Dose escalation
- Low toxicity

Author, study (ref.)	Patients (n)	SBRT dose (Gy/fraction)	CT gemcitabina-based	FFLP (%)	PFS (months)	OS (months)	GI toxicity (≥ G2) (%)
Koong [12]	15	15–25 Gy/1fx	no	77%	2	11 from diagnosis	none
Hoyer [13]	22	45 Gy/3fx	no	57%	4.8	5.7 from diagnosis	18%
Schellenberg [14]	16	25 Gy/1fx	sequential chemotherapy	81%	9	11.4 from diagnosis	47%
Chang [15]	77	25 Gy/ 1fx	For same patients prior CT	84%	-	11.4 from diagnosis	13%
Schellenberg [16]	20	25 Gy/1fx	sequential chemotherapy	94%	9.2	11.8 from diagnosis	20%
Polistina [17]	33	30 Gy/3fx	Prior chemotherapy	82.6%	7.3	10.6	none
Didolkar [18]	85	15–30 Gy/3 fx	sequential chemotherapy	91.7%	-	18.6 from diagnosis 8.6 from SBRT	22%
Mahadevan [19]	39	24-36 Gy/3fx	sequential chemotherapy	85%	15 from diagnosis	20 from diagnosis	9%
Rwigema [20]	71	18–25 Gy/1fx	no	64.8%	-	10.3	10%
Present study	30	36-45Gy/6 fx	Prior chemotherapy	85% (96% for group of 45 Gy)	8 from SBRT 14 from diagnosis	11 from SBRT 19.5 from diagnosis	none

Our experience on SBRT : preliminary report

SBRT in unresectable advanced pancreatic cancer: preliminary results of a mono-institutional experience

Angelo Tozzi[1], Tiziana Comito[1], Filippo Alongi[1,3*], Pierina Navarria[1], Cristina Iftode[1], Pietro Mancosu[1], Giacomo Reggiori[1], Elena Clerici[1], Lorenza Rimassa[1], Alessandro Zerbi[1], Antonella Fogliata[2], Luca Cozzi[2], Stefano Tomatis[1] and Marta Scorsetti[1]

2013 RADIATION ONCOLOGY

2010-2011: 30 patients.

- 21 patients (70%) with unresectable locally advanced disease
- 9 patients (30%) with local recurrence after surgery.

Gemcitabine-based chemotherapy was administered to all patients before SBRT:

- 10 patients (33%) Gemcitabine
- 11 patients (37%) GEMOX
- 7 patients (23%) GEM-5FU
- 2 patients (7%) PEF-G.

Table 1 Summary of patient characteristics

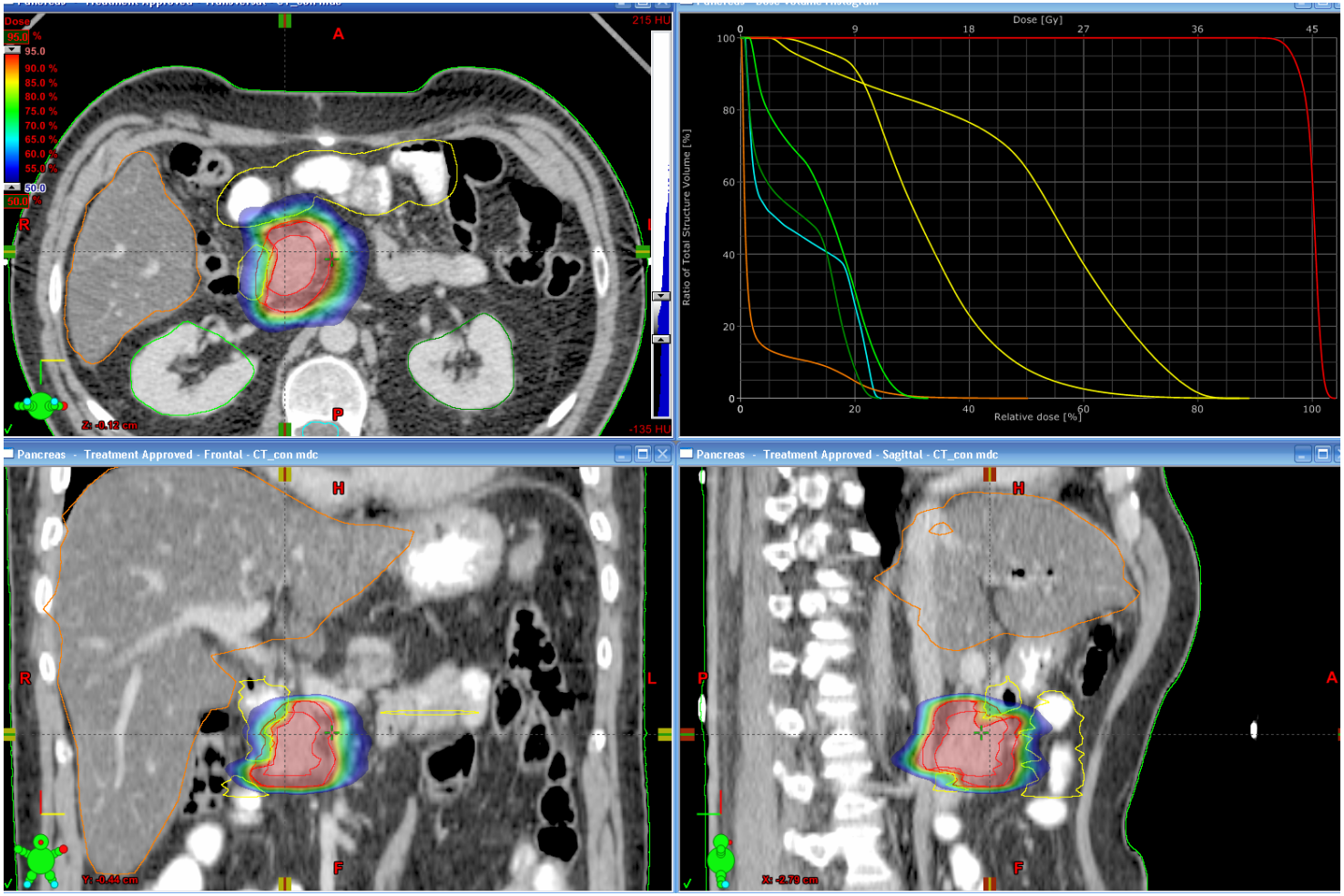
Patients number	**30**
Mean age (range)	67 (43–87)
Gender (M:F)	20:10
Initial tumor characteristics	
T2	8 (27%)
T3	13 (43%)
T4	9 (30%)
N1	12 (40%)
Tumor location (number of patients):	
Head	21 (70%)
Body / Tail	9 (30%)
Mean volume (range) [cm^3]	
CTV	25.6 (3.2-78.8)
PTV	70.9 (20.4-205.2)
Prior therapy (no. of patients)	
Surgery	9 (30%)
Chemotherapy	30 (100%)
Radiation therapy	0 (0%)

- **Prescription dose** was **45Gy in 6 daily fractions of 7.5Gy.**
- In 5 patients (17%) the dose prescription was reduced to **36Gy in 6 fractions** not to exceed dose constraints of duodenum and stomach

The required target coverage was defined as V95% = 100% for the CTV. The maximum acceptable dose heterogeneity to the CTV was D98% > 95% and D2% < 107%.

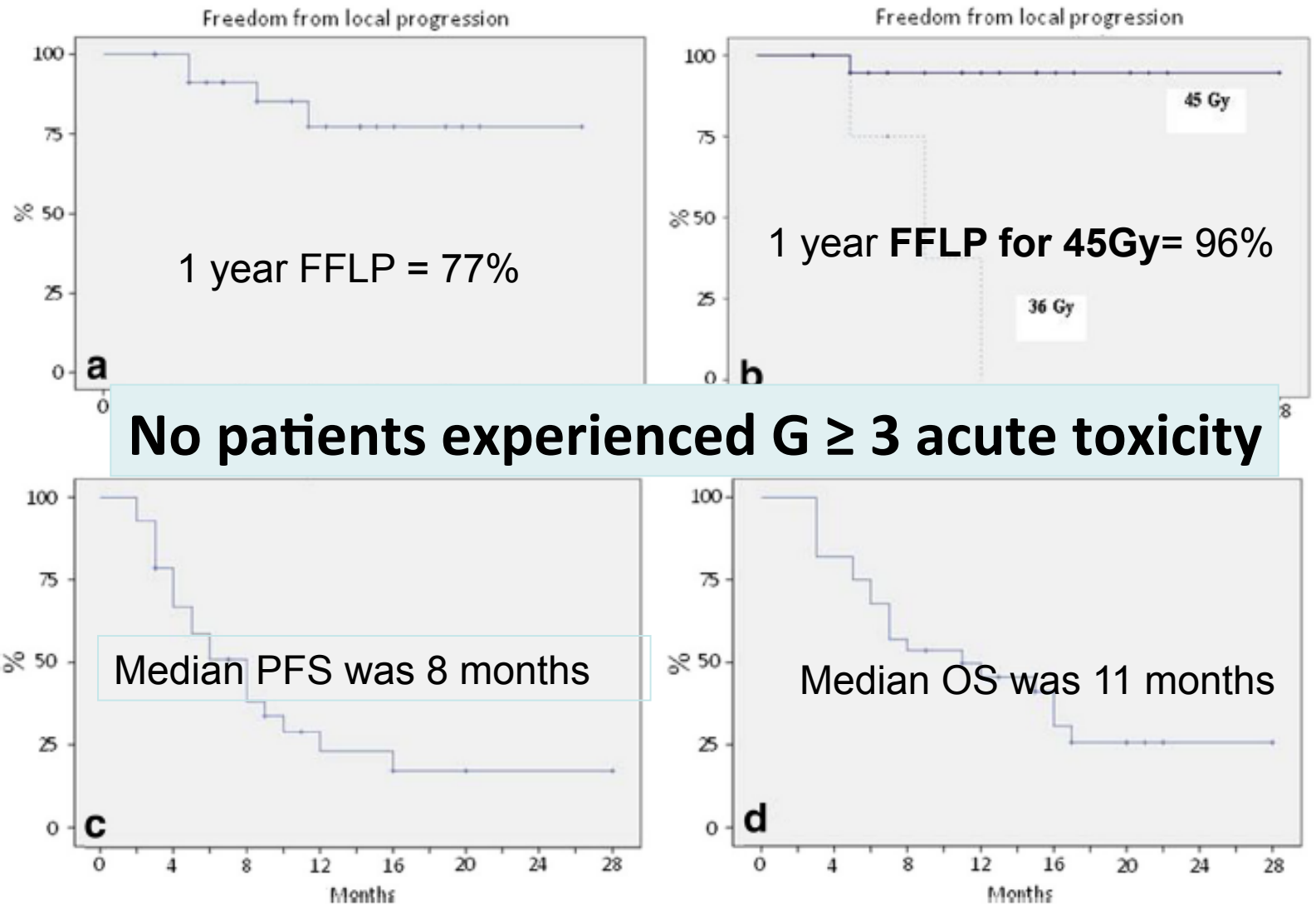
ORGAN	Dose-Volume Limits
Liver	> 700 cm^3 at < 21 Gy
Spinal cord	D 1cm^3 < 18 Gy
Kidneys (R+L)	V15 Gy < 35%
Duodenum	D 1cm^3 < 36 Gy
Stomach, small intestine	D 3cm^3 < 36 Gy

Pz 56 y. Pancreatic unresectable adenoca;
GEM + FOLFIRI -> RP -> SBRT (**45Gy/6fr**.) -> surgery (R0).



Our experience on SBRT pancreas: preliminary data

- **Median FU** was **11 months** (range2–28 months)



Our Phase II trial on SBRT pancreas

INCLUSION CRITERIA:

- Unresectable or recurrence disease
- Maximum tumor diameter < 5cm
- N0
- M0

END POINTS:

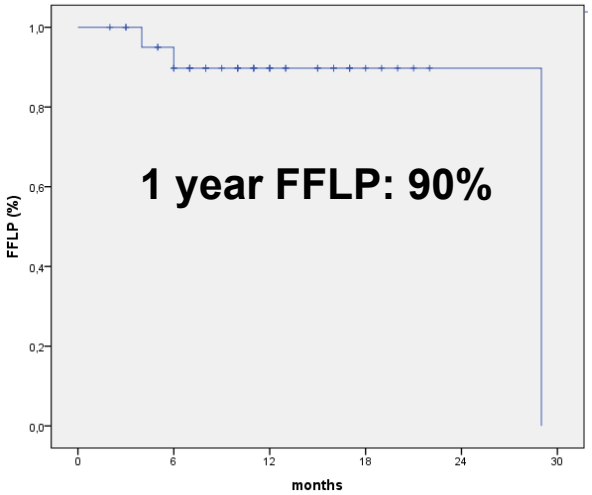
PRIMARY: in-field local control

SECONDARY: toxicity and overall survival

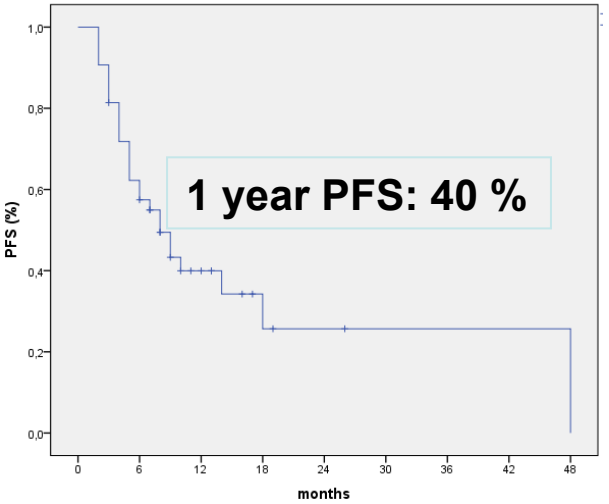
Median FUP 12 months (3-48 months)

Patients number	**62**
Mean age (range)y	**68 (40–87)**
Sex (M:F)	**24:38**
Unresectable tumor	**45 (74%)**
Ca 19.9 pre- SBRT	**28 (45%)**
>300 U/ml	**12 (43%)**
<300 U/ml	**16 (57%)**
Recurrence	**17 (26%)**

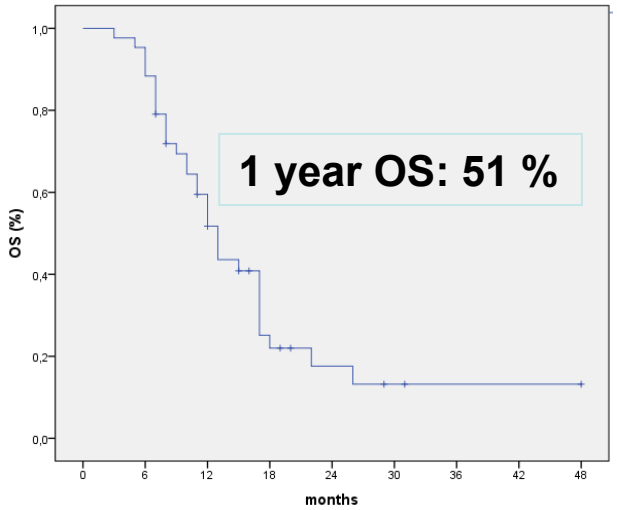
Phase II trial on SBRT pancreas: results on unresectable disease (45pts)

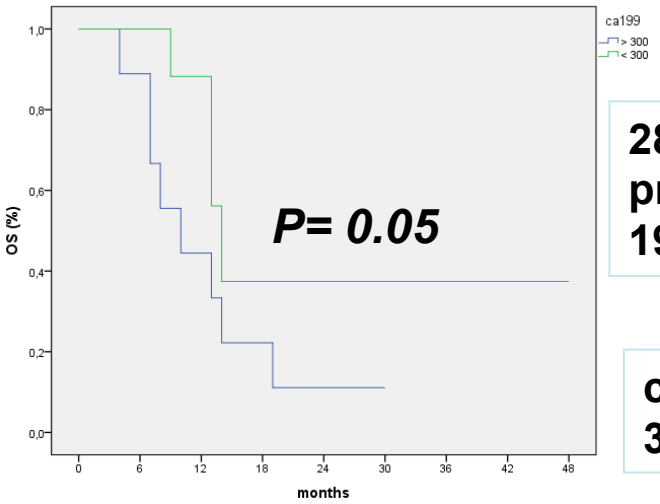


Median PFS : 8 months



Median OS : 13 months

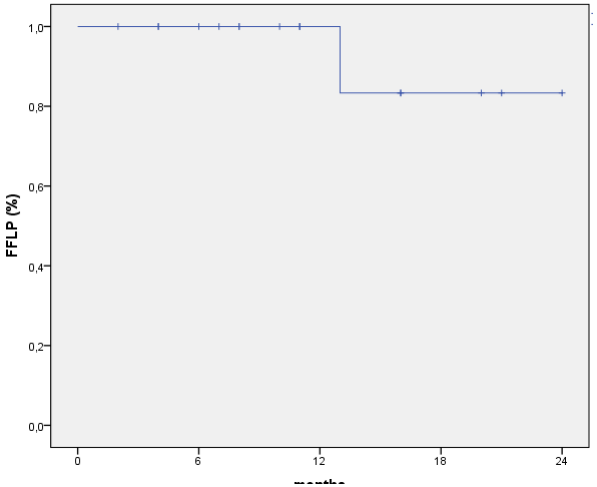




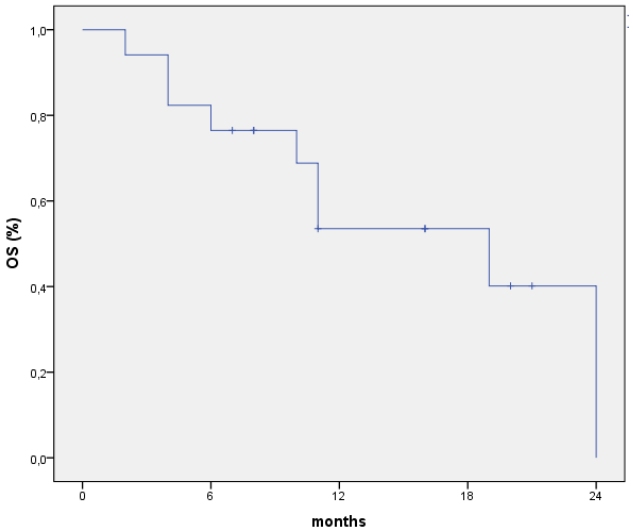
28 patients with pre-treatment Ca 19.9 value

cut-off Ca 19.9: 300 U/ml

Phase II trial on SBRT pancreas: results on recurrence of disease(17pts)

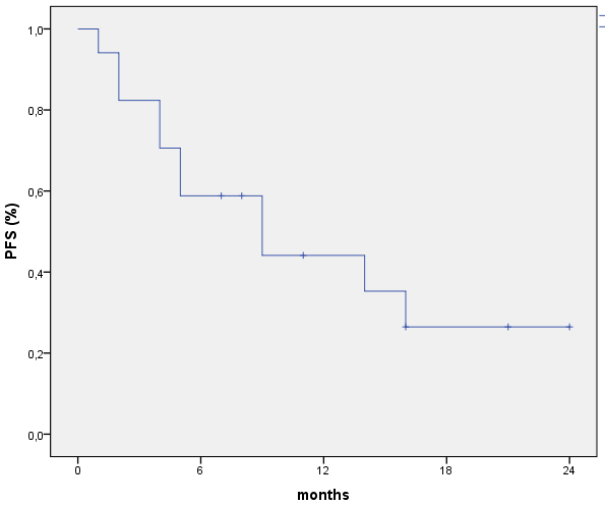


1 year FFLP: 85%



Median OS : 19 months

1 year OS: 53 %

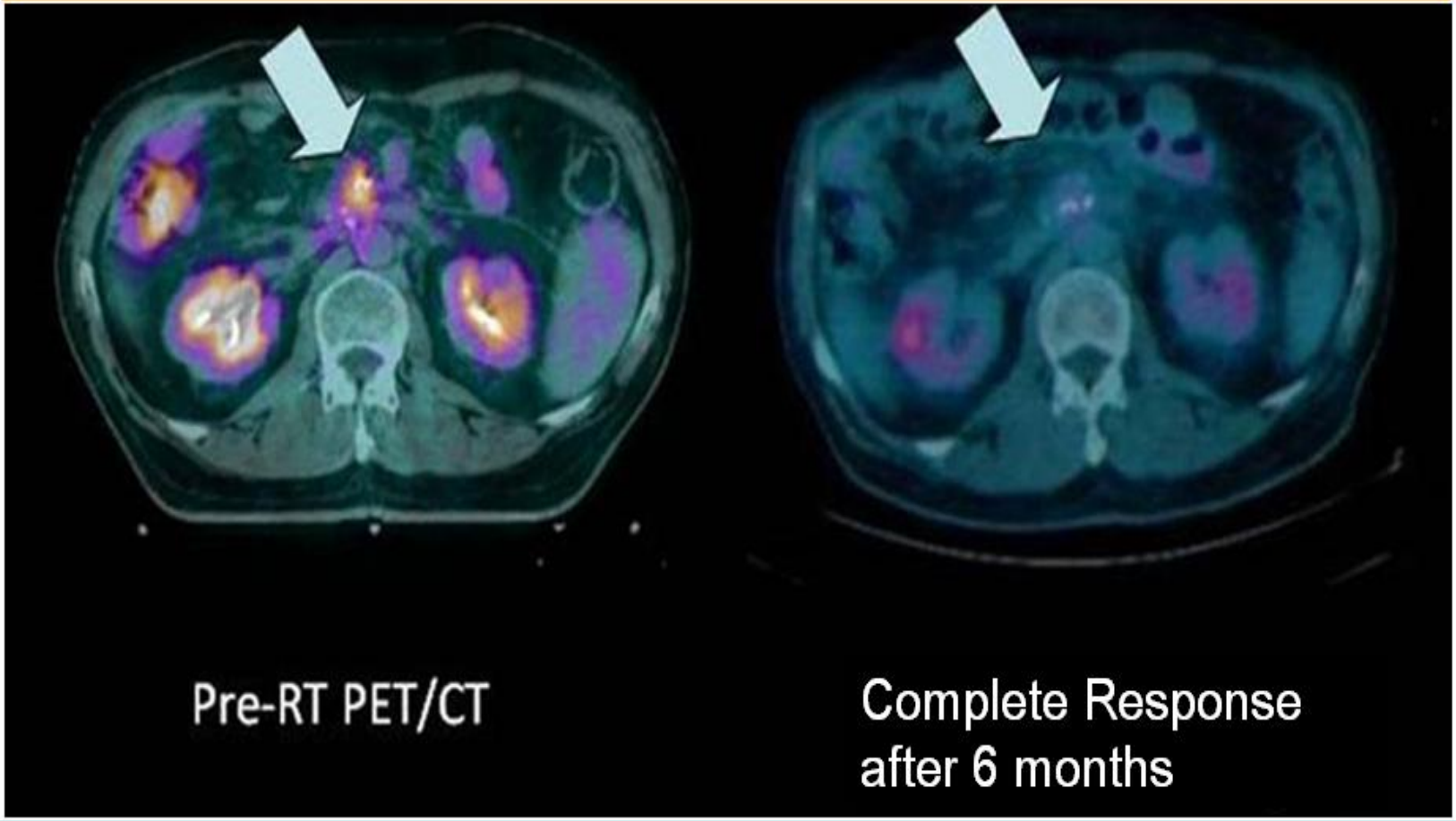


Median PFS : 9 months

1 year PFS: 44 %

- **No patients experienced G ≥ 3 acute toxicity.**

62 yo patient with pancreatic carcinoma local relapse, showing CR after SBRT at 6 months follow-up.



Pancreatic tumors: conclusions

Current evidence:

Feasibility: Non invasive and low toxicity

Efficacy: Acceptable local control rate

Future directions:

1. Selection of patients with molecular factors prognostic of locally failure pattern
2. Escalation RT dose

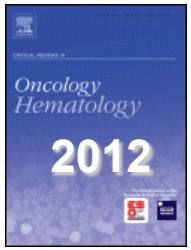
HUMANITAS
CANCER CENTER

SBRT nel distretto addome-pelvi:

- **Tumori del fegato:**
  - **Metastasi epatiche**
  - **HCC**
- **Tumore del pancreas**
- **Tumore della prostata**

SBRT and (Extreme) Hypofractionation for prostate cancer

ELSEVIER



Critical Reviews in Oncology/Hematology xxx (2012) xxx–xxx

CRITICAL REVIEWS IN
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Will SBRT replace conventional radiotherapy in patients with low-intermediate risk prostate cancer? A review

Stefano Arcangeli*, Marta Scorsetti, Filippo Alongi

Radiotherapy and Radiosurgery department, Istituto Clinico Humanitas, Humanitas Cancer Center, Rozzano, Milano, Italy

Accepted 23 November 2011

SBRT and (Extreme) Hypofractionation for prostate cancer

Table 3 Summary of outcomes from SBRT trials with a follow-up of more than 30 months and at least 40 enrolled patients

Study	Schedule	# of patients	Risk class	Medi F/U (mos)	Late grade 3 GU toxicity	Late grade 3 GI toxicity	FFBF
Katz et al. 2010 [5]	35 – 36.25 Gy in 5 fx	304	L-I-H	48	2%	-	97, 93, 75% at 4 year
Freeman, King, 2011. [6]	7-7.25 Gy in 5 fx	41	L	60	< 1%	-	93% at 5 year
McBride et al. 2012 [7]	36.25-37.5 Gy in 5 fx	45	L	44.5	< 1%	-	97.7% at 3 years
Fuller et al. [8]	38 Gy in 4 fx †	54	L-I	36	4%	-	96% at 3 years
Kang et al. [9]	32-36 Gy in 4 fx	44	L-I-H	40	-	-	100%, 100%, 90.9% at 5 years
King et al. 2012 [10]	36.25 Gy in 5 fx	67	L	32.4	3.5%	-	94% at 4 years
Gantry-based Systems							
Madsen et al. 2007 [11]	33.5 Gy in 5 fx	40	L	41	-	-	90% at 4 years
Boike et al. 2011 [12]	45-50 Gy in 5 fx	45	L-I	30, 18, 12	4%	2% plus 1 Grade 4	100% at 1–2.5 years

Abbreviations: L = low; I = intermediate; H = high.

Alongi et al. Radiation Oncology 2013

Our phase II study: inclusion criteria

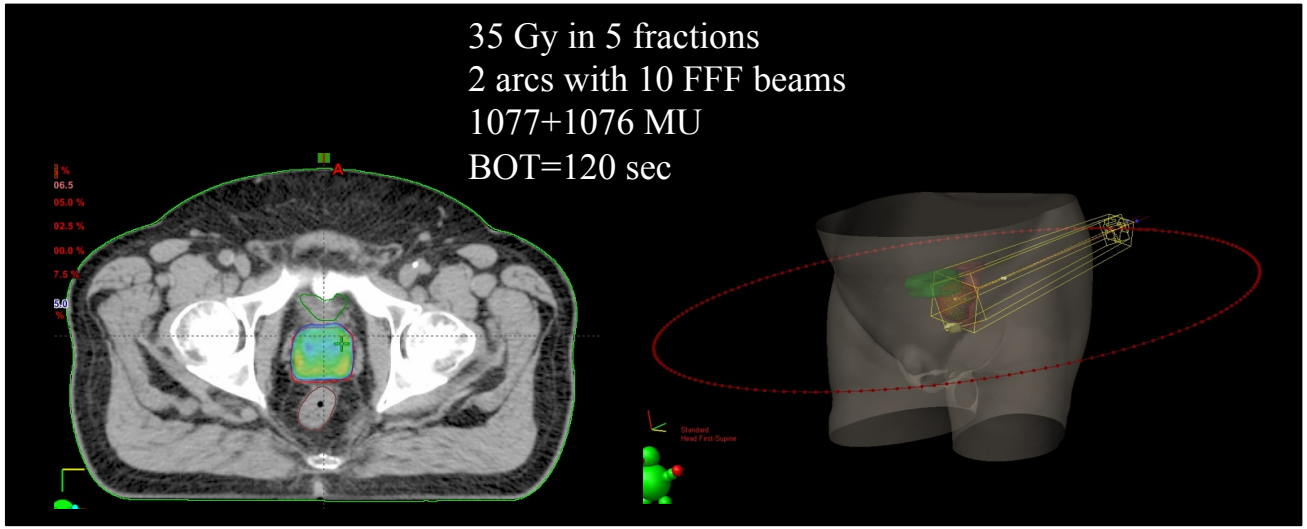
- Age ≤ 80 years
- WHO performance status ≤ 2.
- Histologically proven prostate adenocarcinoma
  →Any case where prophylactic lymph node irradiation is not required (risk of microscopic involvement ≤ 15%)
- PSA ≤ 20 ng/ml.
- T1-T2 (localized)-stage
- No pathologic lymph nodes at CT/ MR and no distant metastases
- No previous prostate surgery other than TURP
- No malignant tumors in the previous 5 years
- IPSS 0-7
- Combined HT according to risk factors.
- Informed consent

Treatment

The schedule is [5 x 7 Gy = 35 Gy] delivered in 5 alternative days

OARs constraints:

- Rectum: V18Gy < 35%; V28Gy < 10%; V32Gy < 5%; D1% < 35 Gy
- Bladder D1% < 35 Gy;



Simulation and Target definition

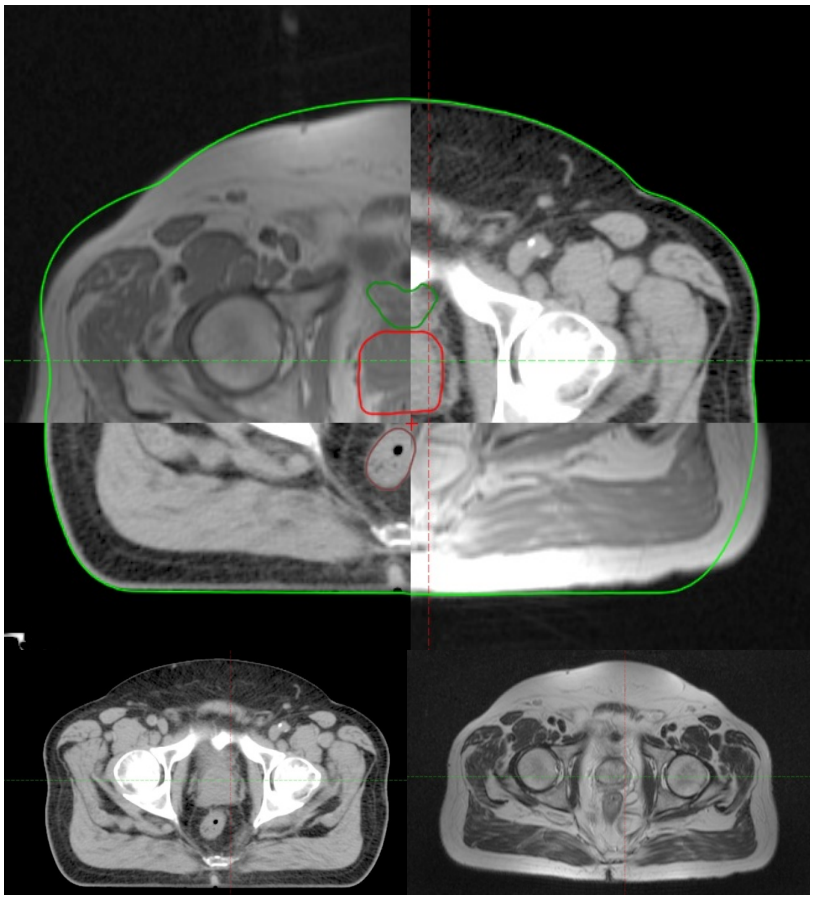
- Simulation CT

- Simulation MRI

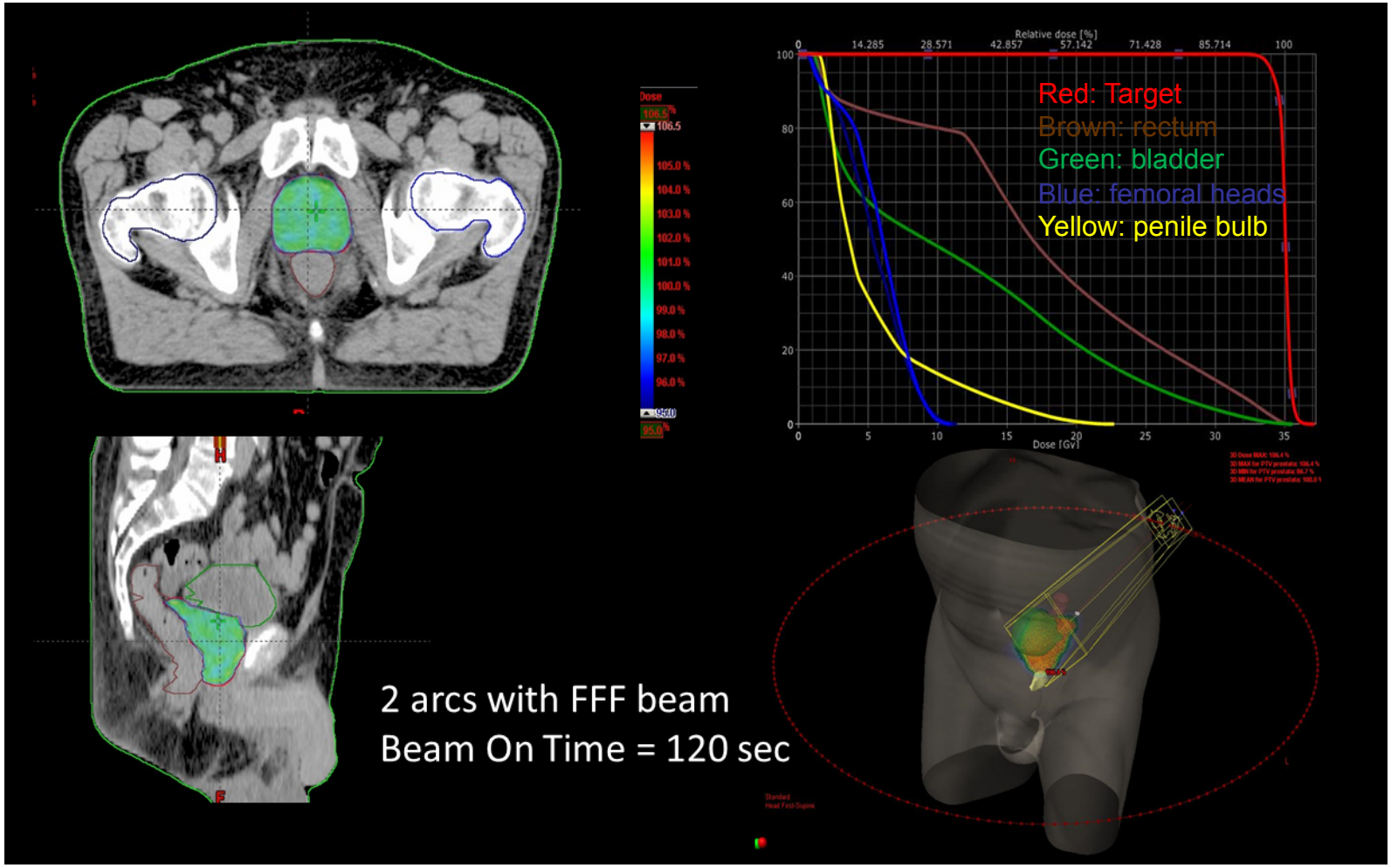
- CT/MRI registration

CTV: prostate + SV, except for T1-T2 lesions with risk of SV involvement ≤ 15% in which case CTV is prostate only

PTV: CTV + 5 mm margin in each direction



Treatment planning

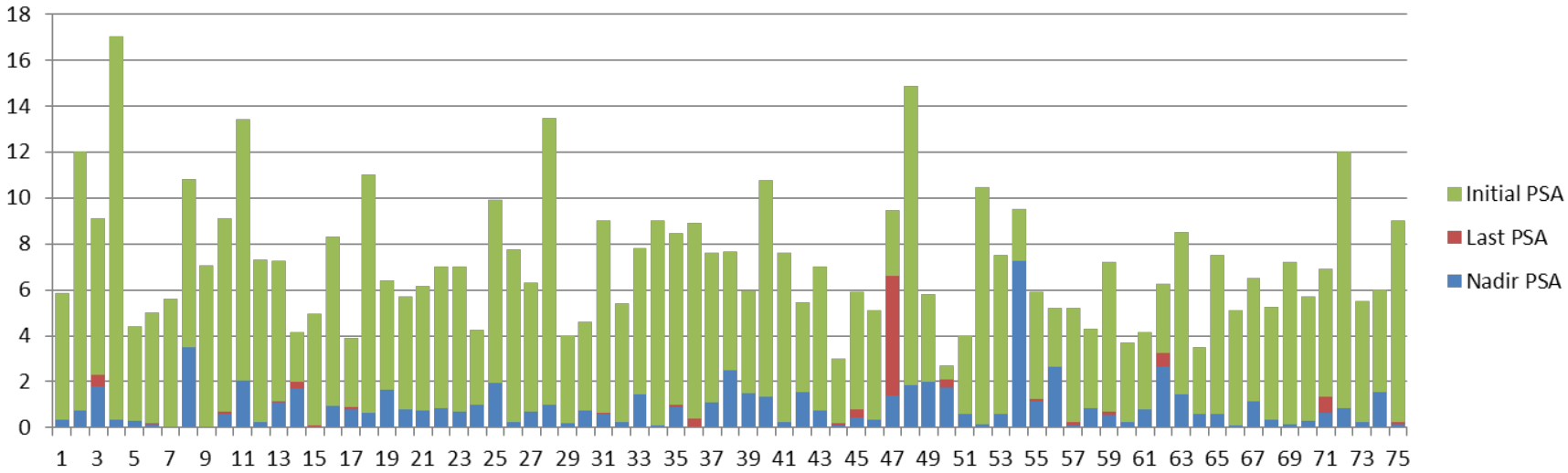


Results

N. of patients	75
Recruitment	Dec 2011- Apr 2014
Median Age [year]	70 [48 - 80]
Median Gleason Score	6 [6-7]
Initial PSA [ng/mL]	Median: 7.17 [0.5-17]
NCCN Low Risk Class	47
NCCN Intermediate Risk Class	28
CTV [cm3]	Mean: 58.4 [25,1-110,2]
PTV [cm3]	Mean: 108.6 [52.8-182.2]

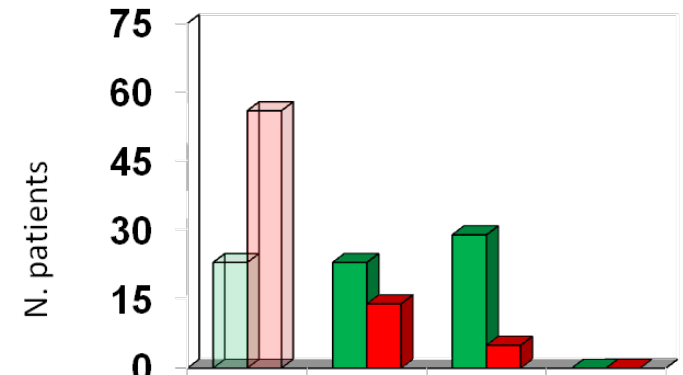
Results

Follow-up [months]	Mean: 17.1 Range: 6-29 Median: 17,8
Nadir PSA [ng/mL]	Mean: 0,97 Range: 0.02-7.25
Last PSA [ng/mL]	Mean: 1.10 Range: 0.02-7.25



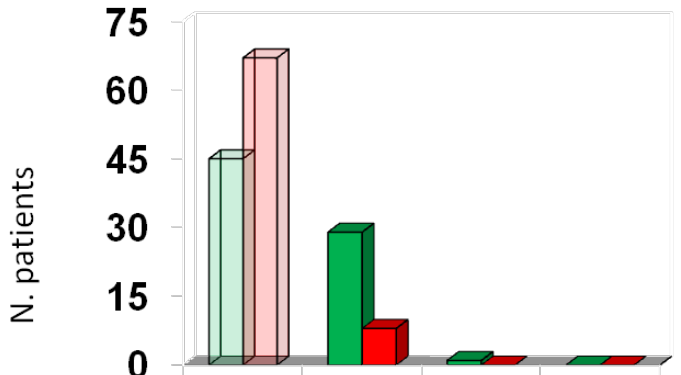
Results

Acute toxicity



	G0	G1	G2	G3
Genito-urinary	23	23	29	0
Rectal	56	14	5	0

Late toxicity



	G0	G1	G2	G3
Genito-urinary	45	29	1	0
Rectal	67	8	0	0

SBRT and (Extreme) Hypofractionation for prostate cancer

Linac based SBRT for prostate cancer in 5 fractions with VMAT and flattening filter free beams: preliminary report of a phase II study

Filippo Alongi[1,4*], Luca Cozzi[2], Stefano Arcangeli[1], Cristina Iftode[1], Tiziana Comito[1], Elisa Villa[1], Francesca Lobefalo[1], Pierina Navarria[1], Giacomo Reggiori[1], Pietro Mancosu[1], Elena Clerici[1], Antonella Fogliata[2], Stefano Tomatis[1], Gianluigi Taverna[3], Pierpaolo Graziotti[3] and Marta Scorsetti[1]

Methods: A prospective phase I-II study, started on February 2012. The schedule was 35 Gy in 5 alternative days. SBRT was delivered with RapidArc VMAT, with 10MV FFF photons.

Results: Median follow-up was 11 months (range: 5–16); 40 patients were recruited in the protocol and treated. All patients completed the treatment as programmed (median 11.8 days (9–22). Acute Toxicities were as follow: Rectum G0: 30/40 cases (75%); G1: 6/40 (15%); G2: 4/40 (10%). Genito-urinary: G0: 16/40 (40%); G1: 8/40 (20%); G2: 16/34 (40%). In two G2 urinary retention cases, intermittent catheter was needed. No acute G3 or greater toxicity was found. Median treatment time was 126 sec (120–136). PSA reduction from the pre-treatment value of the marker was documented in all patients.

Conclusions: Early findings suggest that SBRT with RapidArc and FFF beams for prostate cancer in 5 fractions is feasible and tolerated in acute setting. Longer follow-up is needed for assessment of late toxicity and outcome.

SBRT and (Extreme) Hypofractionation for prostate cancer

Stereotactic body radiotherapy with flattening filter-free beams for prostate cancer: assessment of patient-reported quality of life

Marta Scorsetti · Filippo Alongi · Elena Clerici · Tiziana Comito · Antonella Fogliata · Cristina Iftode · Pietro Mancosu · Piera Navarria · Giacomo Reggiori · Stefano Tomatis · Elisa Villa · Luca Cozzi

In the framework of a prospective mono-institutional phase II trial, EPIC questionnaire was dispensed (up to 1 year after treatment) to a cohort of 46 patients of 72 treated with 5 fractions of 7 Gy each to the prostate. SBRT was delivered with RapidArc VMAT with 10 MV flattening filter-free photon beams.

Conclusions Stereotactic body radiotherapy (SBRT) treatment of prostate with RapidArc and high-intensity photon beams resulted to be **well tolerated by patients with mild toxicity profiles and good patient-reported quality of life perception** for the first year after treatment.

Prostate motion

JOURNAL OF APPLIED CLINICAL MEDICAL PHYSICS, VOLUME 12, NUMBER 1, WINTER 2011

Cone beam CT pre- and post-daily treatment for assessing geometrical and dosimetric intrafraction variability during radiotherapy of prostate cancer

Giacomo Reggiori,[1] Pietro Mancosu,[1a] Angelo Tozzi,[1] Marie C Cantone,[2] Simona Castiglioni,[1] Paola Lattuada,[1] Francesca Lobefalo,[1] Luca Cozzi,[3] Antonella Fogliata,[3] Piera Navarria,[1] Marta Scorsetti[1]

Radiation Oncology Dept.,[1] IRCCS Istituto Clinico Humanitas, Milano (Rozzano), Italy; Physics Dept.,[2] Università degli studi di Milano, Milano, Italy; Medical Physics Unit,[3] Oncology Institute of Southern Switzerland, Bellinzona, Switzerland

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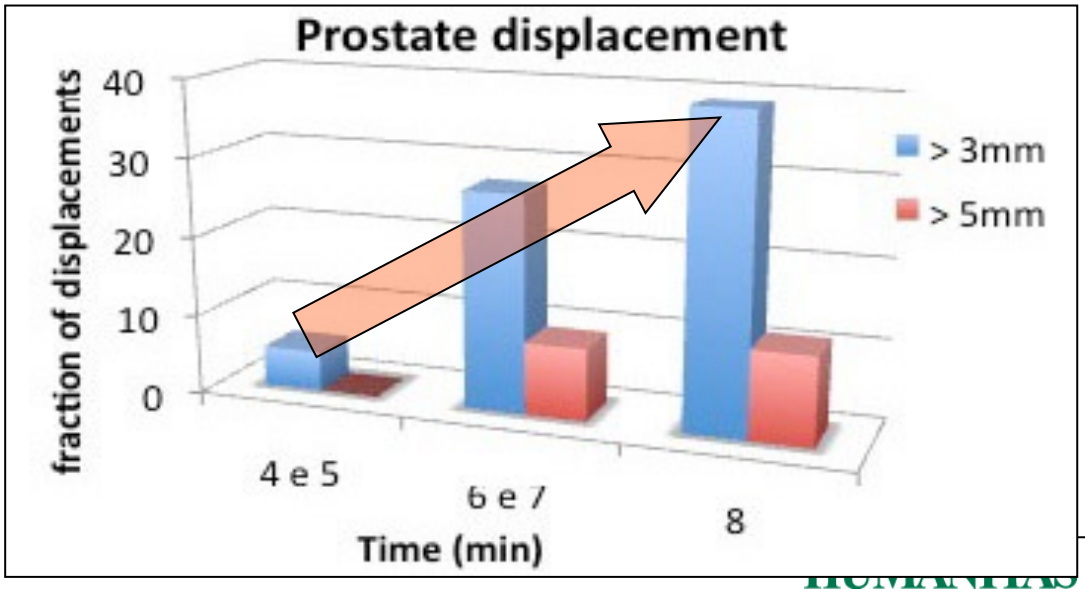
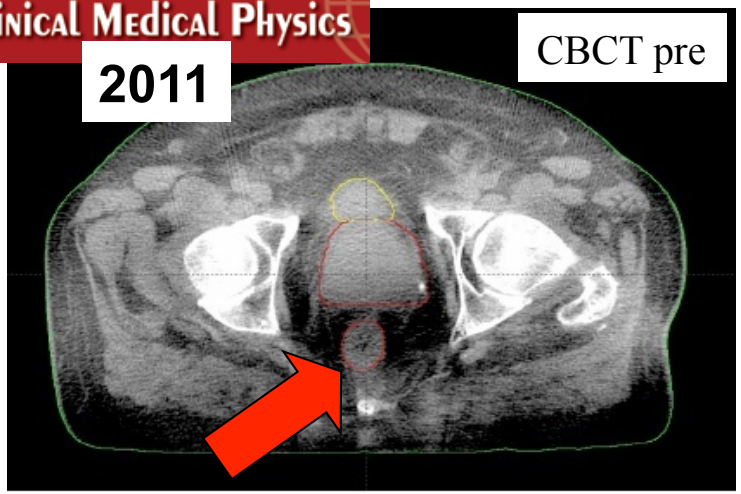
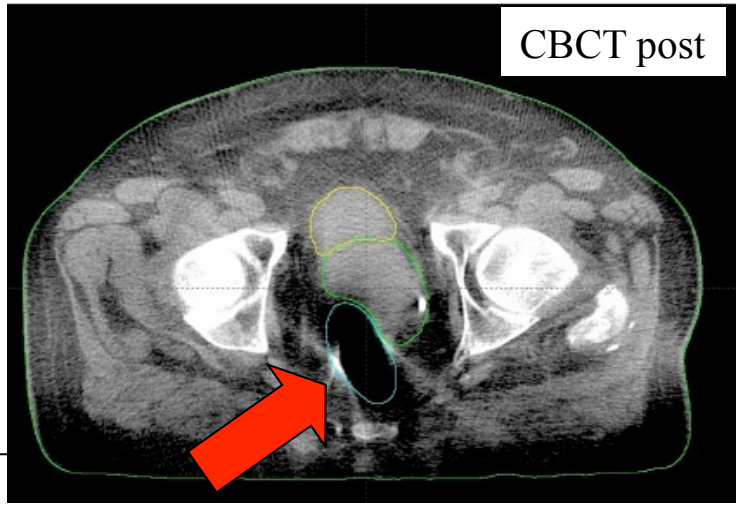
Journal of Applied Clinical Medical Physics

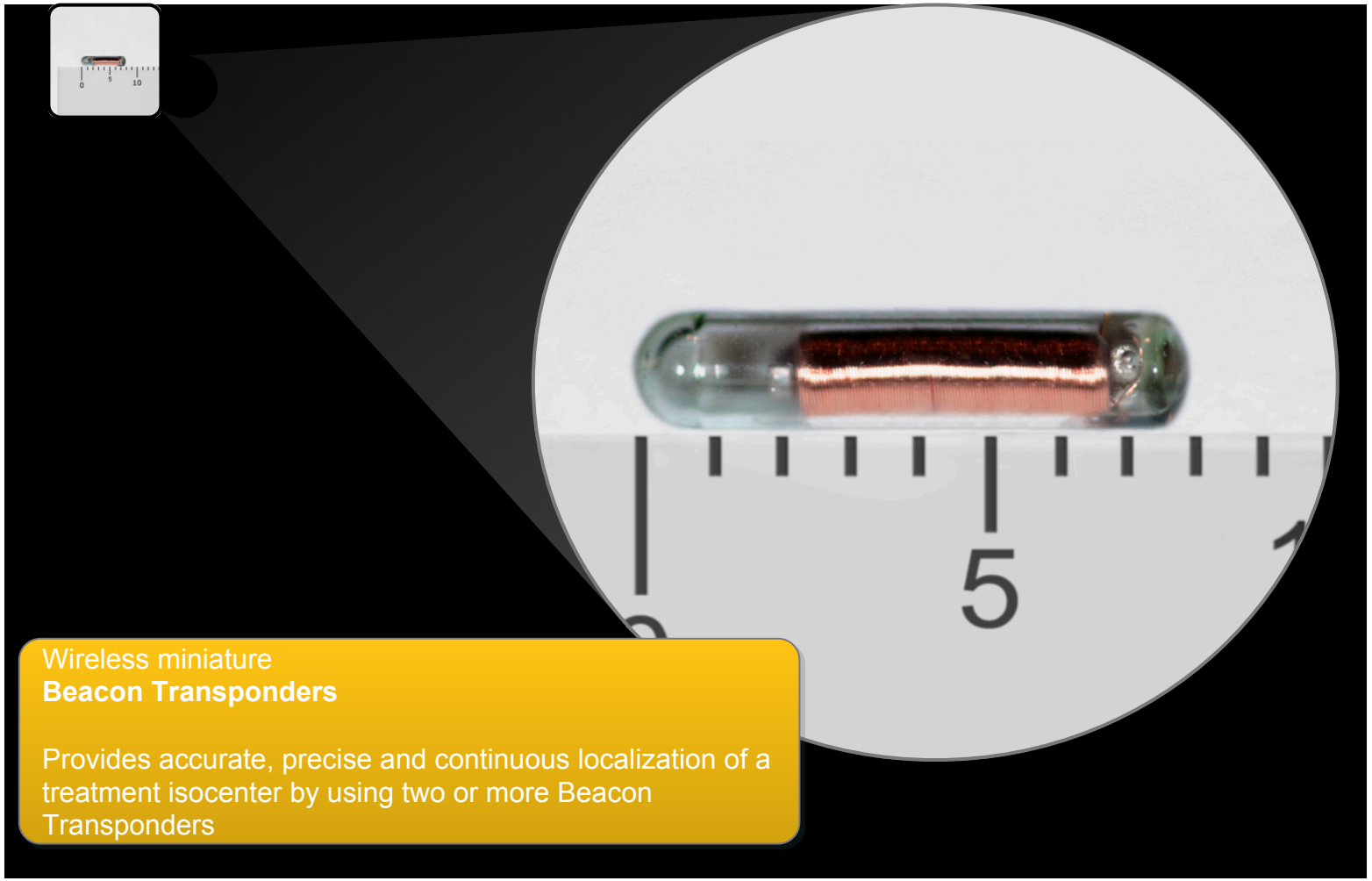
2011





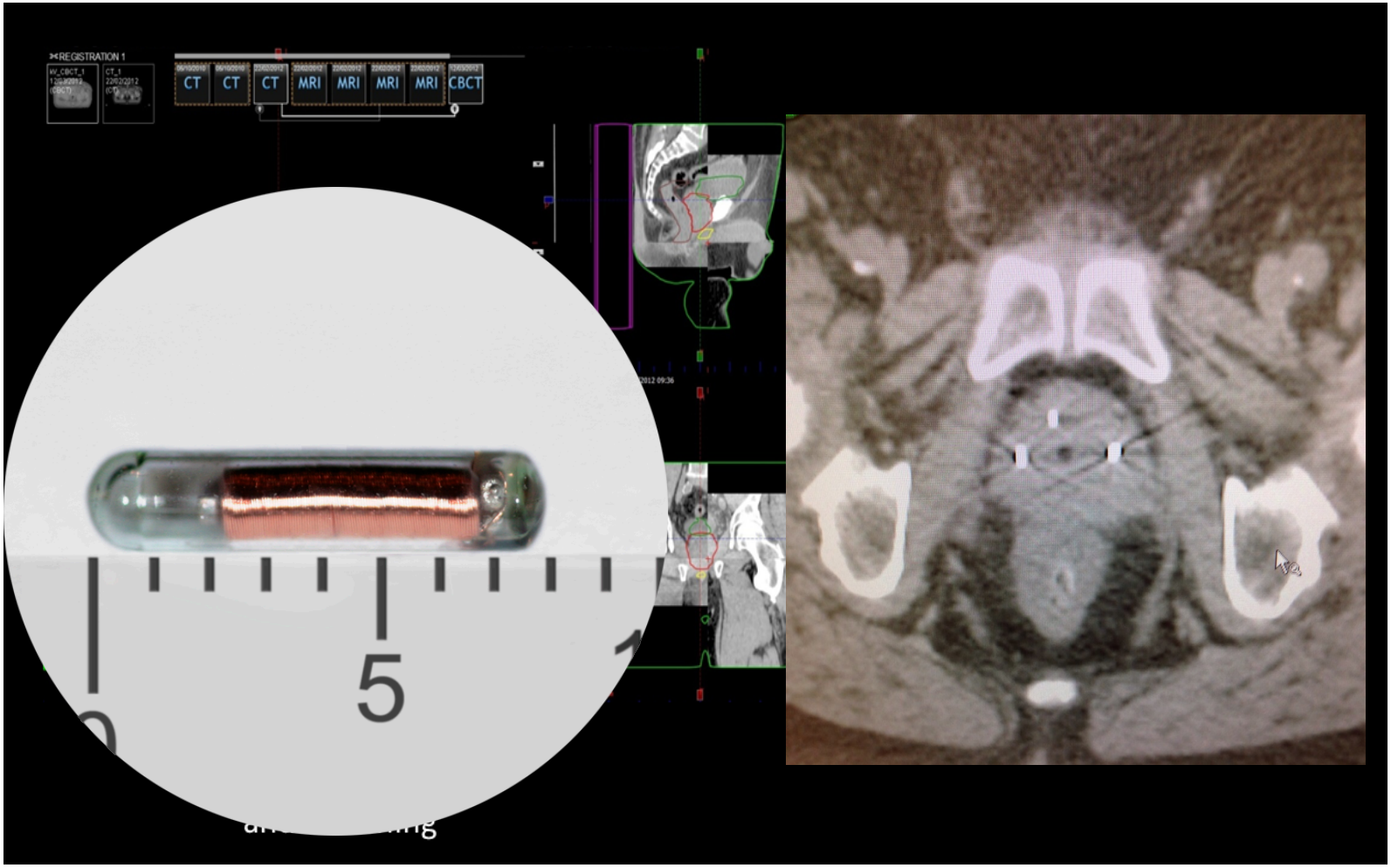


Calypso – Beacons and SBRT prostate

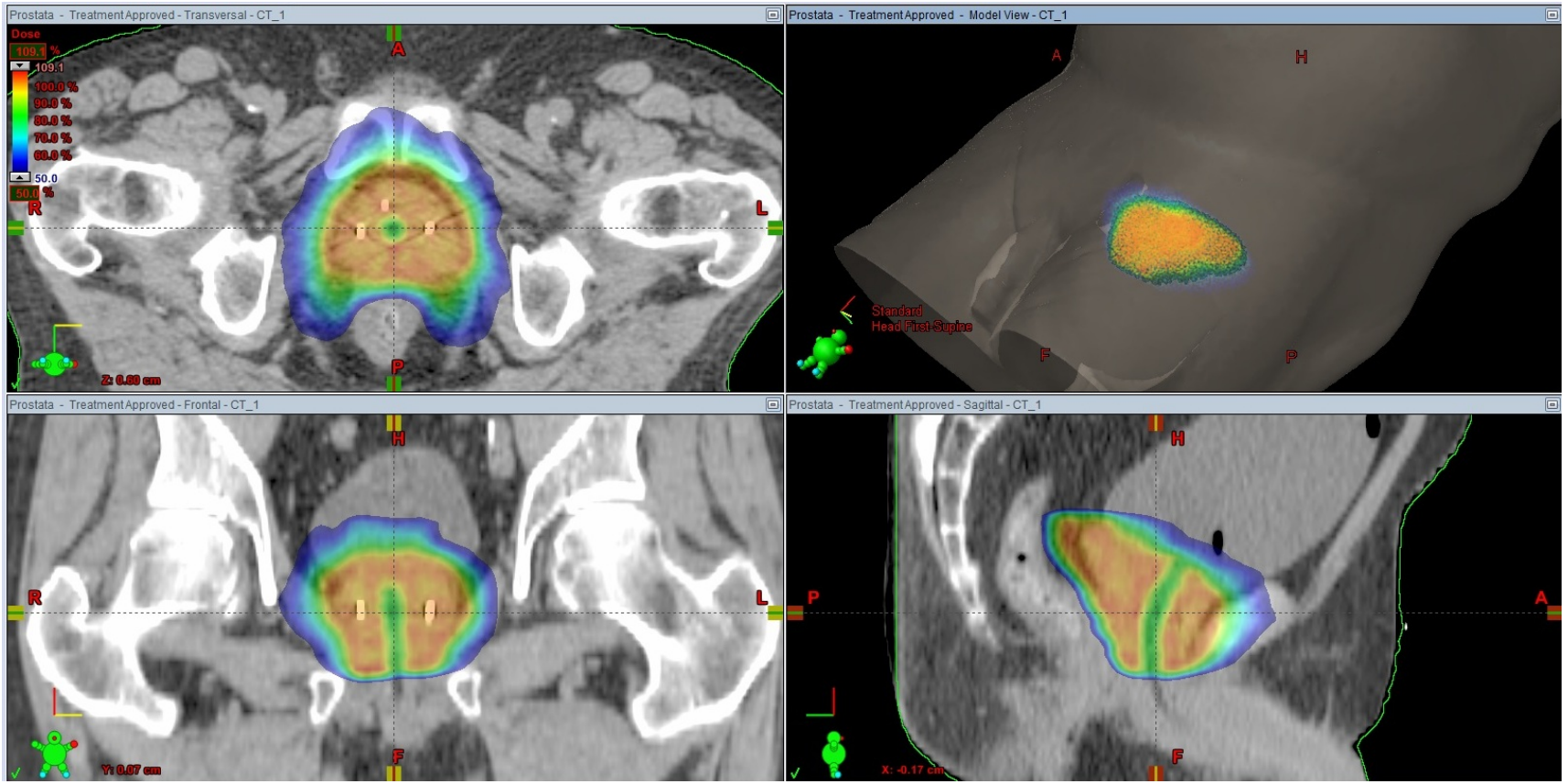


Calypso – Beacons and SBRT prostate

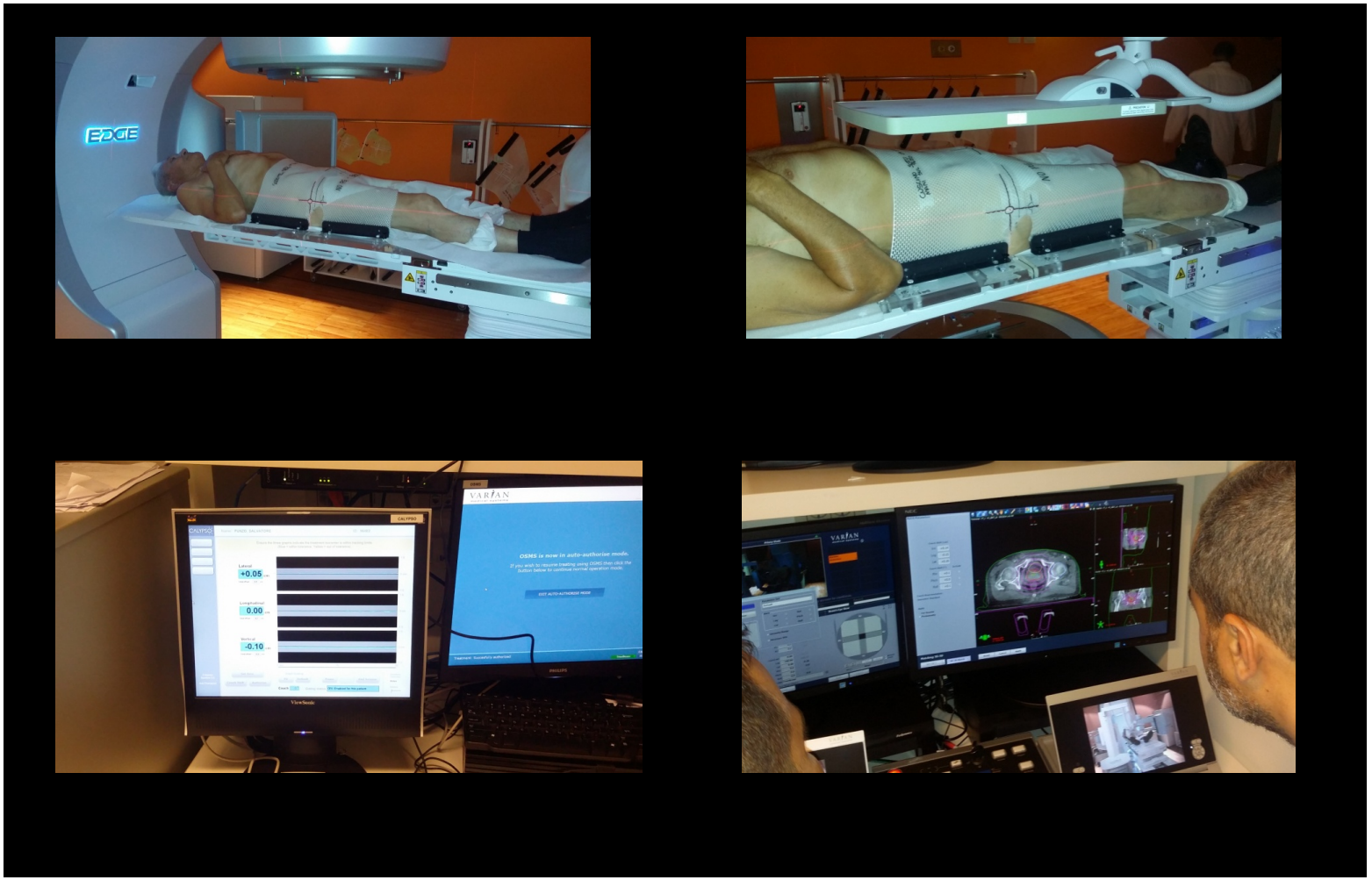
Treatment verification



Calypso – Beacons and SBRT prostate



Calypso – Beacons and SBRT prostate



Prostatic tumors: conclusions

Current evidence:

Feasibility: well tolerated with mild toxicity profiles

Future directions:

1. Longer follow-up is needed for definitive assessment of late toxicity and clinical outcome.

Thank you!

“We can not solve our problems with the same level of thinking that created them”

A. Einstein