HUMANITAS
CANCER CENTER

La radioterapia stereotassica ablativa: addome-pelvi

Metastasi epatiche

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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.

3. Alongi F, Arcangeli S, Filippi AR, Ricardi U, Scorsetti M. the oncologist. 2012
Hoyer, I. J. Rad Onc Biol Phys, 2012

CRC Liver metastases treatment: 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

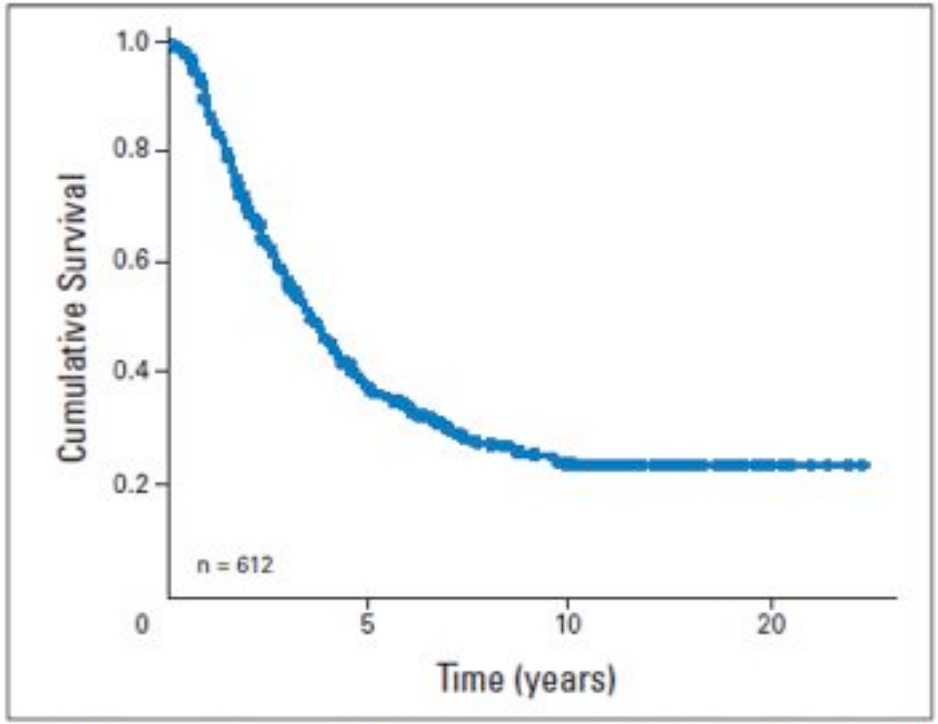


Fig 1. Kaplan-Meier plot of disease-specific survival for 612 patients with potential 10-year follow-up who underwent resection of colorectal liver metastases from 1985 to 1994 at Memorial Sloan-Kettering Cancer Center.

- 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.

CRC Liver metastases treatment: Surgery

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

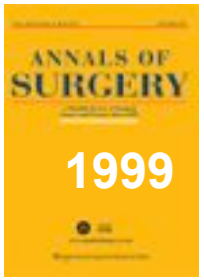


Table 3. UNIVARIATE PREDICTORS OF ADVERSE OUTCOME

	No. of Patients	5-yr Survival (%)	Median Survival (mo)	p
Overall	1001			
Gender				
Male	581			
Female	420			
Age				
<70	802			
>70	199			
Primary tumor				
Node-negative	405			
Node-positive	596			
Primary site				
Colon	743			
Rectum	258			
Disease-free interval				
<12 mo	488			
>12 mo	513			
Carcinoembryonic antigen				
<200 ng/ml	793			
>200 ng/ml	85			
Number of tumors				
1	491			
>1	510			
Largest tumor size				
<5	556			
>5	445			
Tumor distribution				
Unilobar	603			
Bilobar	398			
Extent of resection				
Less than lobectomy	370			
Lobectomy or more	631			
Resection margin				
Negative	895			
Positive	106			
Extrahepatic disease				
No	913			
Yes	88			
Blood loss >2000 cc				
No	884	36	43	0.03
Yes	117	32	35	

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

Fong Y. et al. (1995) CA Cancer J.Clin.

CRC Liver metastases treatment: Surgery

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

Table 2. Comparison of Prognostic Factors Among Survival Cohorts

Factor	< 2-Year Survival* (n = 175) No. of Patients	%	2- to 5-Year Survival* (n = 189) No. of Patients	%	5- to 10-Year Survival* (n = 73) No. of Patients	> 10-Year Survival (n = 102)
Preoperative						
Synchronous disease	23	13	20	11	4	
Node-positive primary†	111	63	101	53	38	
Preoperative CEA > 200 ng/mL†	28	16	21	11	6	
DFI < 12 months†	89	51	86	46	26	
No. of hepatic tumors > 1†	103	59	96	51	23	
Median	2		2			
1	72	41	90	48	50	
2	41	23	50	27	12	
3	22	13	15	8	3	
≥ 4	40	23	31	16	8	
Size of hepatic tumor > 5 cm†	92	53	78	41	30	
Median size of largest hepatic tumor, cm	5		4		4	
Postoperative						
Margin positive	35	20	18	10	6	
Resection ≥ hemihepatectomy	109	62	114	60	44	
Bilateral resection	80	46	55	29	21	

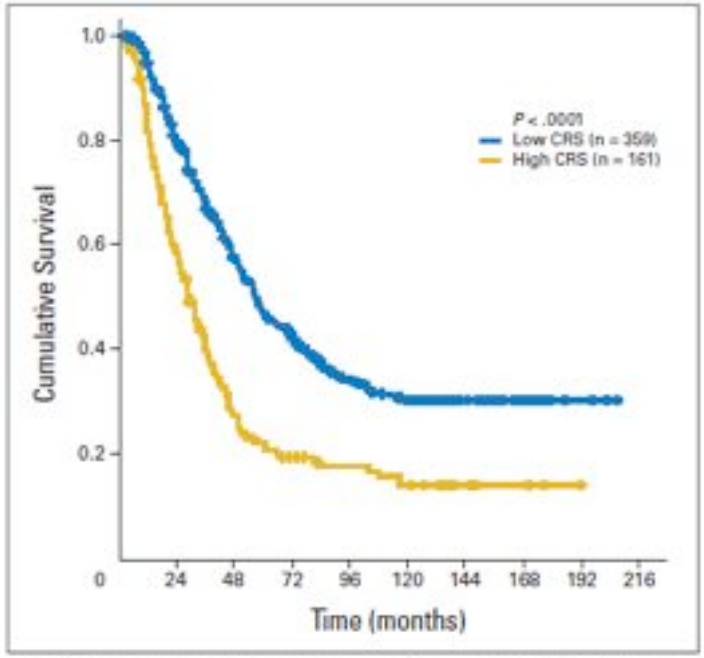
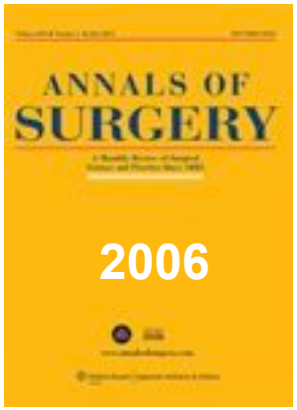


Fig 2. Kaplan-Meier plots of disease-specific survival stratified by low-risk clinical risk score (CRS; top curve) and high-risk CRS (bottom curve).

Non-CRC Liver metastases treatment

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

Only neuroendocrine metastases subgroup had a better prognosis ?



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

Non-CRC Liver metastases treatment

TABLE 2. Five-Year and Median Survivals for Patients With Concolorectal Nonendocrine Liver Metastases From Individual Primary Tumor Sites Grouped by Favorable (Group 1), Intermediate (Group 2), and Poor Outcomes (Group 3)

Study Population	No.	5-Year Survival (%)	Median Survival (mo)
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

Non-CRC Liver metastases treatment

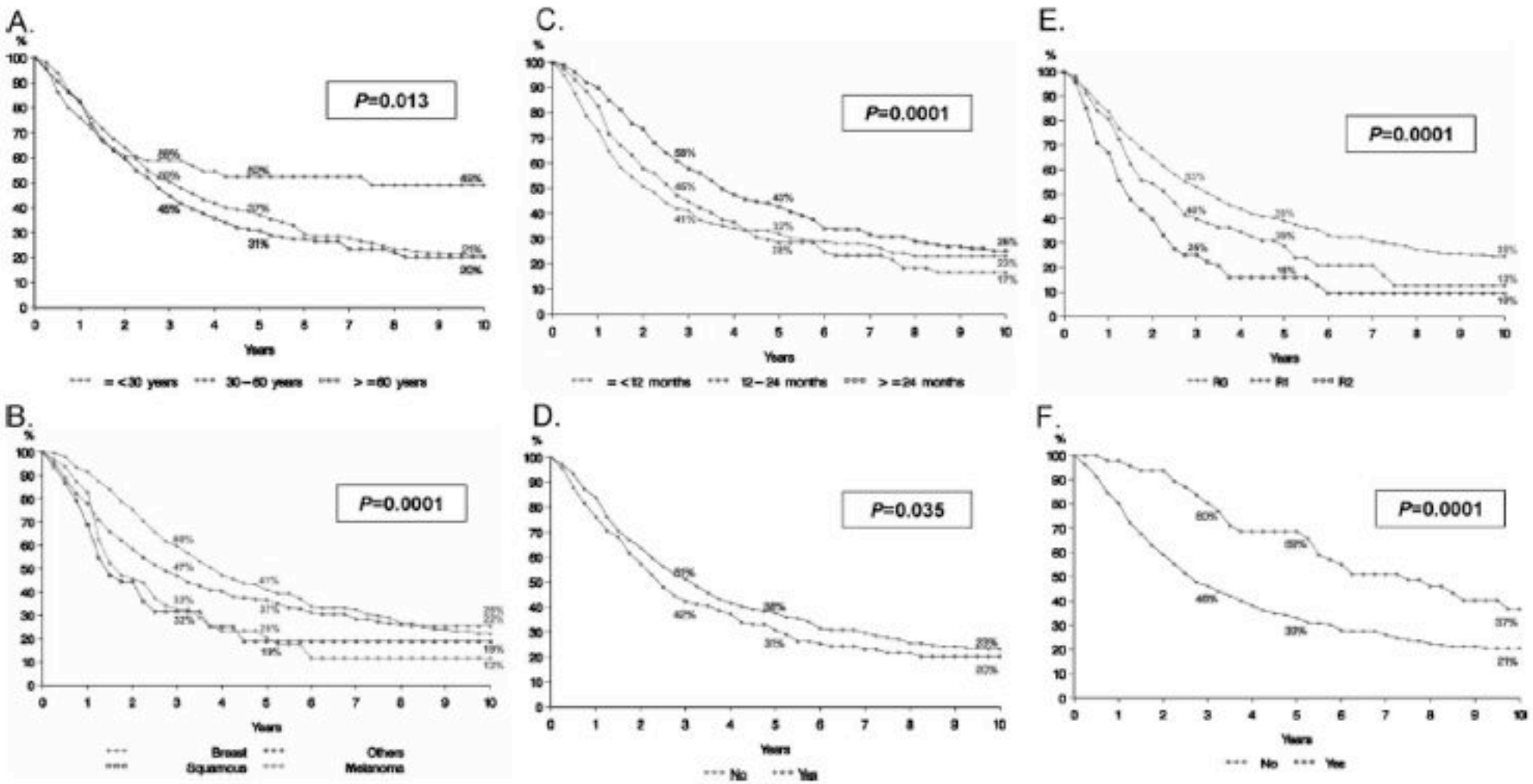
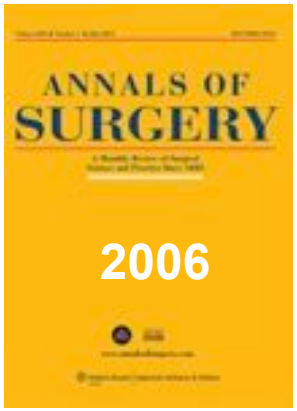


FIGURE 3. Survivals for individual prognostic factors based on univariate and multivariate analysis. A, Age. B, Primary tumor site and histology. C, Disease-free interval from treatment of primary tumor to diagnosis of liver metastases. D, Extrahepatic disease. E, Resection margin. F, Repeat hepatectomy for hepatic recurrence.

Adam R et al. (2006) Ann Surg

Non-CRC Liver metastases treatment



Hepatic Resection for Noncolorectal Nonendocrine Liver Metastases

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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.

Adam R et al. (2006) Ann Surg

Liver metastases treatment: RFA

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

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

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

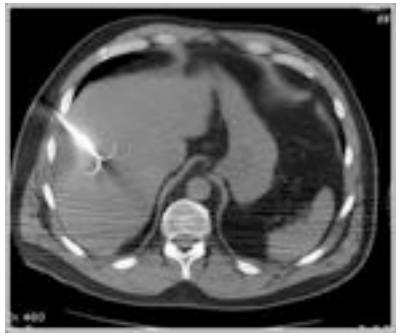
Any patient should be categorized as A1 or A2/B1, B2, or B3. This classification may help to clearly define the type of unresectable patients included in all clinical trials.
[a]Includes all methods, including radiofrequency ablation.

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.

Liver metastases treatment: 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



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

Liver metastases treatment: is there an alternative?

- **Which effective, safe and non invasive alternative therapeutic option for 60-80% of oligometastatic patients unsuitable to locally ablative therapy of liver metastases?**

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)

SBRT on Liver metastases: prospective trials

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	1-yr LC94, 22-mo LC 90.6%
Goodman *et al*[16]	Phase I (HCC and liver mets)	mets)	(median, 32.6 mL)	18-30 Gy (1 fr)	le 3 chest wall ithin 1 year. oxicity 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%

significant heterogeneity

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Nair et al, WJR 2014

SBRT on Liver metastases: significant heterogeneity

Patients selection:

- Colorectal, breast and lung cancer
- Number less than 5
- Maximum tumor size of 6 cm.
- Good performance status
- Absence or stable extrahepatic disease
- Adequate hepatic volume and function

Dose prescription:

- Ranged from 14-30 Gy in 1 fraction
- Ranged from 25 to 60 Gy in 3-6 fractions

Outcomes:

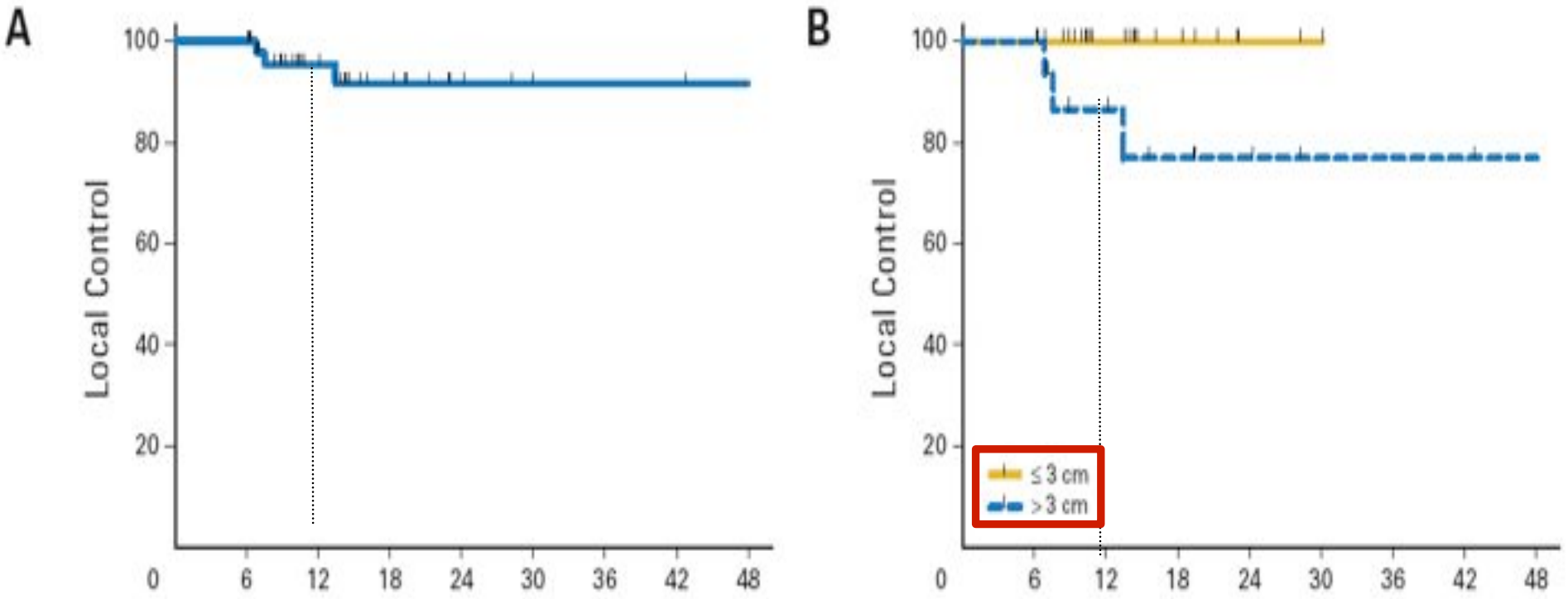
- 1-year LC 70-100%; 2-years LC 60% to 90%
- 1-year OS 70-80%; 2-years OS 30-73%
- Toxicity ≥ G3 1 - 10%; incidence of RILD less than 1%.

Hoyer et al, IJROBP 2012

SBRT on Liver metastases: dose and local control

Correlation between dose prescription and tumor size

60 Gy /3 fr

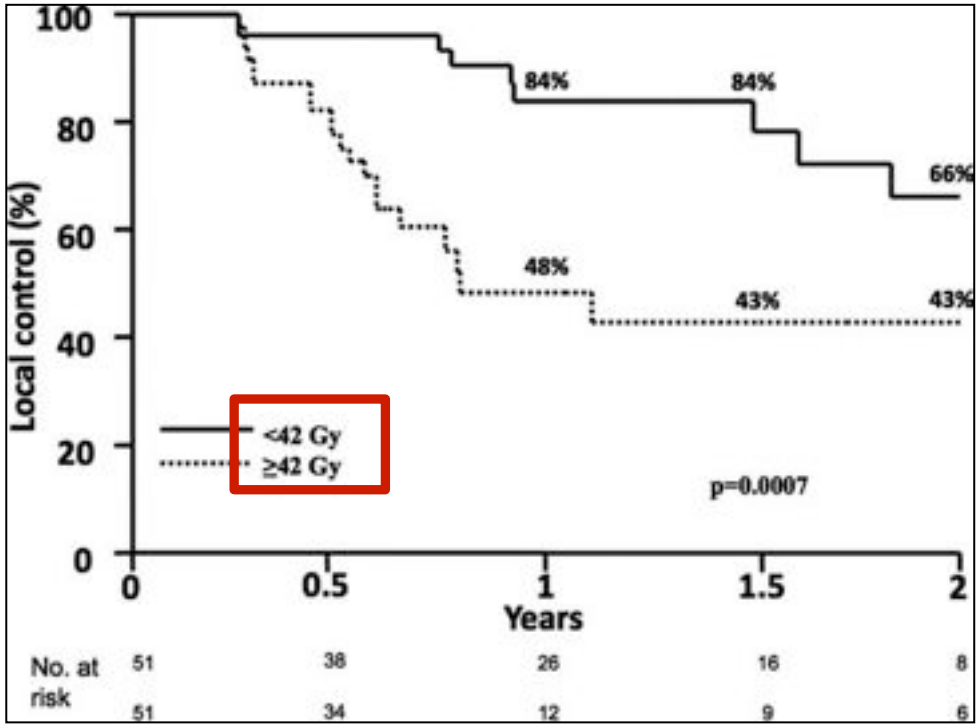


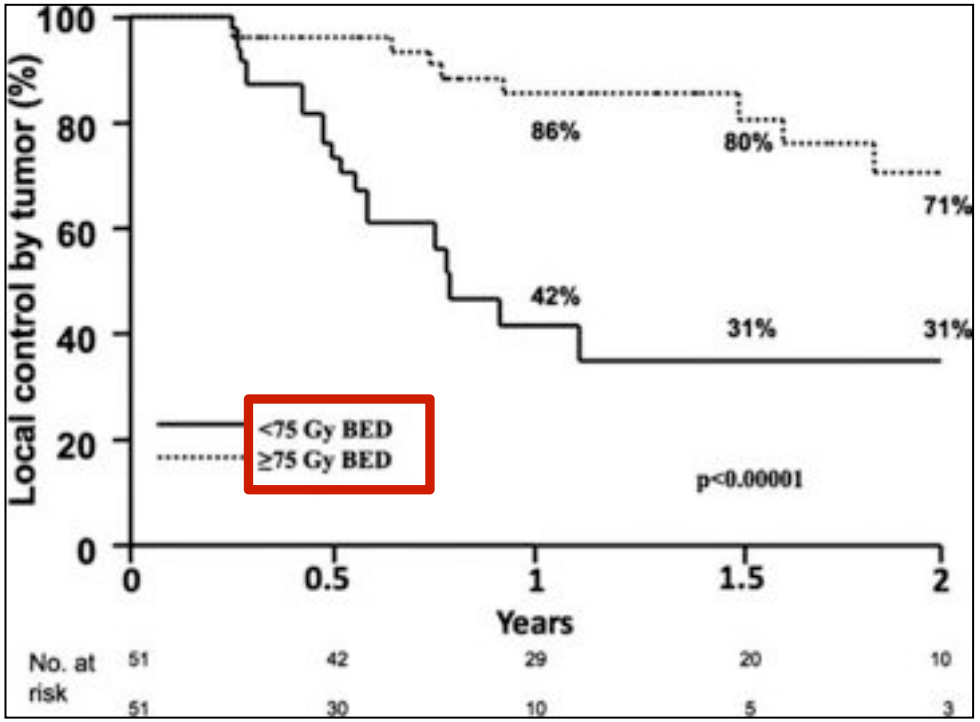
For lesion diameter > 3cm, a prescription dose of >60 Gy should be considered.

Rusthoven et al. (2009) JCO

SBRT on Liver metastases: dose and local control

Correlation between dose prescription and local control



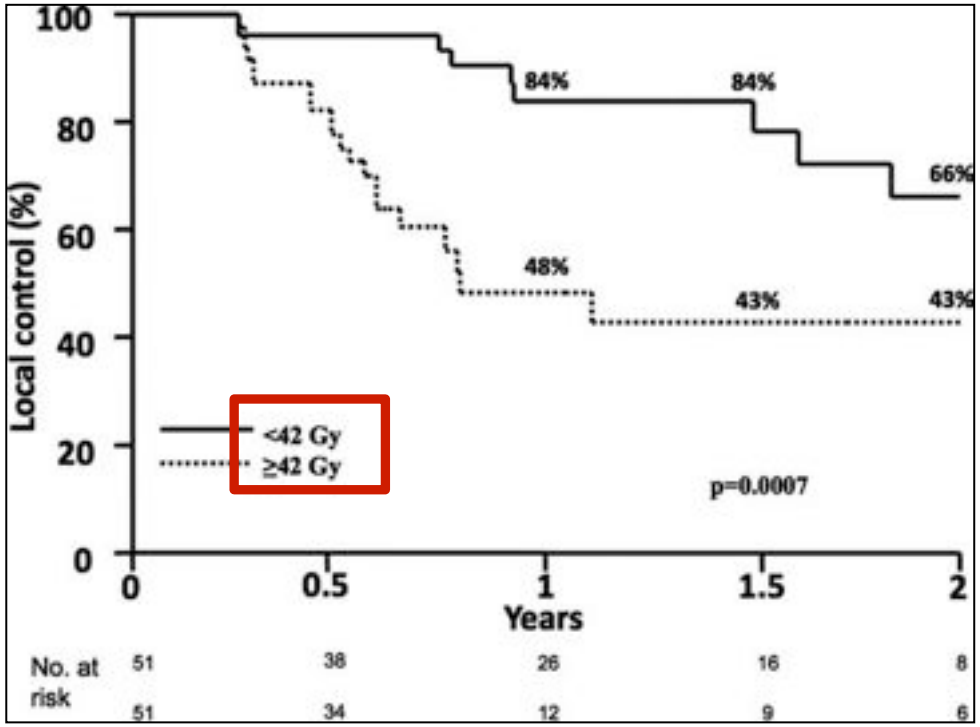


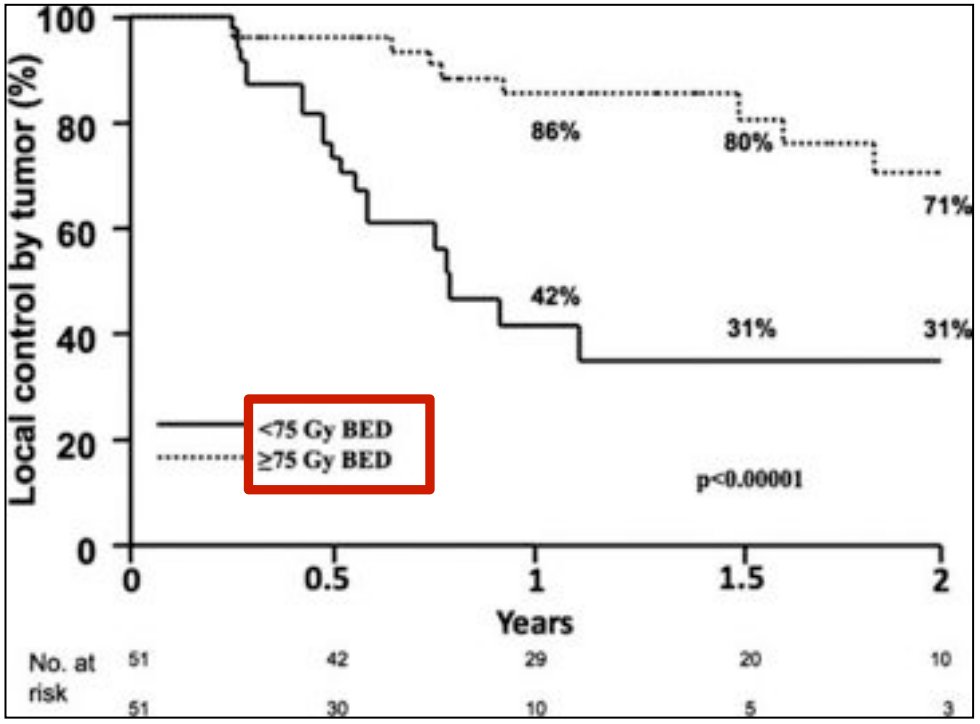
for 1-year local control >90% is 46 to 52 Gy in 3 fractions. **CONCLUSIONS:** Liver stereotactic body radiotherapy is well tolerated and effective for colorectal liver metastases. The strong correlation between local control and OS supports controlling hepatic disease even for heavily pretreated patients. 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

SBRT on Liver metastases: dose and local control

Correlation between dose prescription and local control





single-fraction dose, respectively. Converting these values back into a 3-fraction stereotactic body radiotherapy regimen yields an estimate of the required stereotactic body radiotherapy dose to achieve 90% local control of 46 to 52 Gy in 3 fractions.

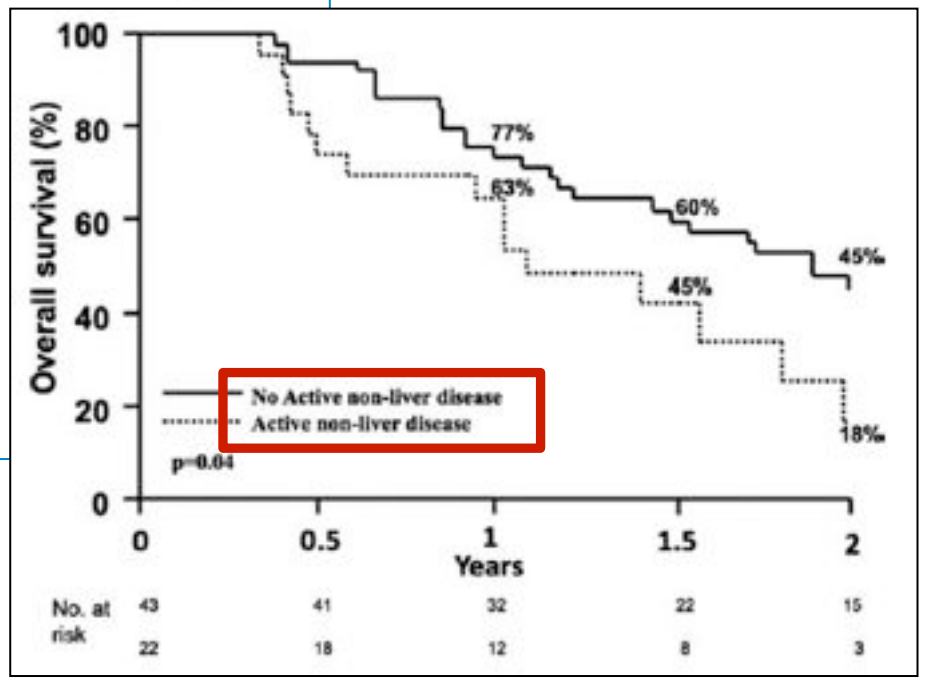
Chang et al.Cancer, 2011

SBRT on Liver metastases: dose and overall survival

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

SBRT on Liver metastases: toxicity

Table 3. Constraints proposed for 3-fraction SBRT schedule

Organ at risk	Wulf *et al.* (36)	Rusthoven *et al.* (37)	Hoyer RAS–Trial (www.cirro.dk)	RTOG 0236 SBRT lung (www.rtog.org)	QUANTEC (48)
Liver (CTV excluded)	30% <21 Gy* 50% <15 Gy*	700 mL < 15 Gy	700 mL < 15 Gy	NA	700 mL ≤15 Gy D_{mean} < 15 Gy
Stomach	$D_{5\ mL}$ <21 Gy	D_{max} ≤30 Gy	$D_{1\ mL}$ <21 Gy	NA	D_{max} <30 Gy ($D_{5\ mL}$ <22.5 Gy)
Bowel	$D_{5\ mL}$ <21 Gy	D_{max} ≤30 Gy	$D_{1\ mL}$ <21 Gy	NA	D_{max} <30 Gy
Esophagus	$D_{5\ mL}$ <21 Gy	NA	$D_{1\ mL}$ <21 Gy	D_{max} ≤27 Gy	NA
Kidney	NA	Total kidney $D_{35\%}$ <15 Gy	Total kidney $D_{35\%}$ <15 Gy	NA	NA
Spinal cord	NA	D_{max} ≤18 Gy	D_{max} <18 Gy	D_{max} ≤18 Gy	D_{max} ≤20 Gy
Heart	$D_{5\ mL}$ <21 Gy	NA	$D_{1\ mL}$ <30 Gy	D_{max} ≤30 Gy	NA

- **Toxicity ≥ G3 1 - 10%; incidence of RILD less than 1%.**
- **Toxicity G2 included a transient hepatic transaminase**
- **Duodenal ulceration and intestinal perforation were observed in 3 patients with maximum doses greater than 30 Gy in 3 fractions to the duodenum and bowel.**
- **One case of Grade 3 soft-tissue toxicity was observed for dose of 48 Gy in 3 fractions to a subcutaneous tissue .**
- **In 2 patients, nontraumatic rib fractures were experienced for maximum doses of 51.8 Gy and 66.2 Gy in 6 fractions to 0.5 cm3 of rib .**

Hoyer et al, IJROBP 2012

SBRT on liver metastases: Preliminay results of our Phase II Trial

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†

END POINTS:

PRIMARY: in-field local control

SECONDARY: toxicity and overall survival

INCLUSION CRITERIA:

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

Phase II trial of liver SBRT: Patients characteristics

- 61 patients
- 76 lesions

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.

Median FU 12 months

Table 1 Baseline patient and treatment characteristics

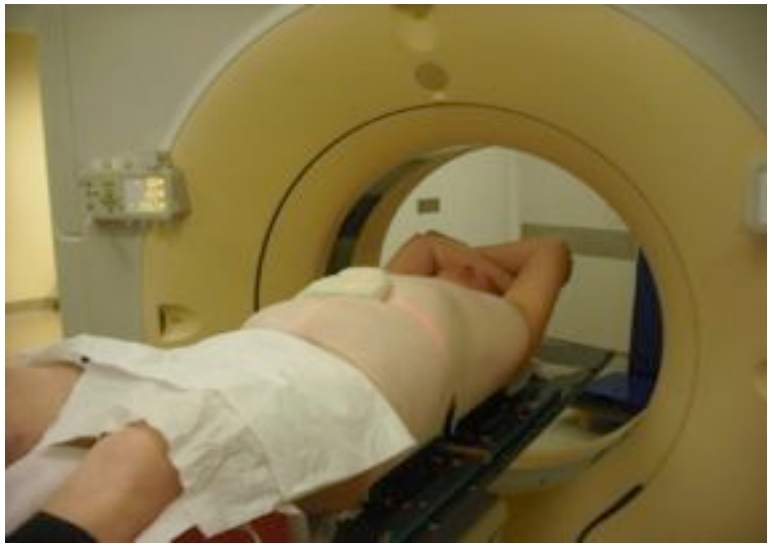
Characteristic	n	%
No. of patients	61	
Male	26	42.6
Female	35	57.4
Median age, y	65	-
Range	39-87	
No. of liver lesions		
1	48	78.7
2	11	18.0
3	2	3.3
Primary		
Colorectal	29	47.5
Breast	11	18.0
Gynecological	7	11.5
Other	14	22.9
Time since diagnosis, mo		
≤12	35	57.4
>12	26	42.6
No. of prior systemic 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

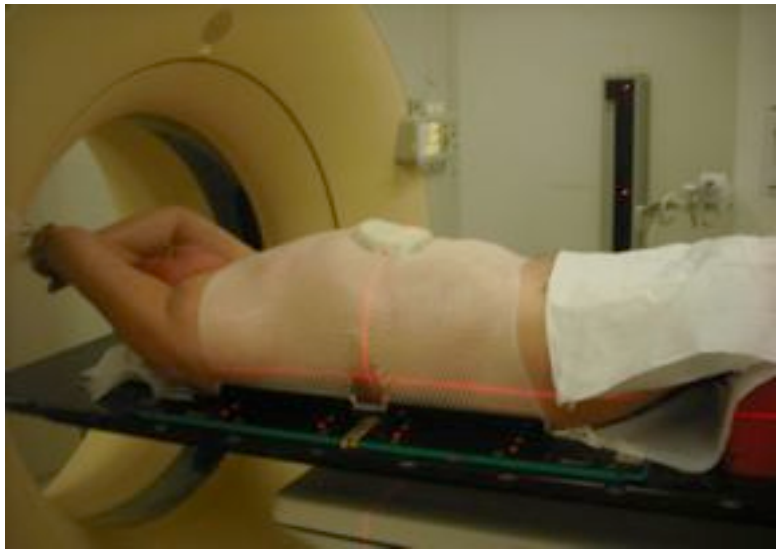
Phase II trial of liver SBRT: Patients characteristics

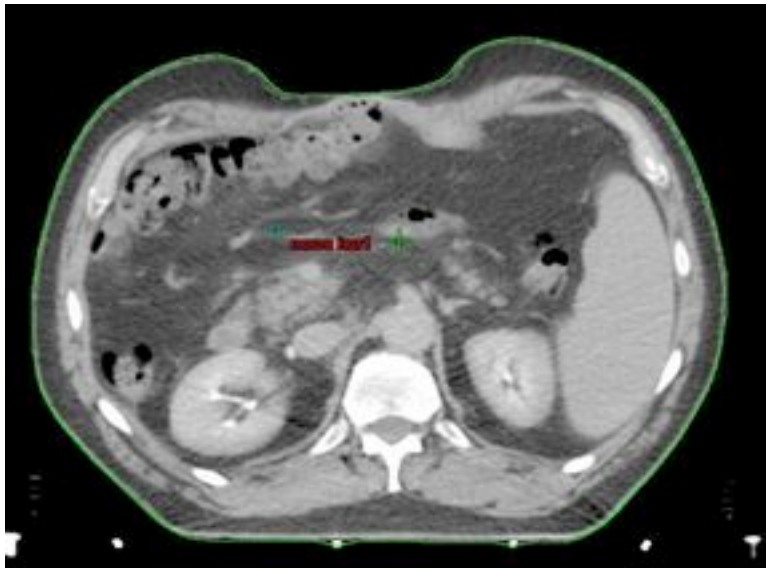
	Dose/ fraction	Number fractions	Total Dose
Standard dose	**25Gy**	**3**	**75 Gy**
Dose reduction 10%	**22.5 Gy**	**3**	**67.5 Gy**
Dose reduction 20%	**20. 63 Gy**	**3**	**61.89 Gy**
Dose reduction 30%	**18.75 Gy**	**3**	**56.25 Gy**

ORGAN	Dose-Volume Limits	Other Conditions
Healthy liver (total liver volume minus cumulative GTV)	> 700 cm^3 at < 15 Gy	Volume of healthy liver > 1000 cc
Spinal cord	D 1cm^3 < 18 Gy	
Kidneys (R+L)	V15 Gy < 35%	
Stomach, duodenum, small intestine	D 3cm^3 < 21 Gy	distant by GTV > 8 mm
Heart	D 1cm^3 <30 Gy	
Rib	D30cm^3 <30Gy	

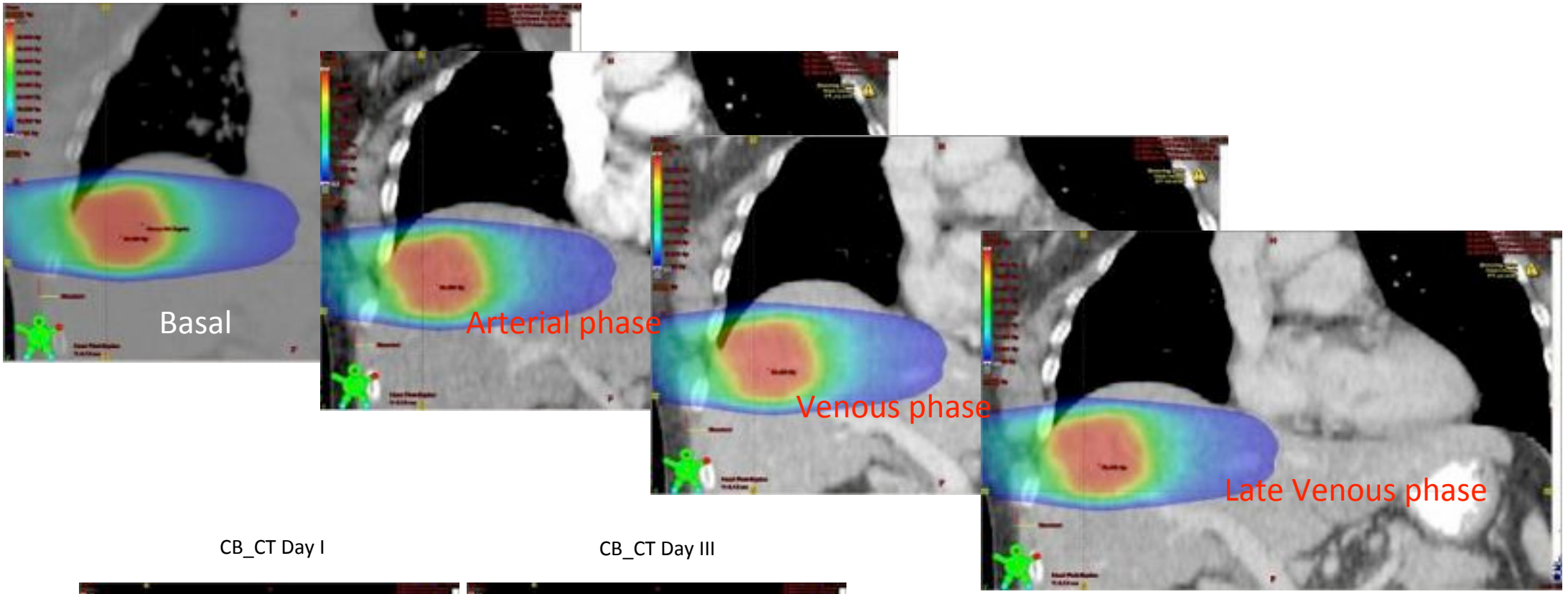
Phase II trial of liver SBRT: Simulation



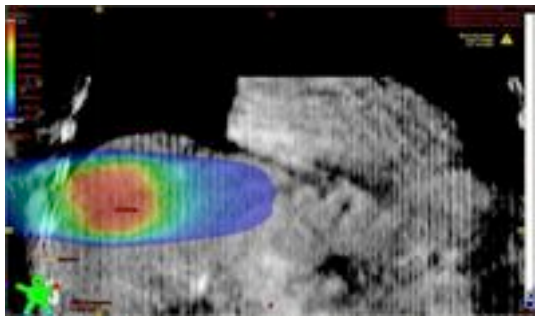




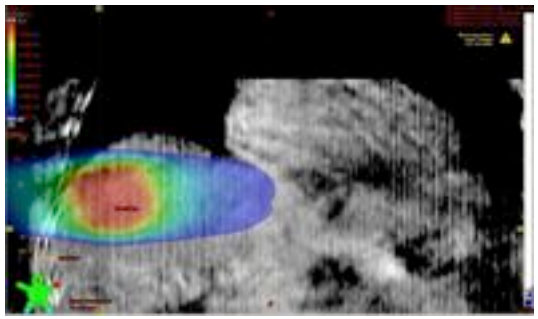
Phase II trial of liver SBRT: CT Simulation and Conebeam CT



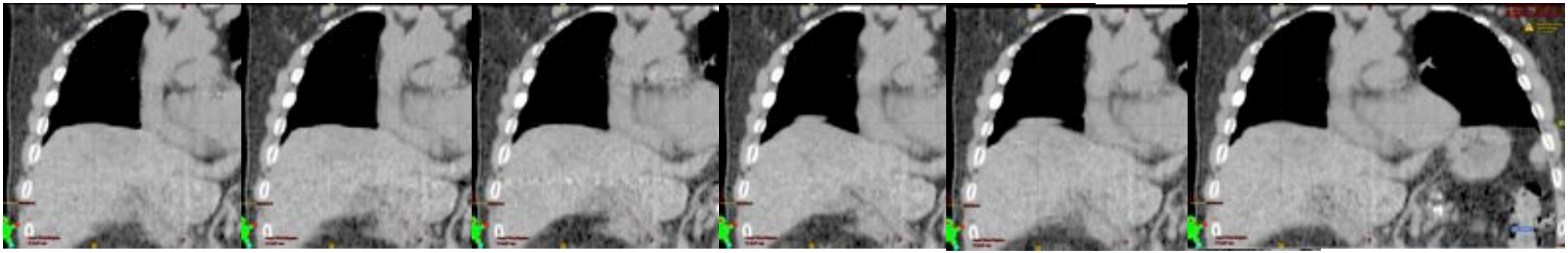
CB_CT Day I

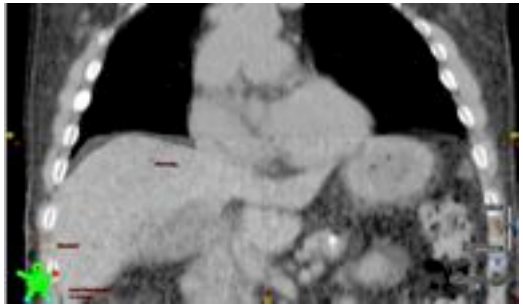


CB_CT Day III

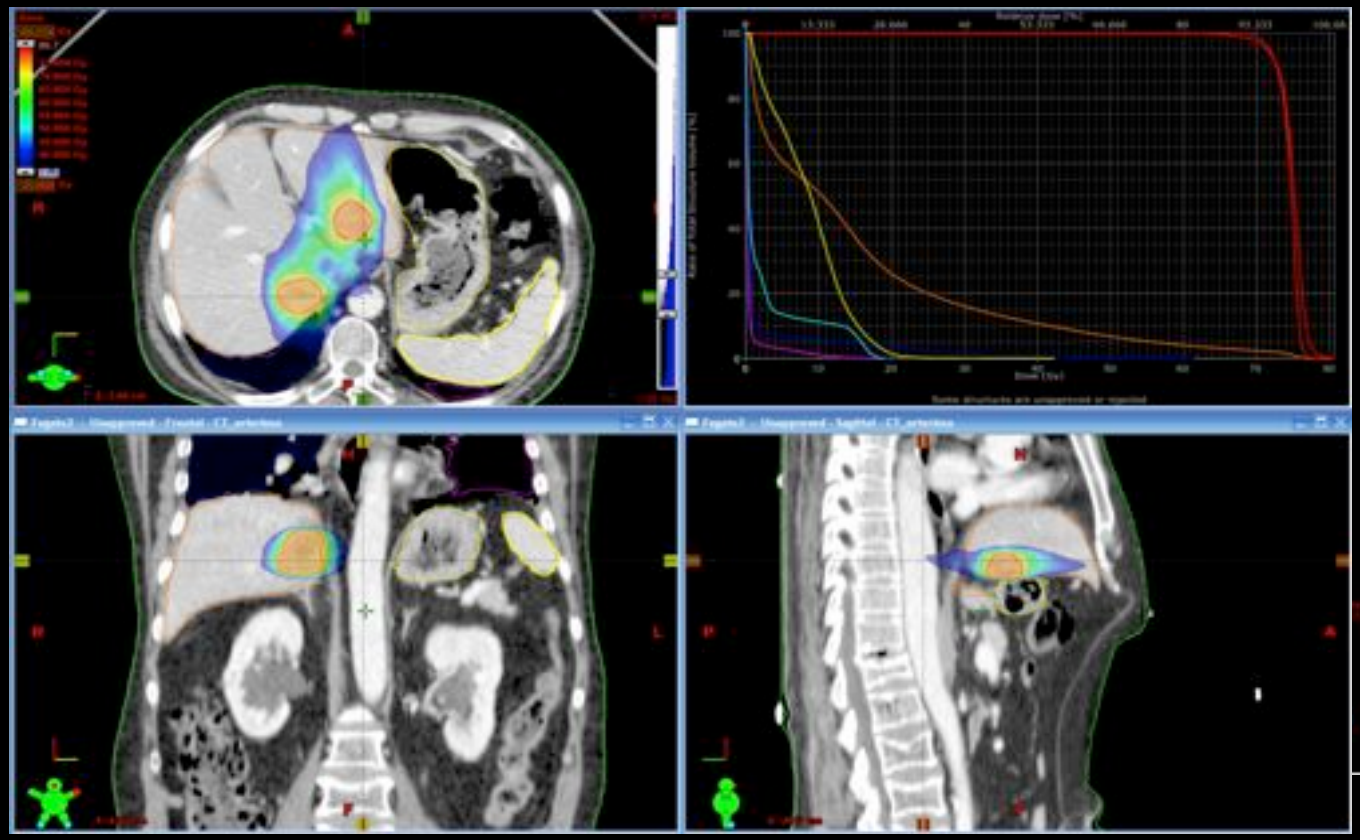


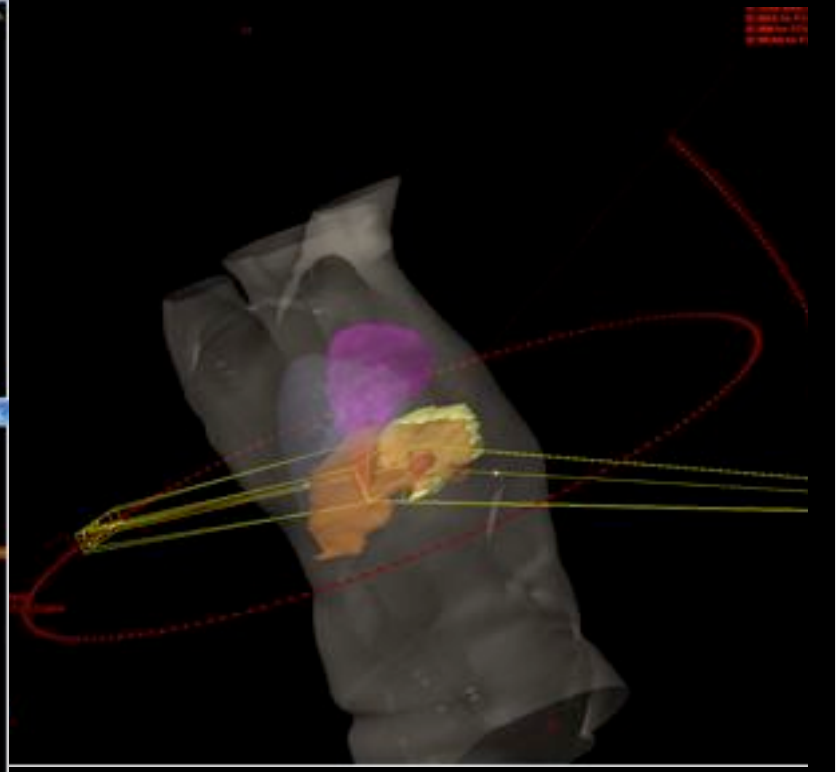
Phase II trial of liver SBRT: 4D CT





Phase II trial of liver SBRT: SBRT liver: 25Gy x 3; 10FFF; DR 2400



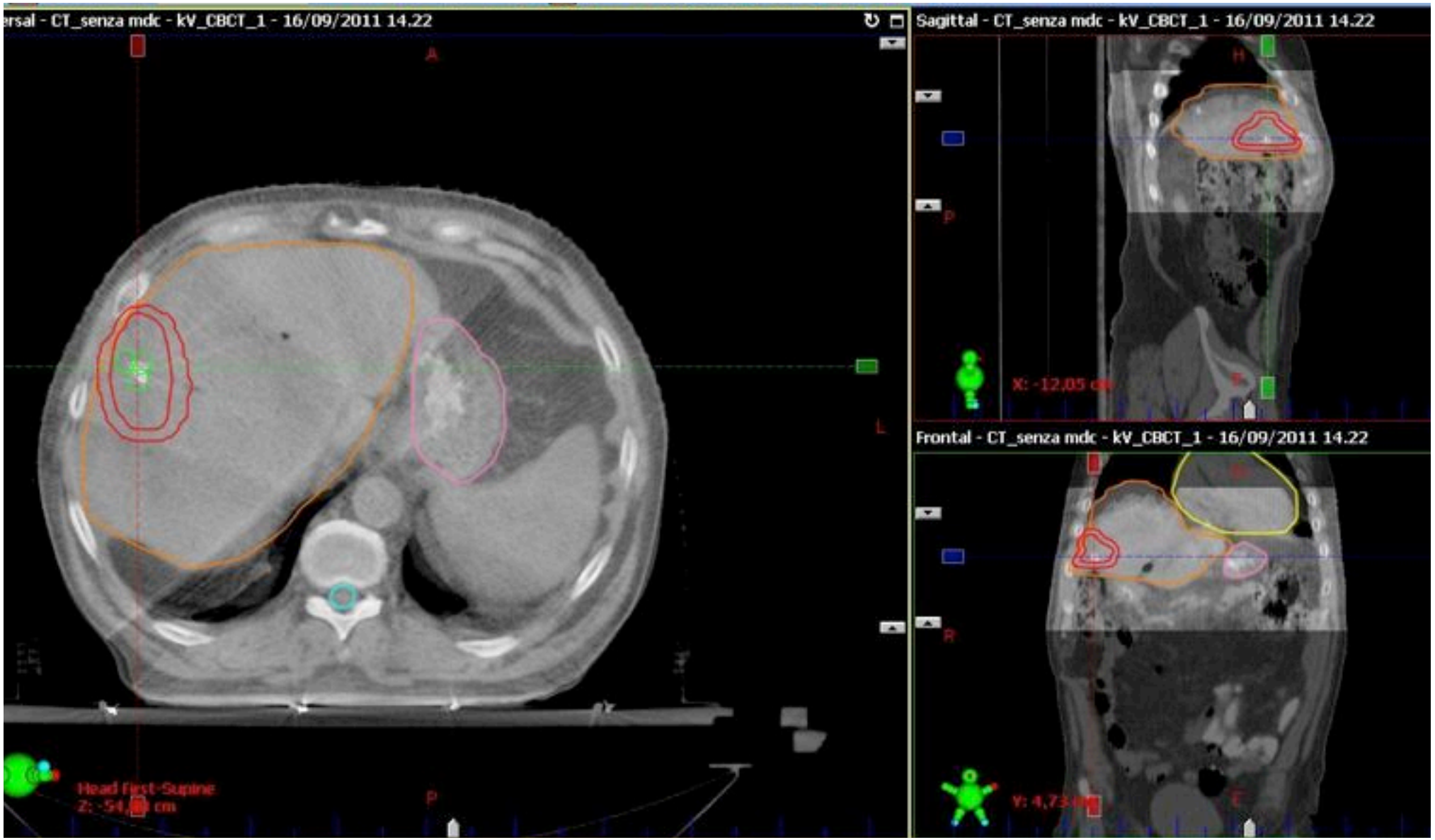


PTV1&PTV2: V95%=99.5%
Spinal cord: Max dose=17.3 Gy
Stomach: Max=21.0Gy, Mean=9.5 Gy
Liver: Mean=15.5 Gy, D15Gyfree=2811cc

1 isocentre, 3 arcs
Jaw tracking

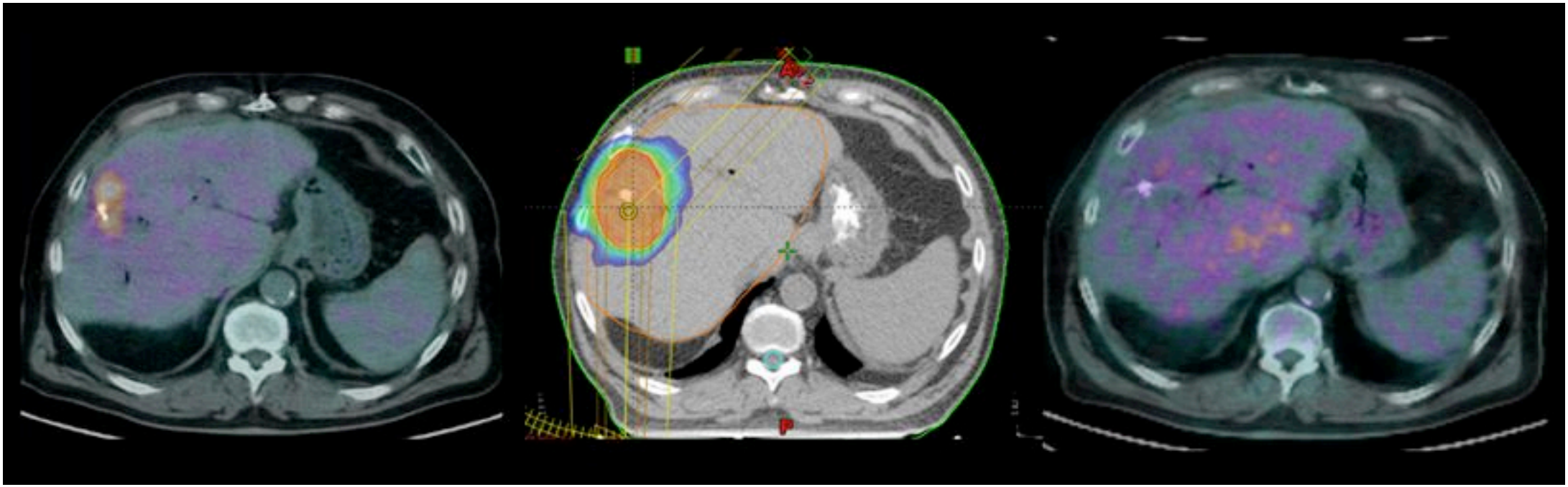
MU:3216+3527+563
BOT: 174s(80+82+14s)

Phase II trial of liver SBRT



Phase II trial of liver SBRT

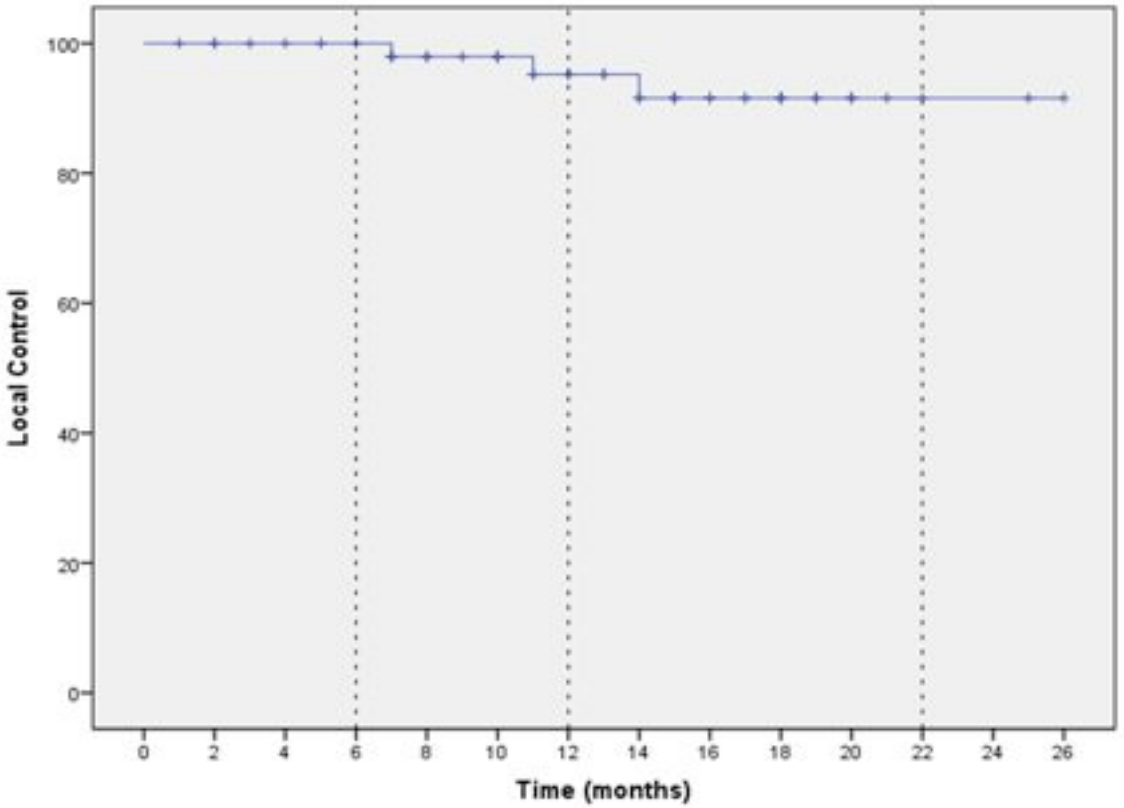
Patient treated with SBRT for local relapse after hepatic surgery for colorectal metastasis



PET –CT pre-treatment, CEA 72

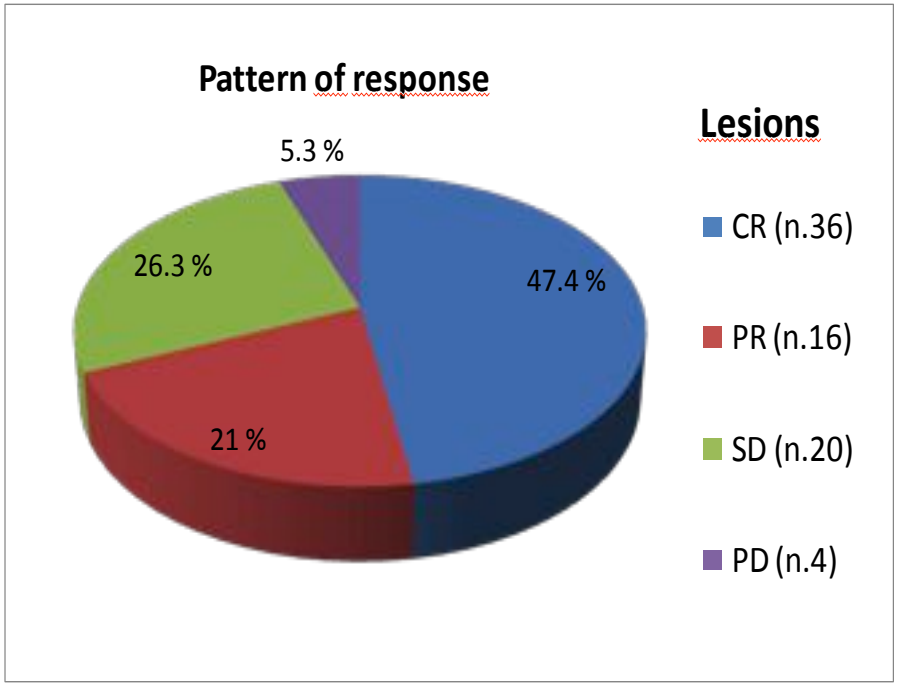
PET –CT post-treatment CEA 2.2

Phase II trial of liver SBRT: Local Control



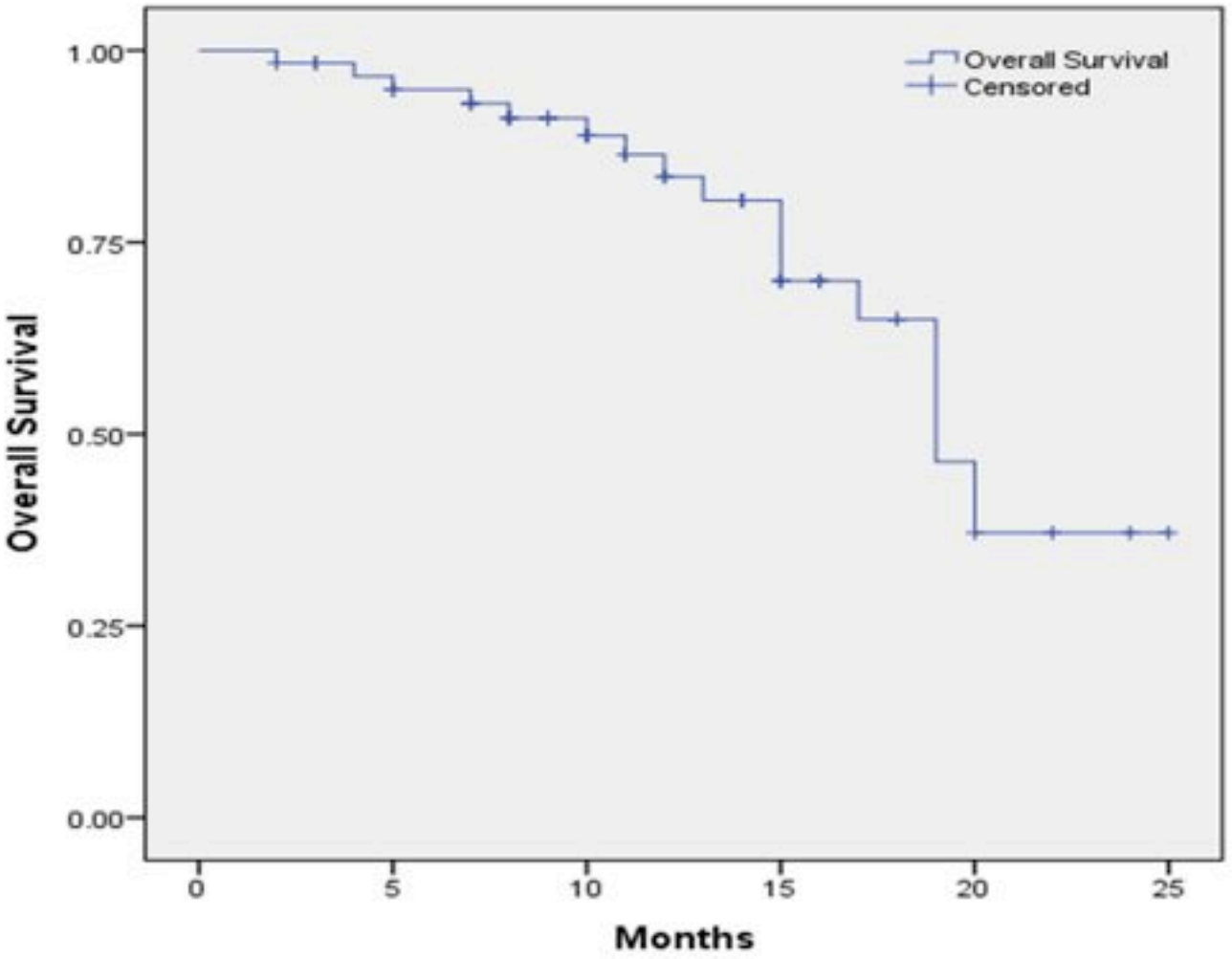
Local Control:

- 6 months=100%
- 12 months=94%
- 22 months =91%



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)

Phase II trial of liver SBRT: Overall Survival



OS:
12 months = 84%
18 months= 65%

Median OS: 19 months

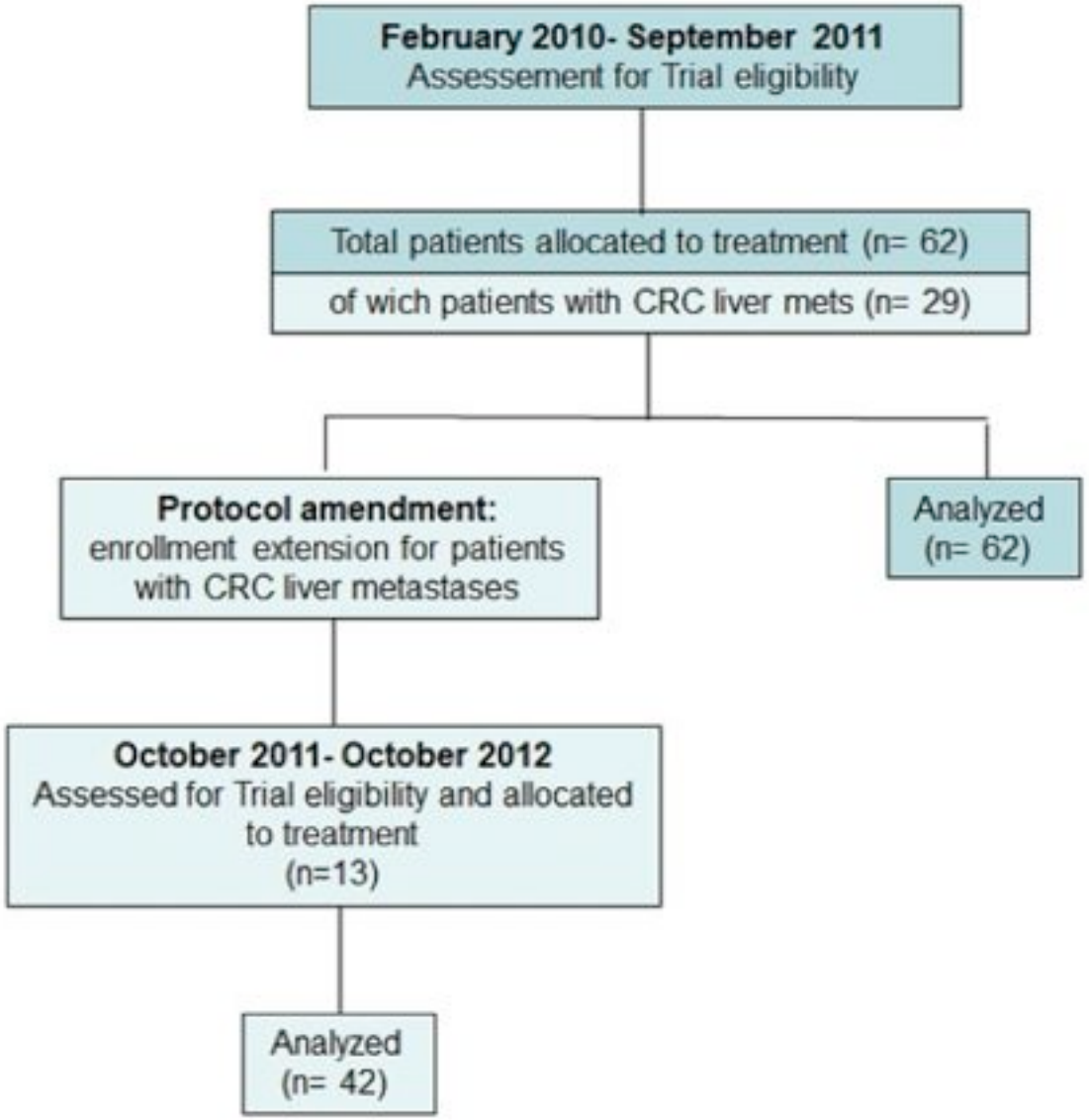
Phase II trial of liver SBRT: Toxicity

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

SABR on liver metastases from CRC: Definitive results of our phase II Trial



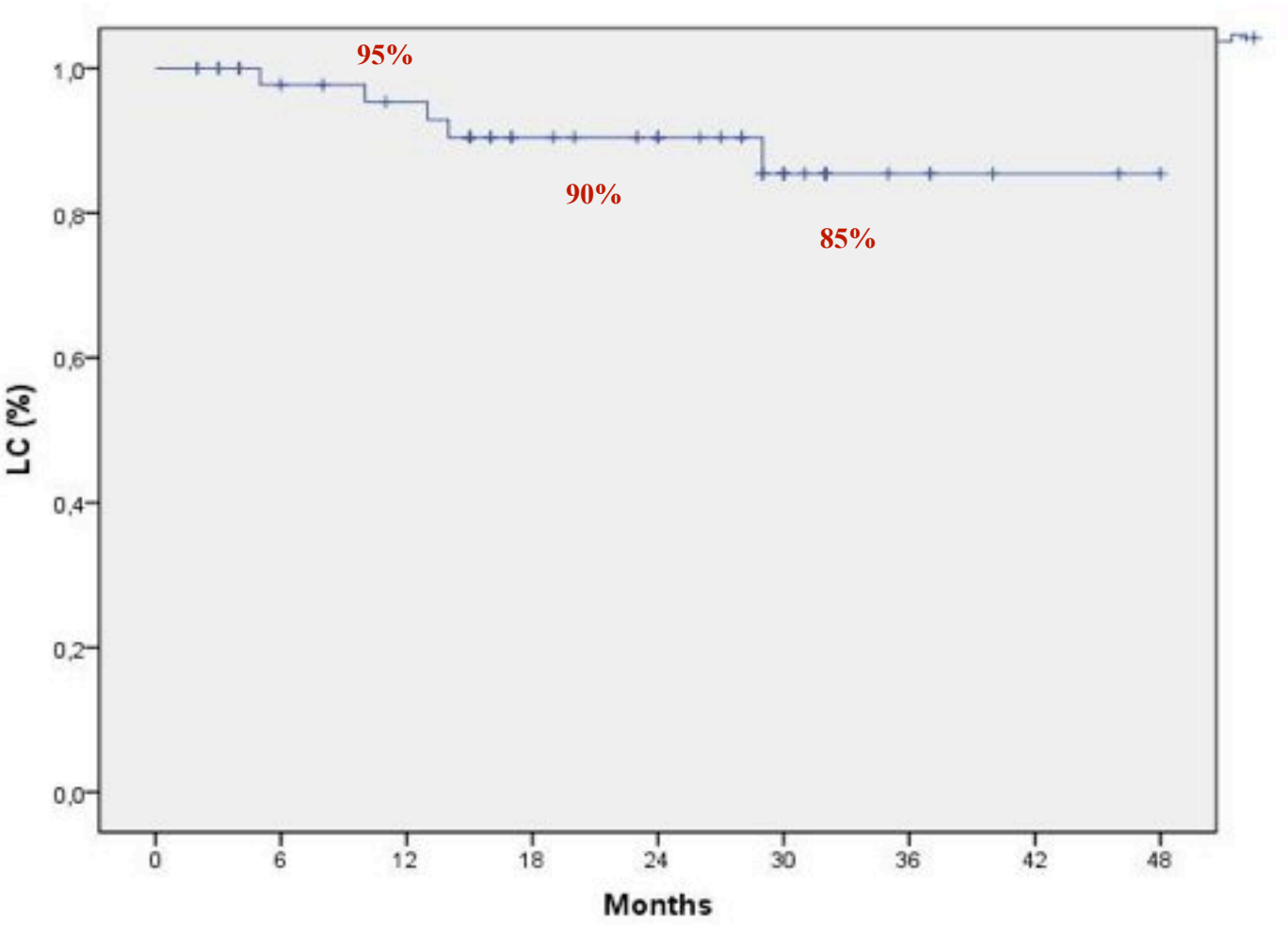
SABR on liver metastases from CRC: Definitive results of our phase II Trial

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%)

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)

Phase II trial of SABR in CRC liver metastases: Local control



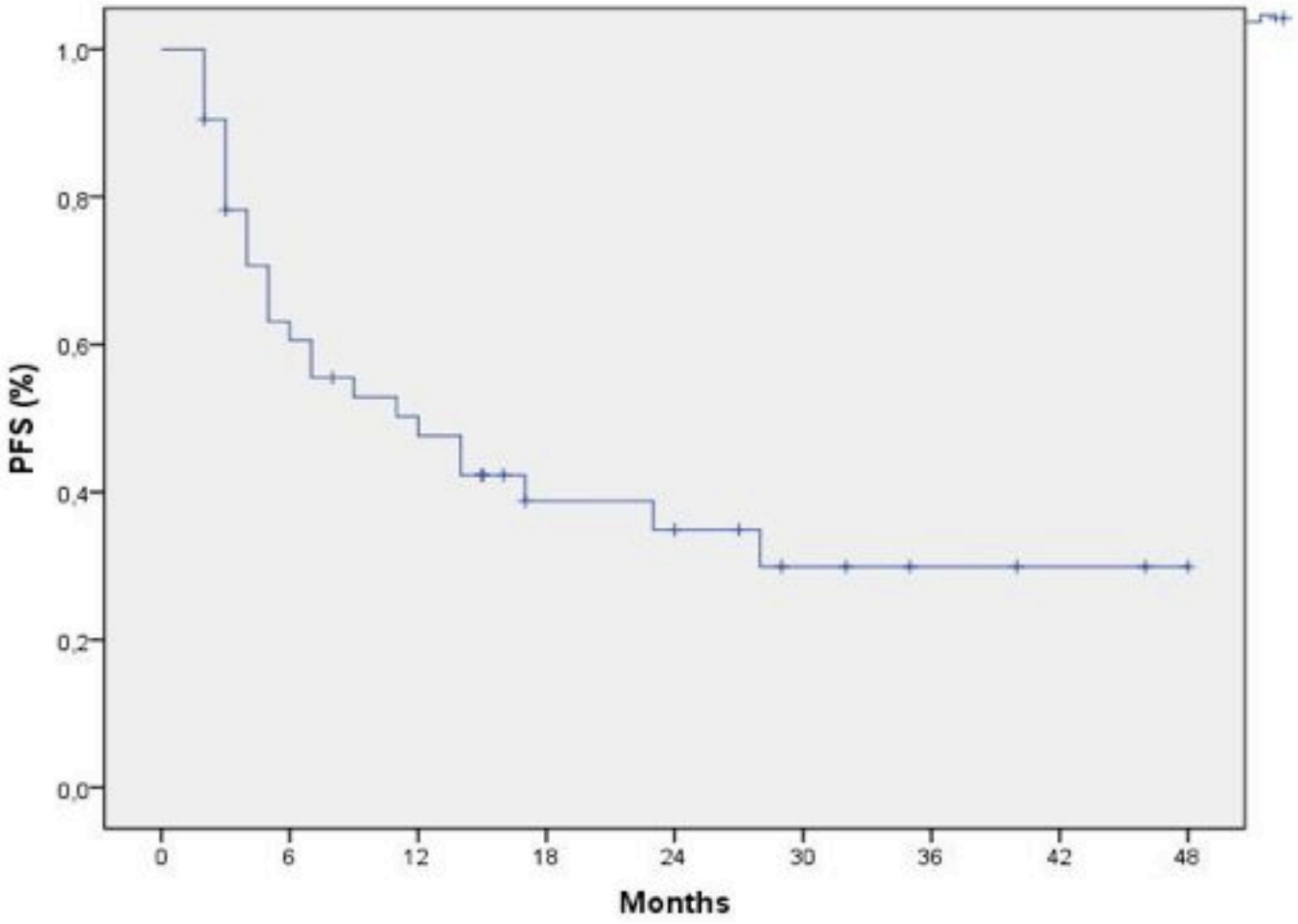
1 - year LC = 95%

2 – years LC = 90%

3 – years LC = 85%

Phase II trial of SABR in CRC liver metastases: Progression-free survival

Median PFS = 12 months.



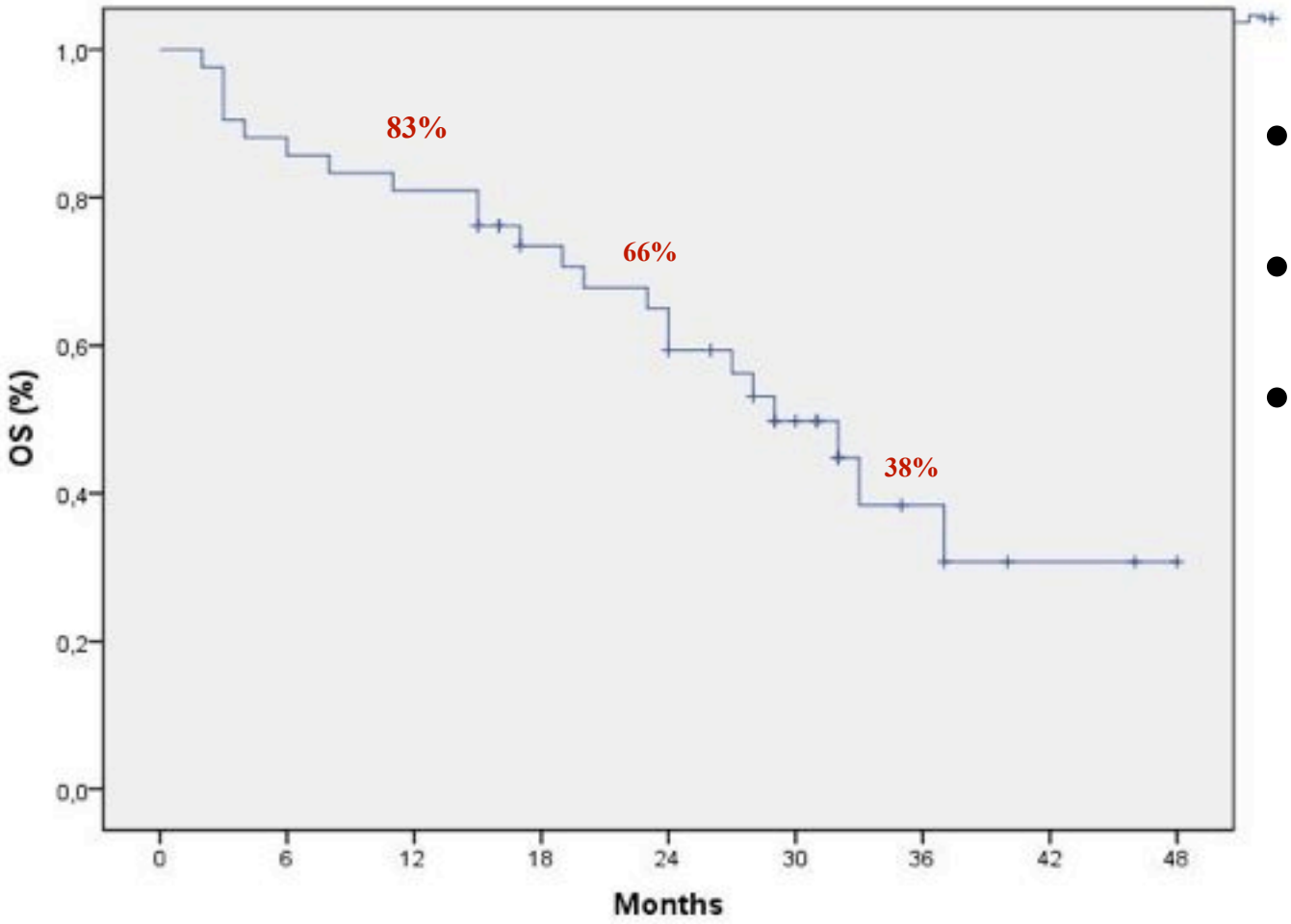
1 - year PFS = 50 %

2 - years PFS = 35%

3 – years PFS = 30%

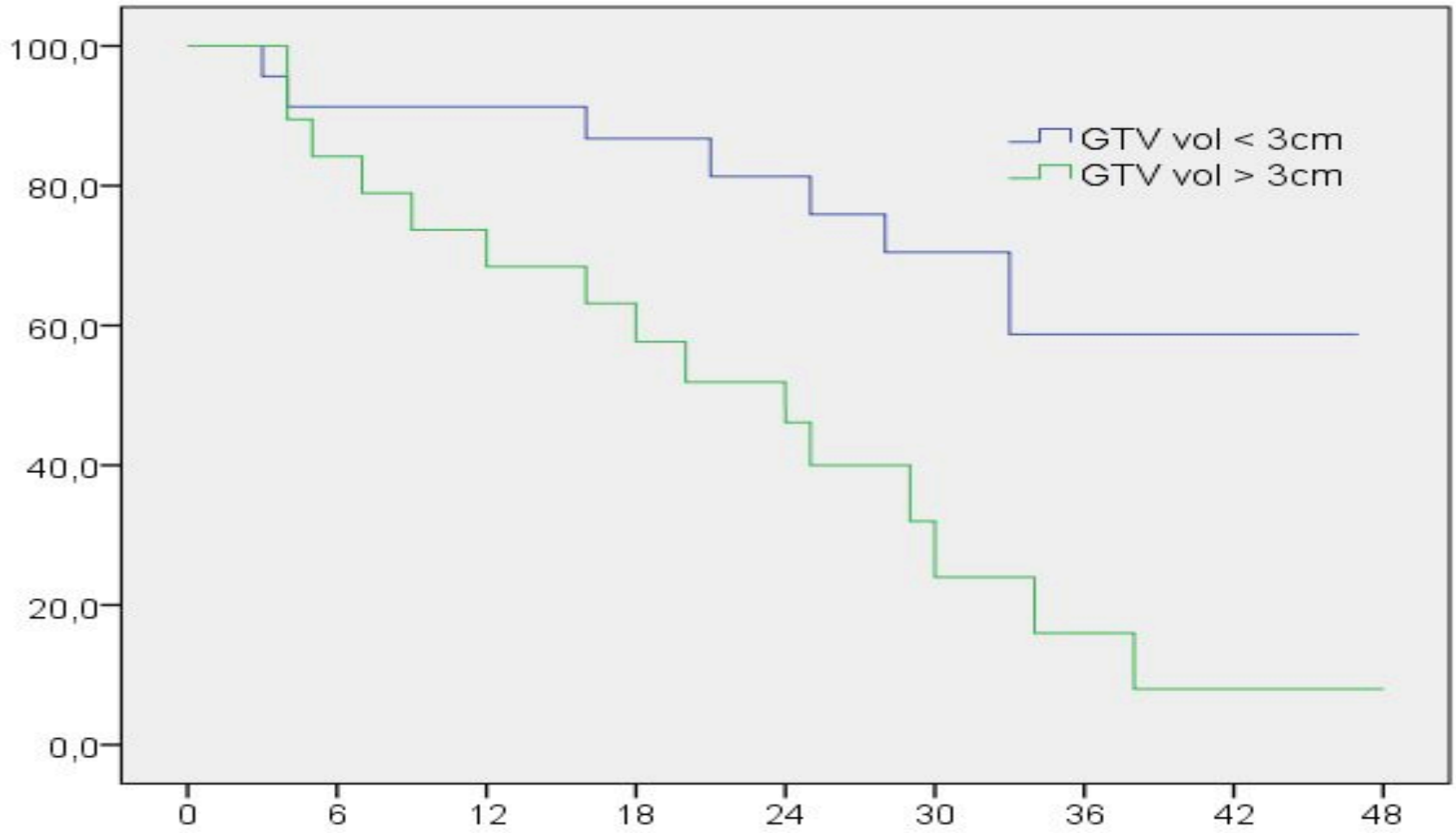
Phase II trial of SABR in CRC liver metastases: Overall Survival

Median OS = 29 months

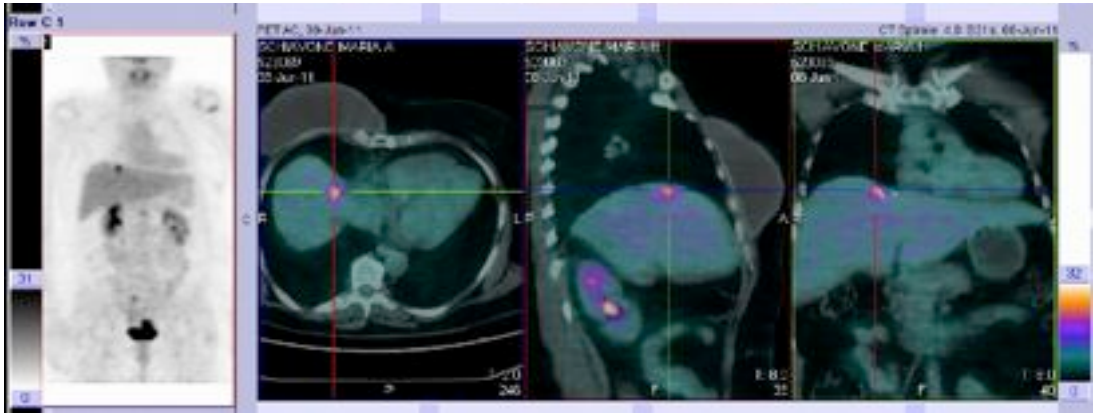


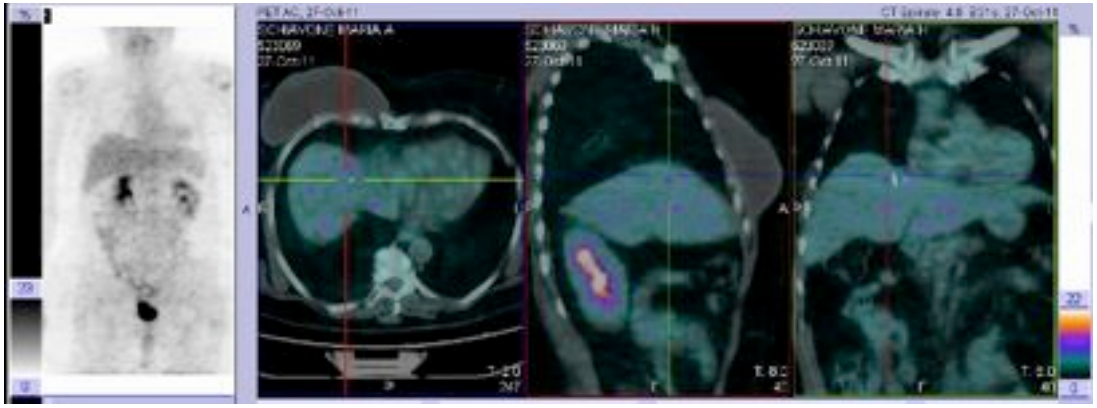
- **1 - year OS = 83%**
- **2 - years OS = 66%**
- **3 - years OS = 38%**

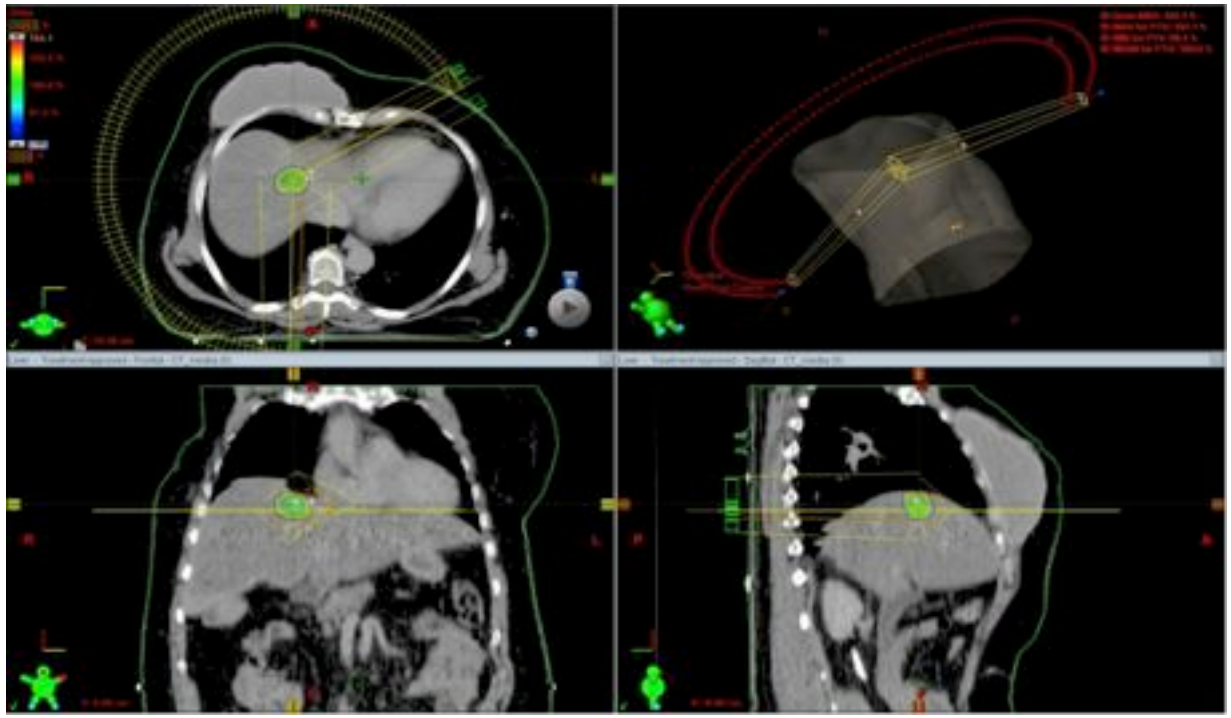
Phase II trial of SABR in CRC liver metastases: Overall Survival



Phase II trial of SABR in CRC liver metastases







Conclusion: current evidences

Selection criteria	*Patients categories*		
	Suitable	**Cautionary**	**Unsuitable**
Lesion Number	< 3	4	> 4
Lesion Diameter	1-3 cm	>3 and ≤ 6cm	> 6cm
Distance from OARs	>8 mm	5-8 mm	< 5mm
Liver Function	Child A	Child B	Child C
Free Liver Volume	>1000cc	< 1000cc and ≥ 700 cc	<700 cc

Lesion diameter	**Prescription Dose**
≤ 3 cm	48 - 60 Gy
3-6 cm	60 – 75 Gy

Conclusion: future directions

Selection of patients with favourable prognosis to evaluate the impact on survival

Comparative RCTs with other local procedures (SR and RF)

Association with chemo\target therapy


Thank you!