



3rd HITRIplus School
SPECIALIZED COURSE ON
CLINICAL ASPECTS OF HEAVY
ION THERAPY RESEARCH
3 - 7 July 2023 ONLINE

Specialized Course on Clinical Aspects of Heavy Ion Therapy Research

Jul 3 - 7, 2023
Online
Europe/Zurich timezone



HITRI
Heavy Ion Therapy Research Integration

Sacro Trial

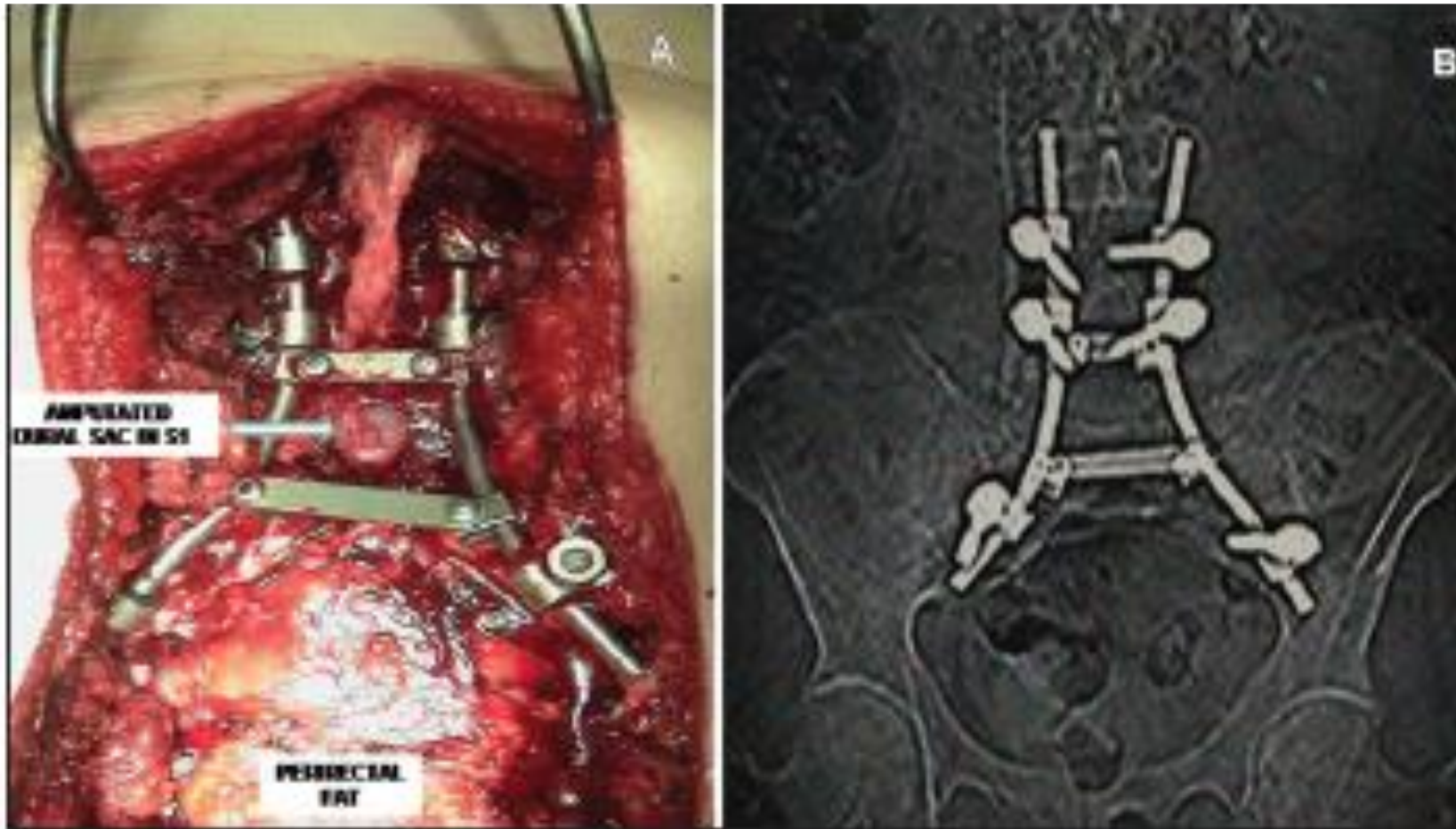
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This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 101008548

TOTAL SACRECTOMY FOR SACRAL TUMOUR

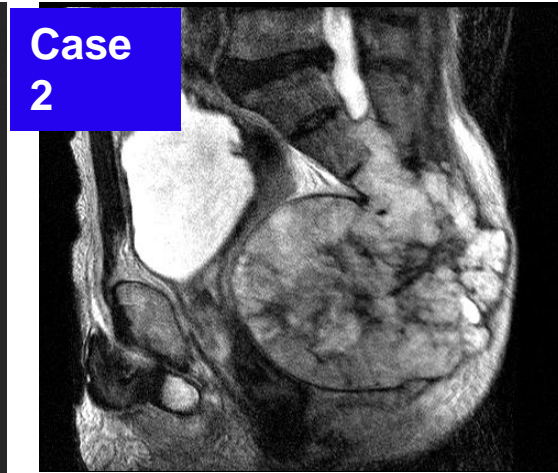


The mean total operating time was 13.3 hrs (range: 8 – 20.1hrs); the mean total blood loss 14.1 ltrs (range: 4.2 – 33 ltrs). The mean length of hospital stay was 8.9mths (range: 2 – 36mths) in 9 cases received total en-bloc sacrectomy. (Molloy,2006)

Chordoma of the sacrum treated with exclusive CIRT in Japan at NIRS



↓ 6 years



↓ 5 years



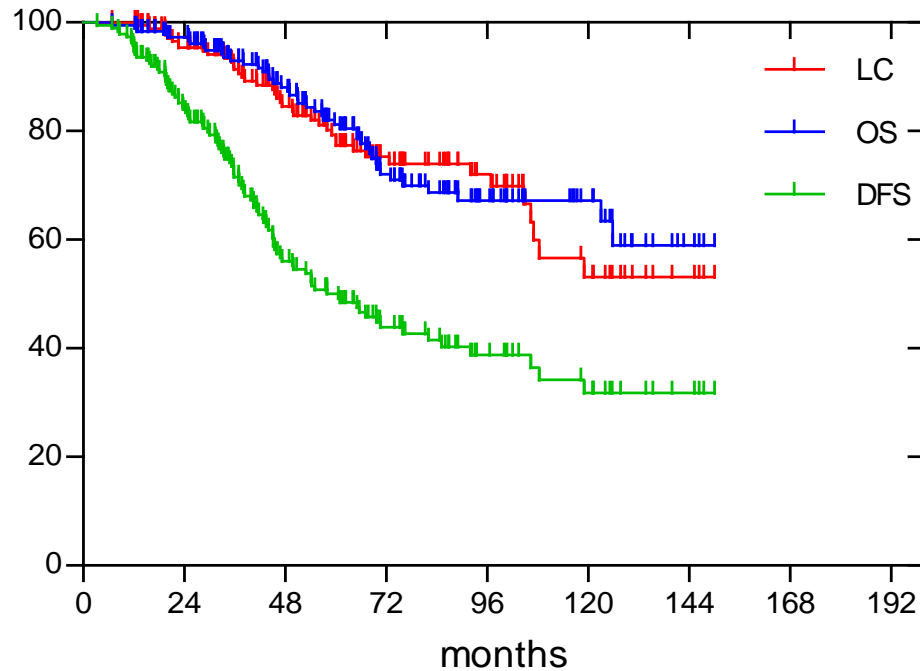
↓ 6 years



The results of CIRT for sacral chordoma (n=188)

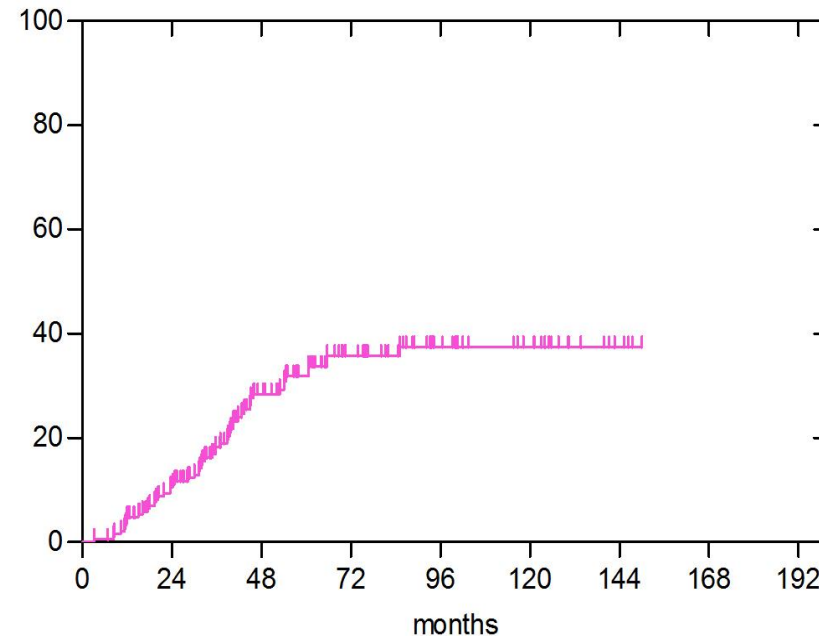
(June 1996 – Feb 2013)

LC, OS and DFS rates



5y	LC	77%
	OS	81%
	DFS	50%

The incidence of metastases



32% of pts had metastases in 5-year

Difficult questions:

- **Can we propose carbon ions as an alternative to surgery?**
- **How much should we insist before accepting patient refusal ?**
- **Are the Japanese data reproducible ?**
- **Is long term toxicity profile really better with carbon ions?**
- **What are the salvage treatment options?**
- **Can we do the same with protons?**

Prospective study on sacral chordoma



SACRO:
Sacral Chordoma,
a Randomized & Observational European study
on Surgery versus Hadron therapy

EudraCT number:

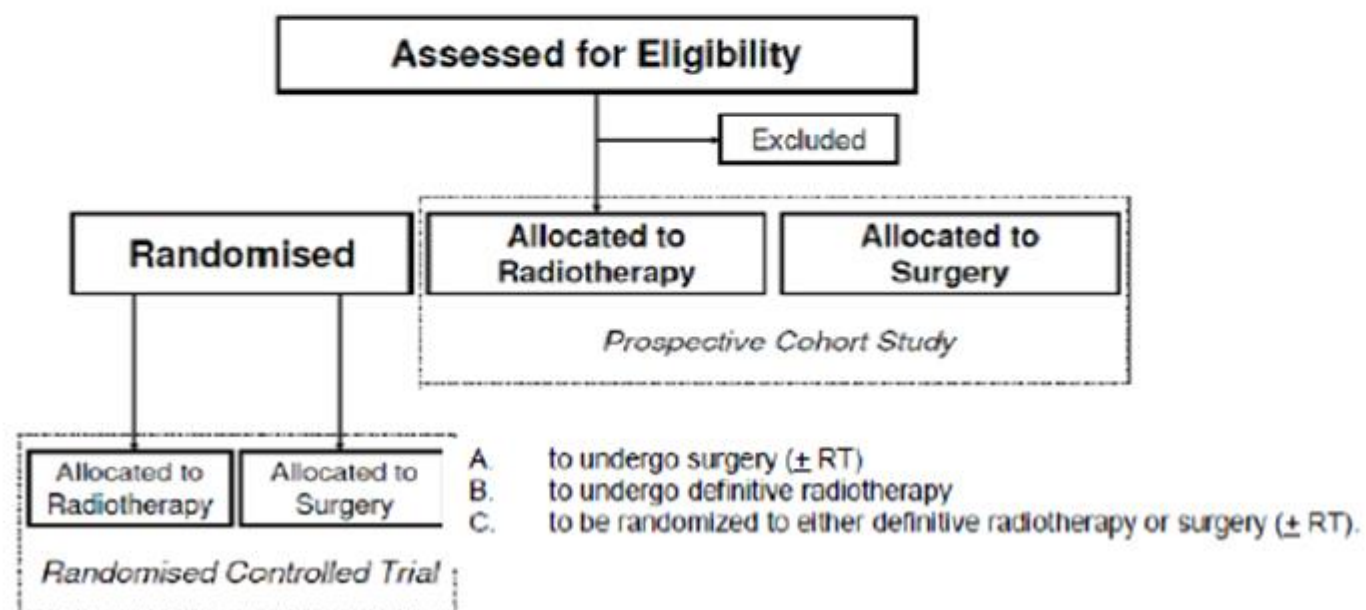


**CHORDOMA
FOUNDATION**



SACRAL Chordoma: a Randomized & Observational study on surgery versus definitive radiation therapy in primary localized disease (SACRO)

Schematic flow-chart



This study is aimed at estimating the effectiveness, safety and activity of radiotherapy as compared to standard surgical treatment for patients with primary sacral chordoma who are candidates to a complete en-bloc resection

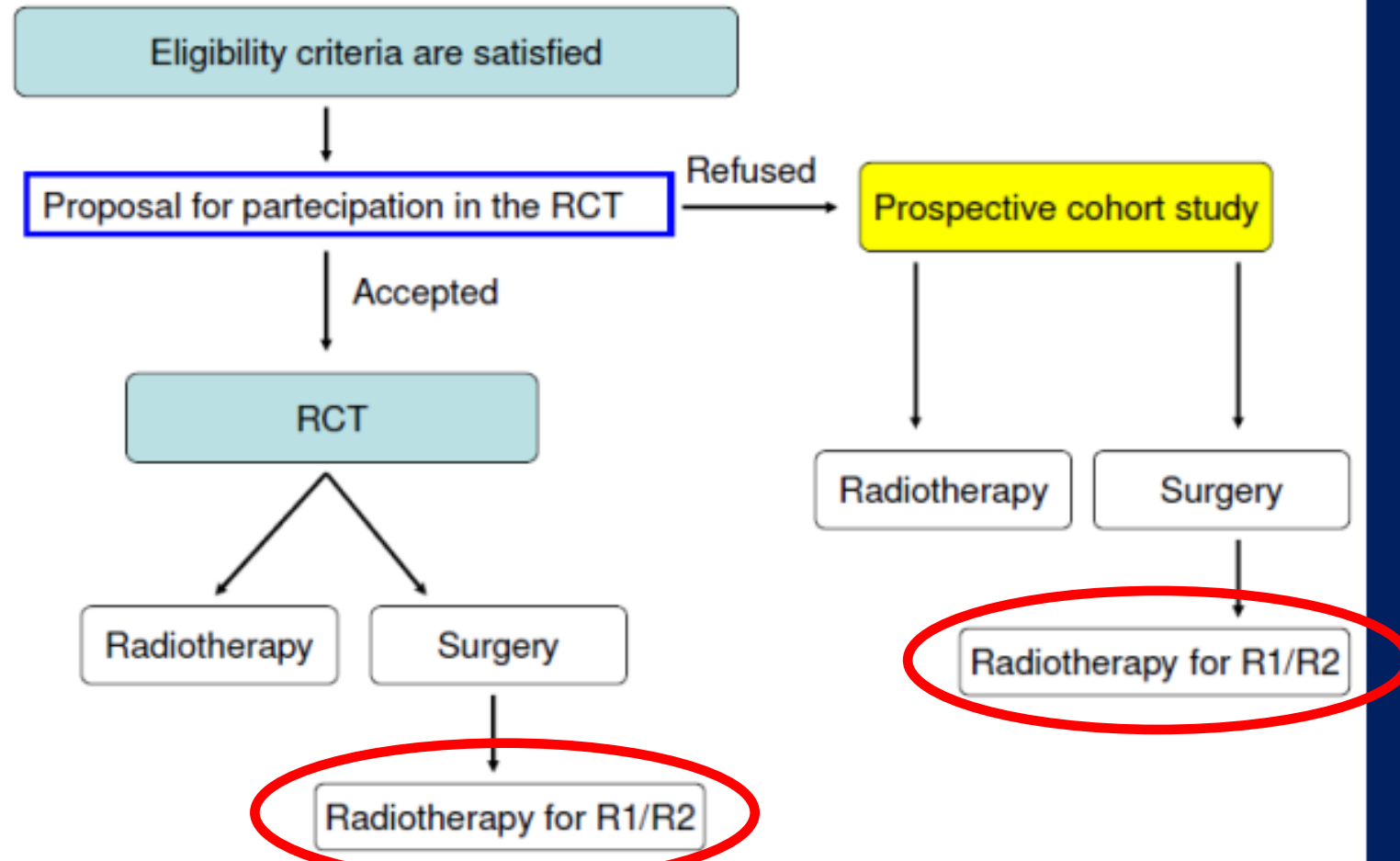
After R1/R2 resection, radiotherapy will be considered

Inclusion criteria

- **path confirmed diagnosis of primary chordoma**
- **tumor arising from sacrum**
- **age ≥ 18 years**
- **no evidence of metastases**
- **en-bloc resection feasible**

Study design, bayesian approach

Flow-chart



Study treatment

- a) to undergo immediate surgery**
- b) to undergo immediate radiotherapy**
- c) to be randomized to either immediate radiotherapy or immediate surgery**

Study end-points

Primary endpoint

Relapse free survival

Secondary end points

Overall Survival (OS)

Morbidity

LRFS

DRFS

Safety

QoL

Open sites

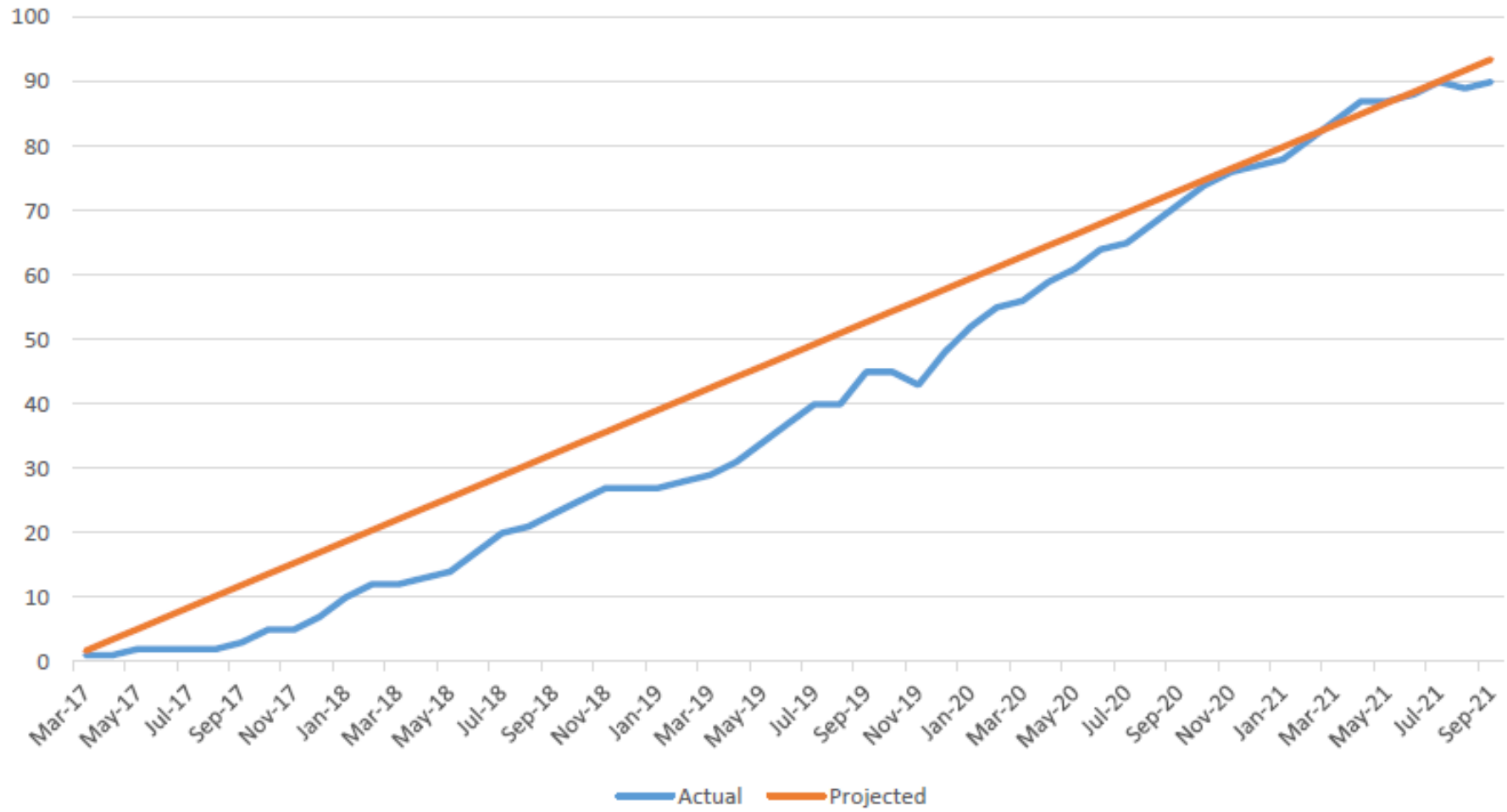
2016	2017	2018	2019	2020	2021	Total
1	7	2	7	4	2	23



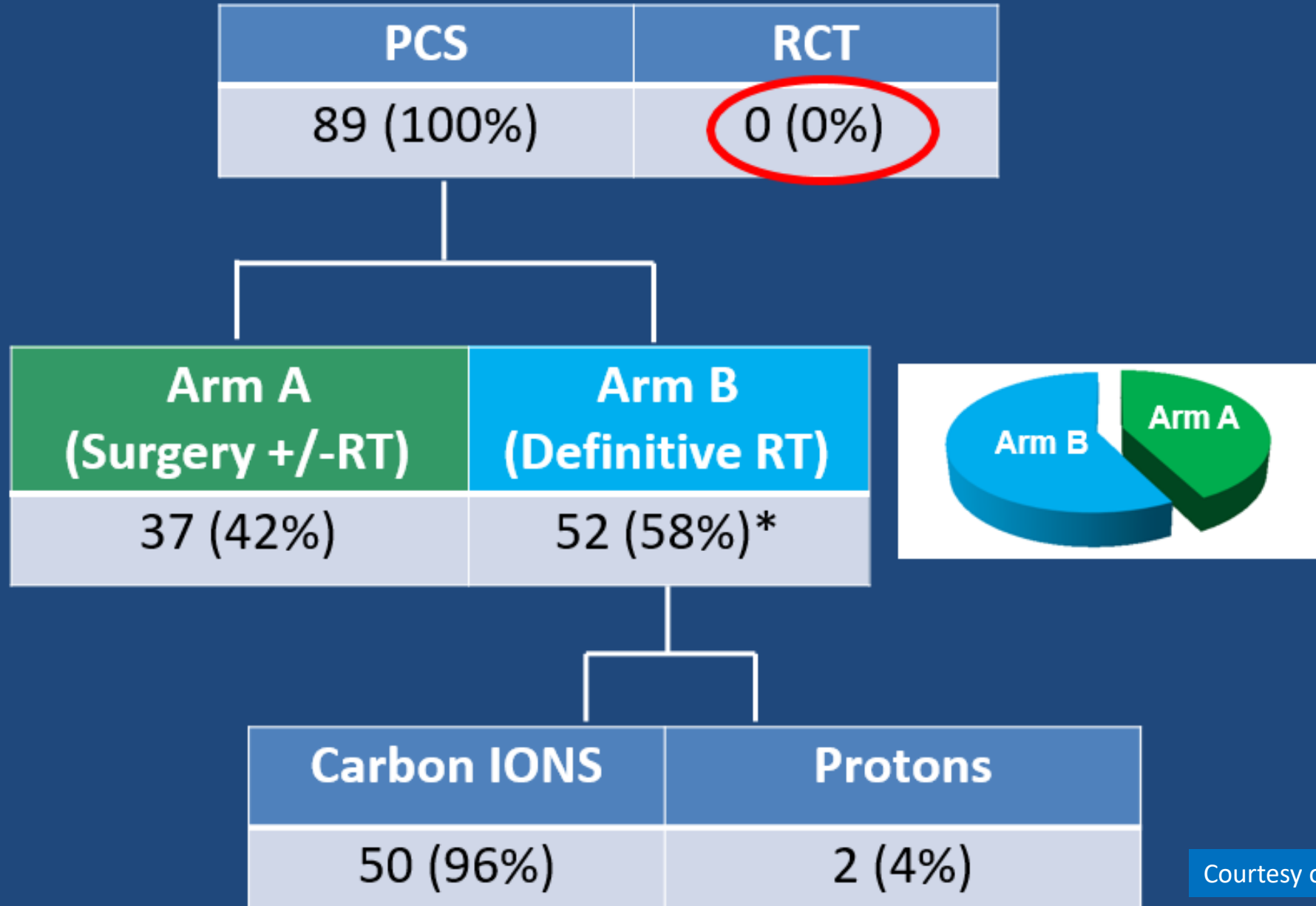
**23 active sites in 7 countries
and more ar joining**

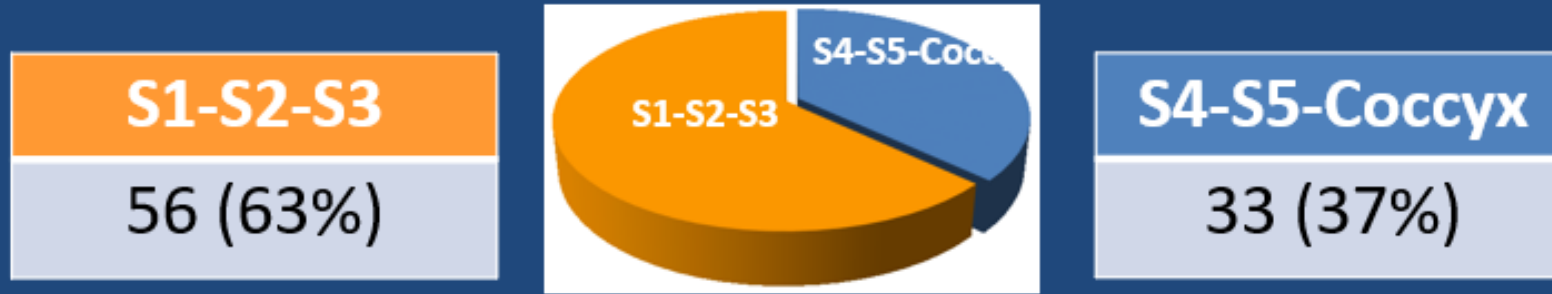
**136 enrolled
patients**

SACRO Accrual

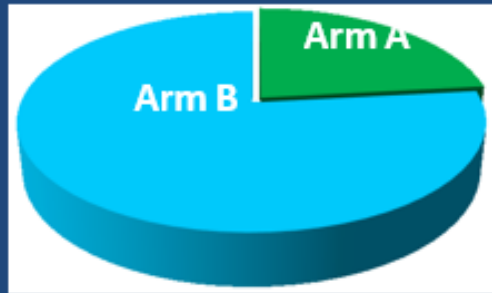


Study Cohorts & Treatment

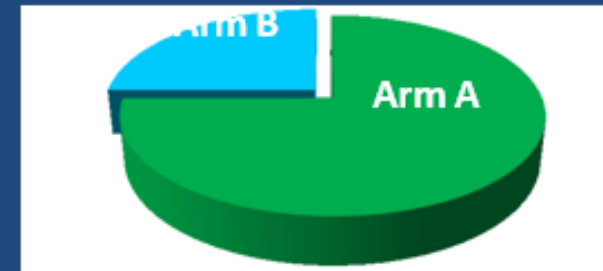




Chosen Treatment



Arm A (Surgery +/-RT)	Arm B (Definitive RT)
11 (20%)	45 (80%)



Arm A (Surgery +/-RT)	Arm B (Definitive RT)
26 (79%)	7 (21%)

Multifocality	Number of patients
Yes	5% (2)
No	81% (30)
Missing/UNK	14% (5)

Quality of surgery	Microscopic margins	Resection type
86% (32) Macros. Complete 3% (1) Macros. Incomplete 4 pts missing data (11%)	70% (26) R0 14% (5) R1 0% (0) R2 3% (1) Tumor spillage 5 pts missing data (14%)	81% (22) Wide 15% (4) Marginal 4% (1) Intralesional 10 pts missing data

Organ resection	Tumor rupture or contamination
None*	6%(2)*

Postoperative RT
None

* 4 Missing data

Definitive RT dose * 51 pts

Carbon IONS	Protons
46 (90%)	5 (10%)

RT total dose (Gy)	Number of patients
64 (16 fractions of 4.0 Gy)	4% (2)
66 (22 fractions of 3.0 Gy)	2% (1)
70.4 (16 fractions of 4.4 Gy)	14% (7)
73.5 (35 fractions of 2,1.6 Gy)	6% (3)
73.6 (16 fractions of 4.6 Gy)	65% (33)
74 (37 fractions of 2 Gy)	2% (1)

4 pts missing data (6%)

RT toxicity

33 pts (87%) experienced RT related toxicity

AE Term	Total	G1	G2	G3	G4
Radiodermatitis	27	52,6% (20)	13,2% (5)	5,3% (2)	0,0% (0)
Peripheral sensory neuropathy	25	26,3% (10)	26,3% (10)	13,2% (5)	0,0% (0)
Peripheral motor neuropathy	22	21,1% (8)	21,1% (8)	15,8% (6)	0,0% (0)
Skin induration	20	26,3% (10)	23,7% (9)	2,6% (1)	0,0% (0)
Rectal toxicity (Constipation)	15	31,6% (12)	2,6%	5,3% (2)	0,0% (0)
Bone fracture	12	28,9% (11)	0,0% (0)	2,6% (1)	0,0% (0)
Sacral/extremities Pain	11	5,3% (2)	13,2% (5)	10,5% (4)	0,0% (0)
Neuralgia	8	0,0% (0)	13,2% (5)	7,9% (3)	0,0% (0)
Urinary toxicity (retention)	8	21,1% (8)	0,0% (0)	0,0% (0)	0,0% (0)
Urinary toxicity (incontinence)	5	5,3% (2)	5,3% (2)	2,6% (1)	0,0% (0)
Skin hyperpigmentation	4	7,9% (3)	2,6% (1)	0,0% (0)	0,0% (0)
Rectal toxicity (Incontinence)	3	5,3% (2)	0,0% (0)	2,6% (1)	0,0% (0)

Data from Interim Analysis (on 33 pts)

Surgery post-operative Complications ≥ 3 according to Clavien-Dindo grade

Pts with surgical complication

41% (13/32*)

5 missing pts (14%)

Nr of post-operative Complications ≥ 3
according to Clavien-Dindo grade

63% (20/32*)

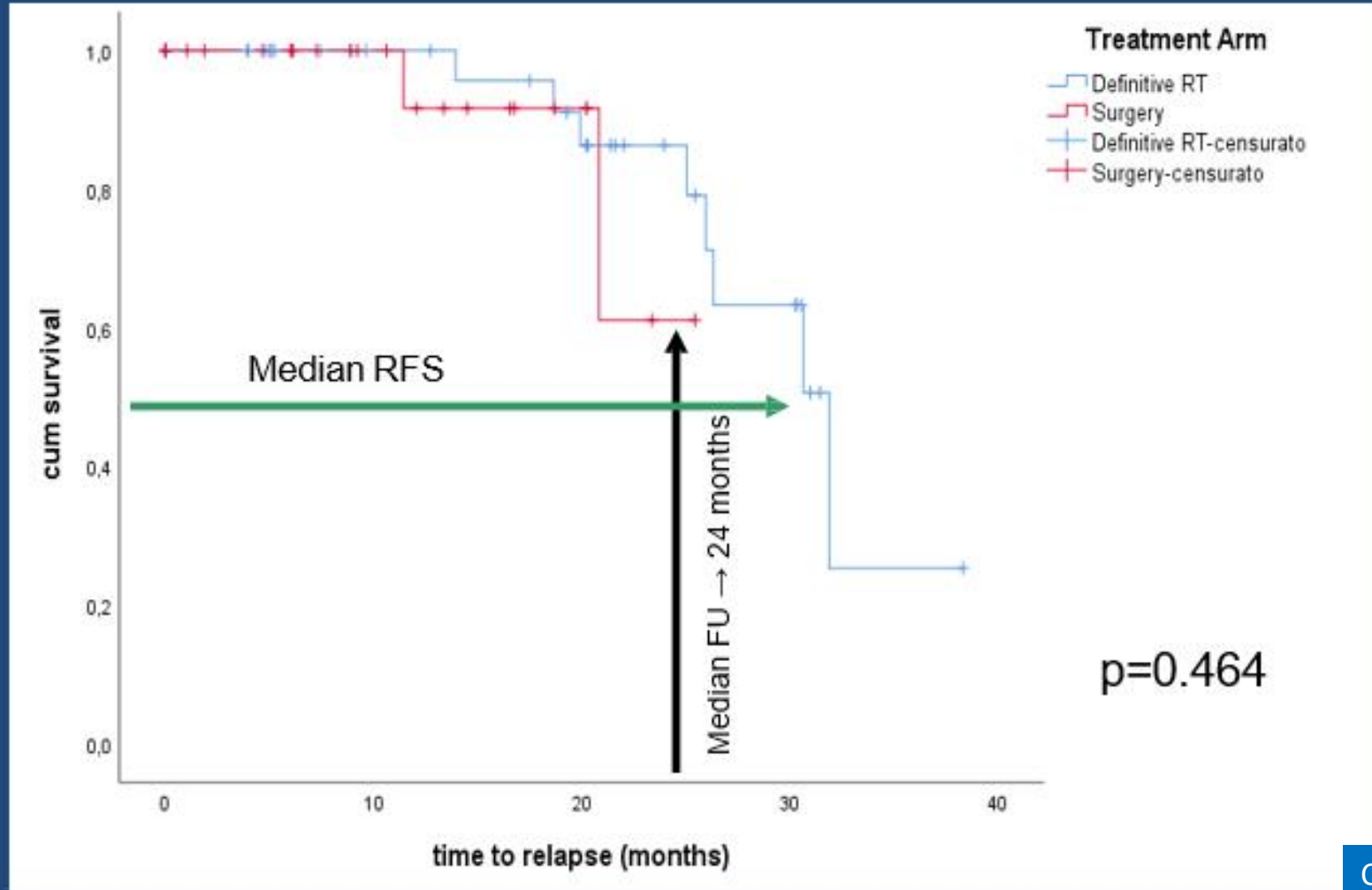
Infection	Wound dehiscence	Hemorrhage	Seroma	CSF leak
40% (8/20)	35% (7/20)	15% (3/20)	5% (1/20)	5% (1/17)

SAE

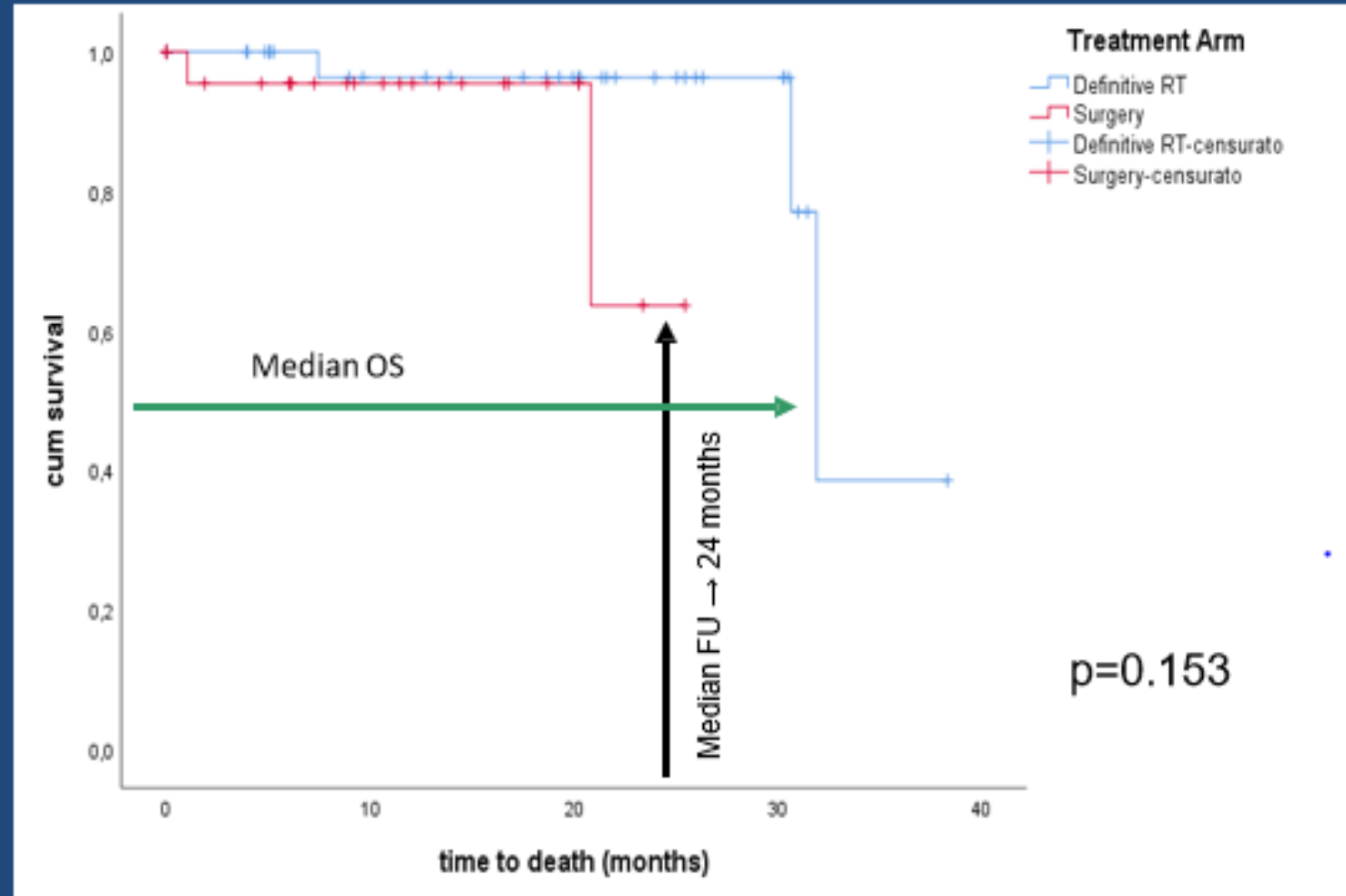
SAE

1 pt had hemorrhagic shock after on 30th pod and died

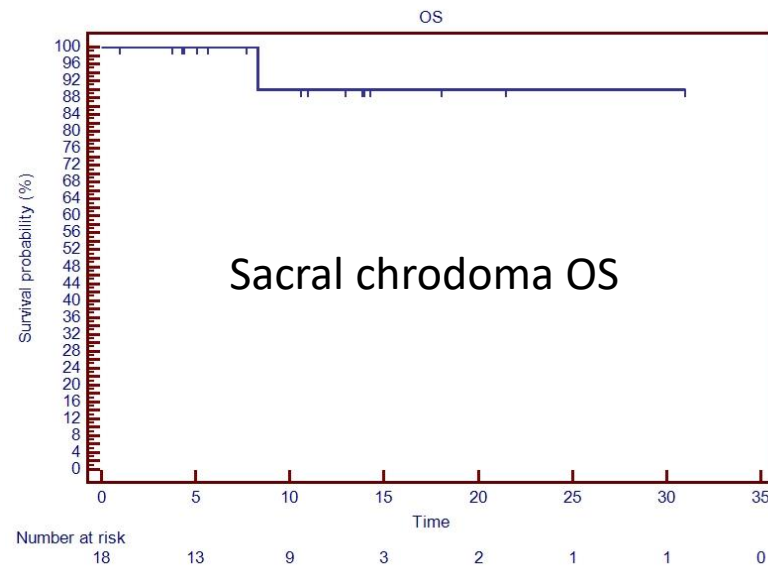
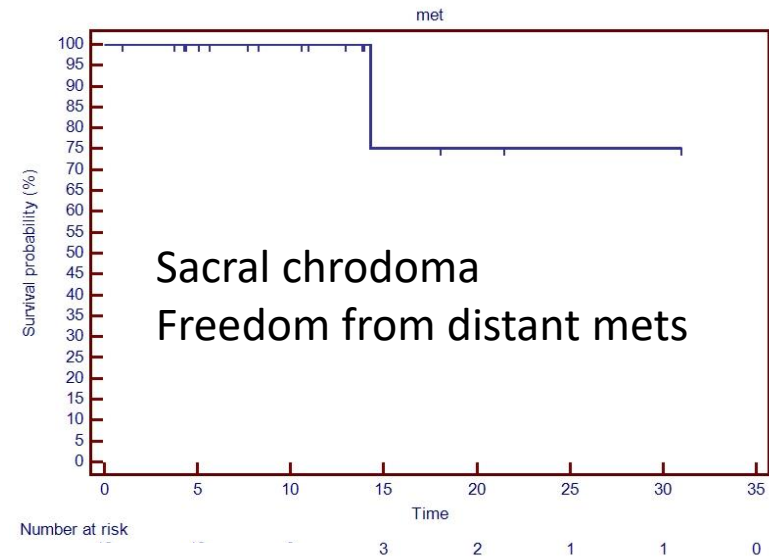
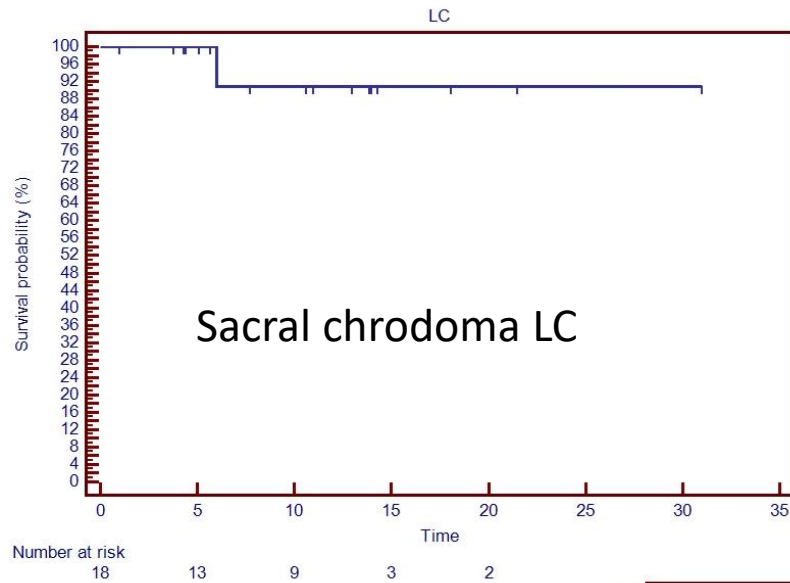
Relapse-Free Survival



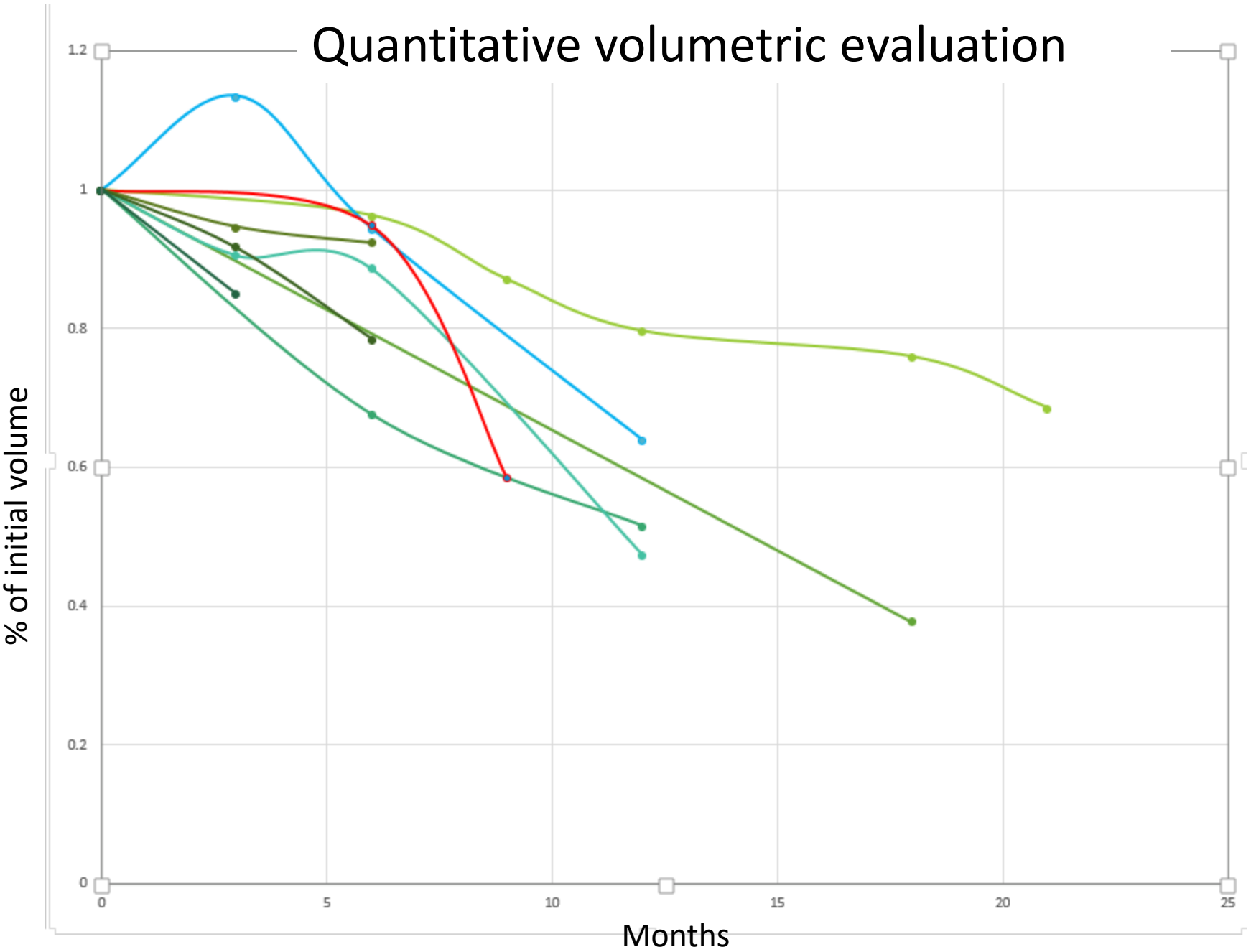
Overall Survival



Sacral chordoma at MedAustron



Quantitative volumetric evaluation



What is different in the new vs. old patients

old

- Dose mostly 70.4 Gy RBE
- Rectum PRV 3 mm 1cc < 60 Gy RBE
- Syngo optimization
- Sometimes spacer
- Very large CTV1

new

- Dose mostly 73.6 Gy RBE
- Rectum 1 cc < 66 Gy RBE
- Raysearch optimization
- Often spacer
- Trend toward smaller CTV1

Male 42 YO

Initial symptom :
incontrollable pain
urinary incontinence
erectile deficit

Diagnosis

Sacral chordoma (1174 ml)

Prescription:

exclusive CIRT

4.6 Gy RBE x 9 to PTV1 (41.4 Gy RBE)

4.6 Gy RBE x 7 to PTV2 (32.2 Gy RBE)

Total dose 73.6 Gy RBE in 16 fr in 4 weeks

Contouring :

Include piriform muscle and
adequate bone and gluteus
margins in PTV1

Dose constraints:

Rectum

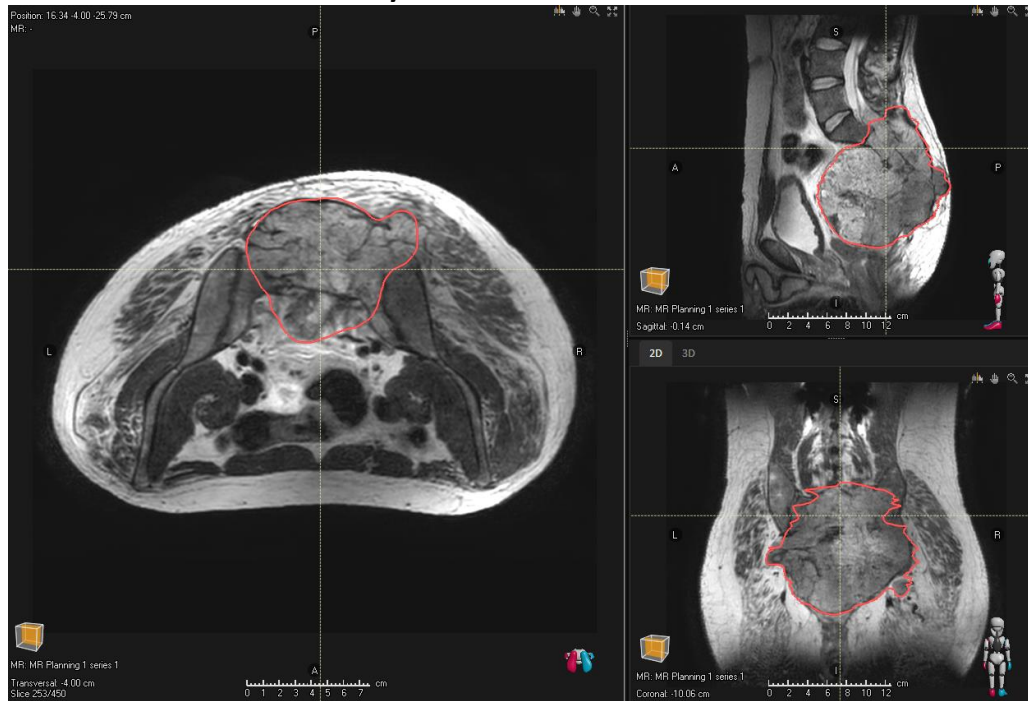
D (RBE, 1 ccm) < 66 Gy RBE,

D (RBE, 5 ccm) < 63 Gy RBE,

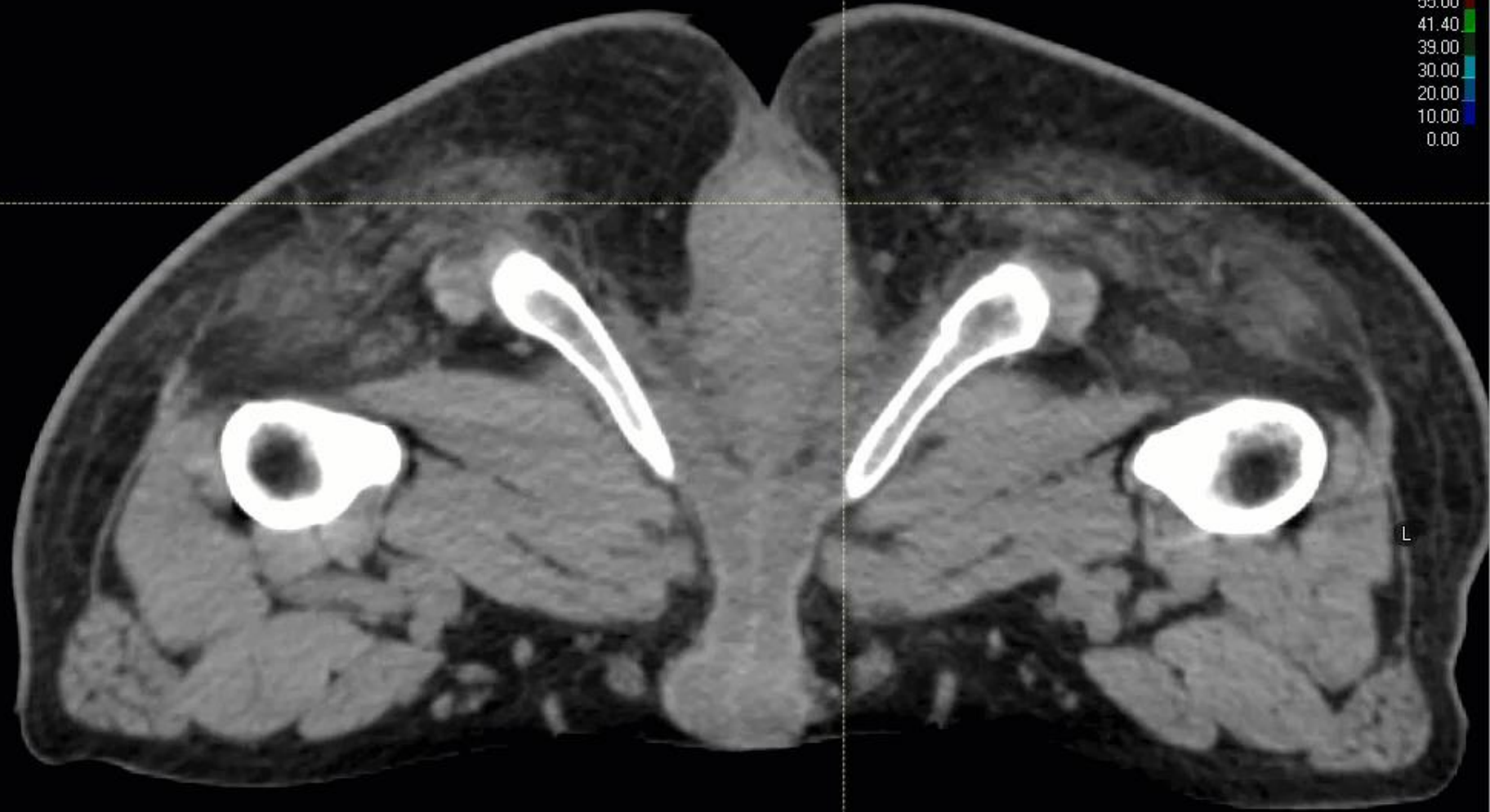
D (RBE, 10 ccm) < 55 Gy RBE

Cauda Equina

D max < 70 Gy RBE



Dose distribution



**Response at 12 Mo.
from 1175 ml to 606 ml (48% reduction)**

