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Carbon-ion Radiotherapy for Retroperitoneal Sarcomas

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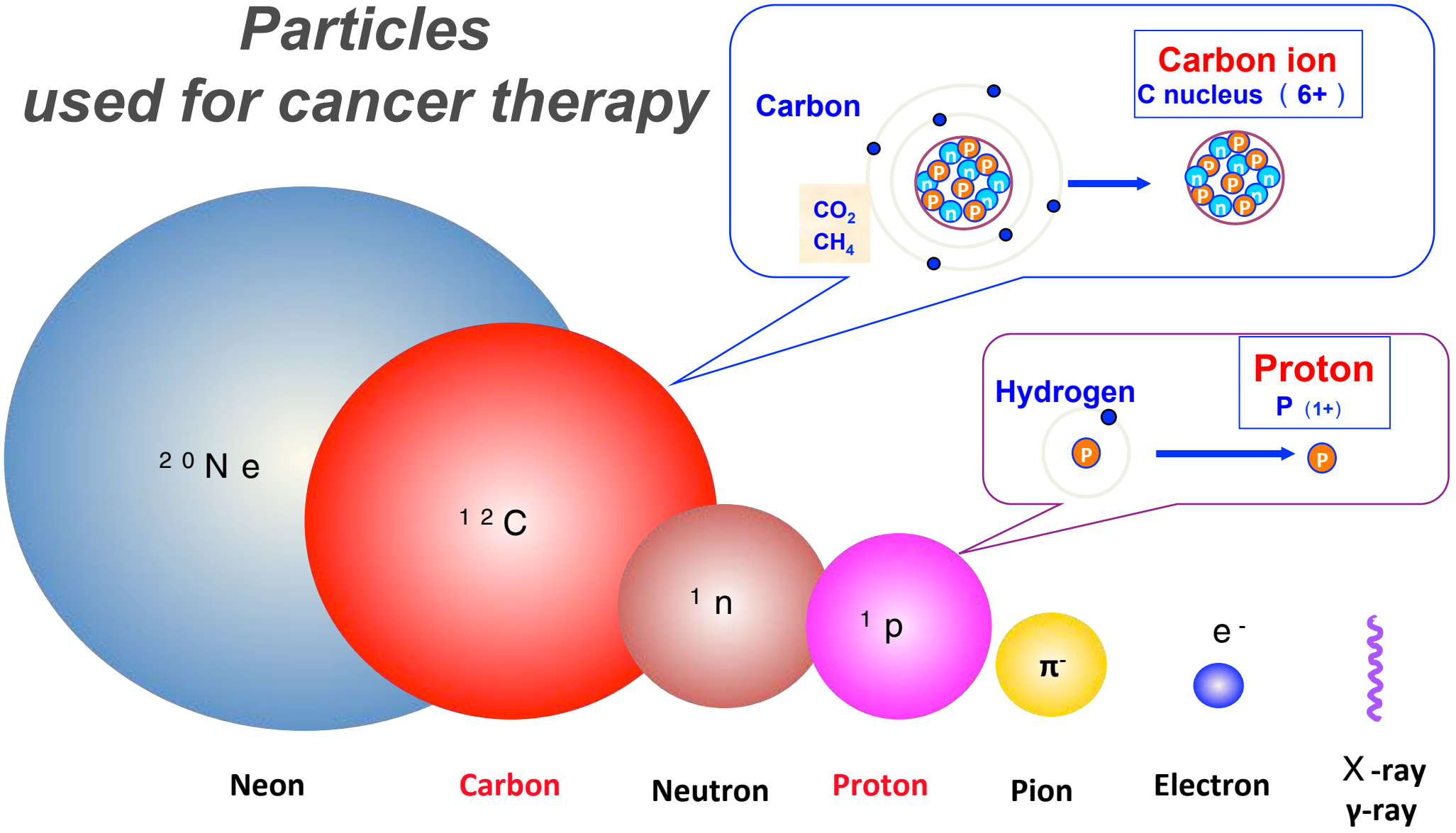
Contents

1. Characteristics of C-ion RT
2. Unresectable bone & soft tissue sarcoma
3. Bone sarcoma
    1) Sacral chordoma
    2) Osteosarcoma
    3) Chondrosarcoma
4. Soft tissue sarcoma
5. Retroperitoneal sarcoma including paracervical tumor
    1) General aspects
    2) Preliminary results
    3) Update results
6. Summary

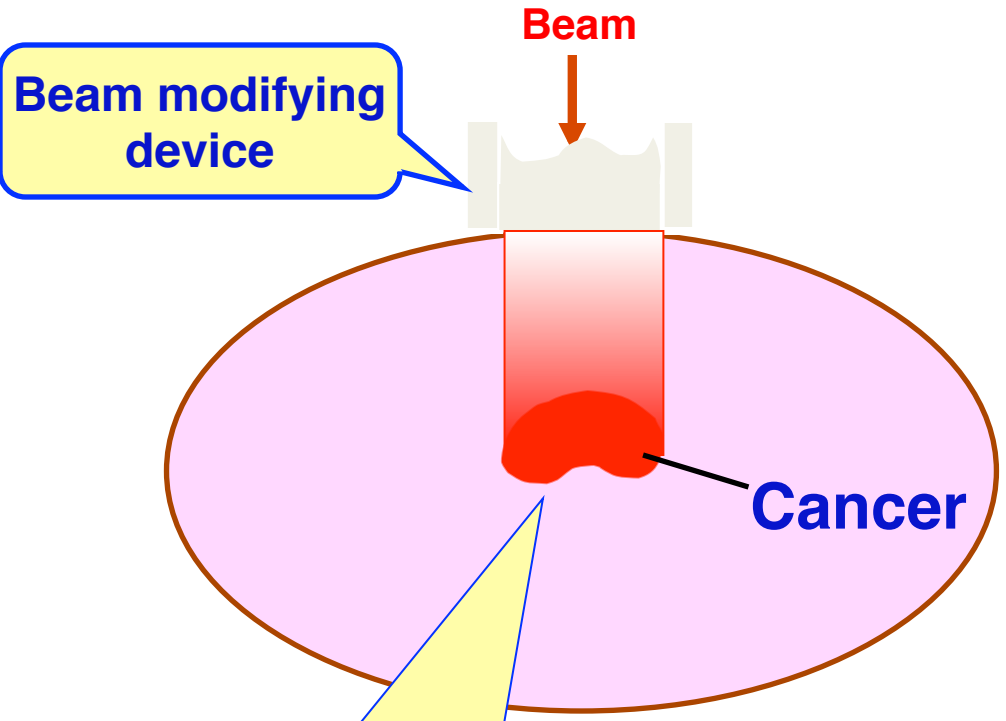
Particles used for cancer therapy



Mass	20	:	12	:	1	:	1	:	1/7	:	1/1800	:	-

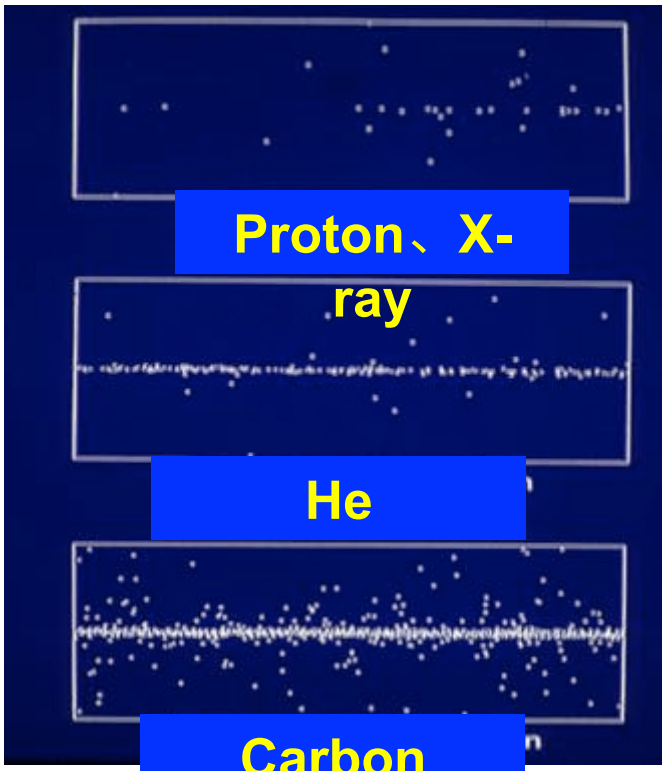
Characteristics of Carbon Ion Beams

1. Superior dose localization



Ion beams can be localized precisely in the target.

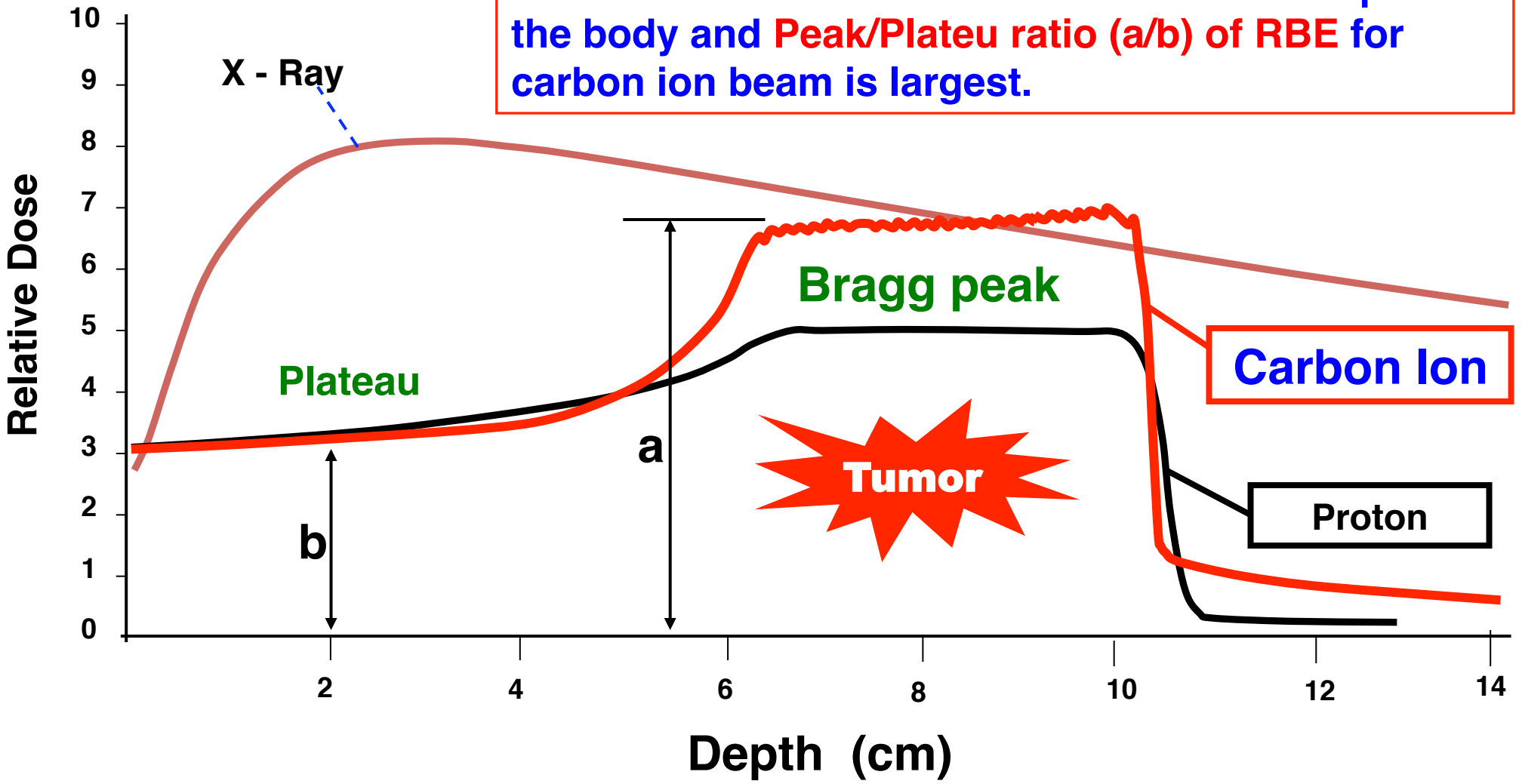
2. High biological effets



Carbon ion beam produces dense ionization and its RBE is 2~3 times larger than X-rays.

Dose Distribution

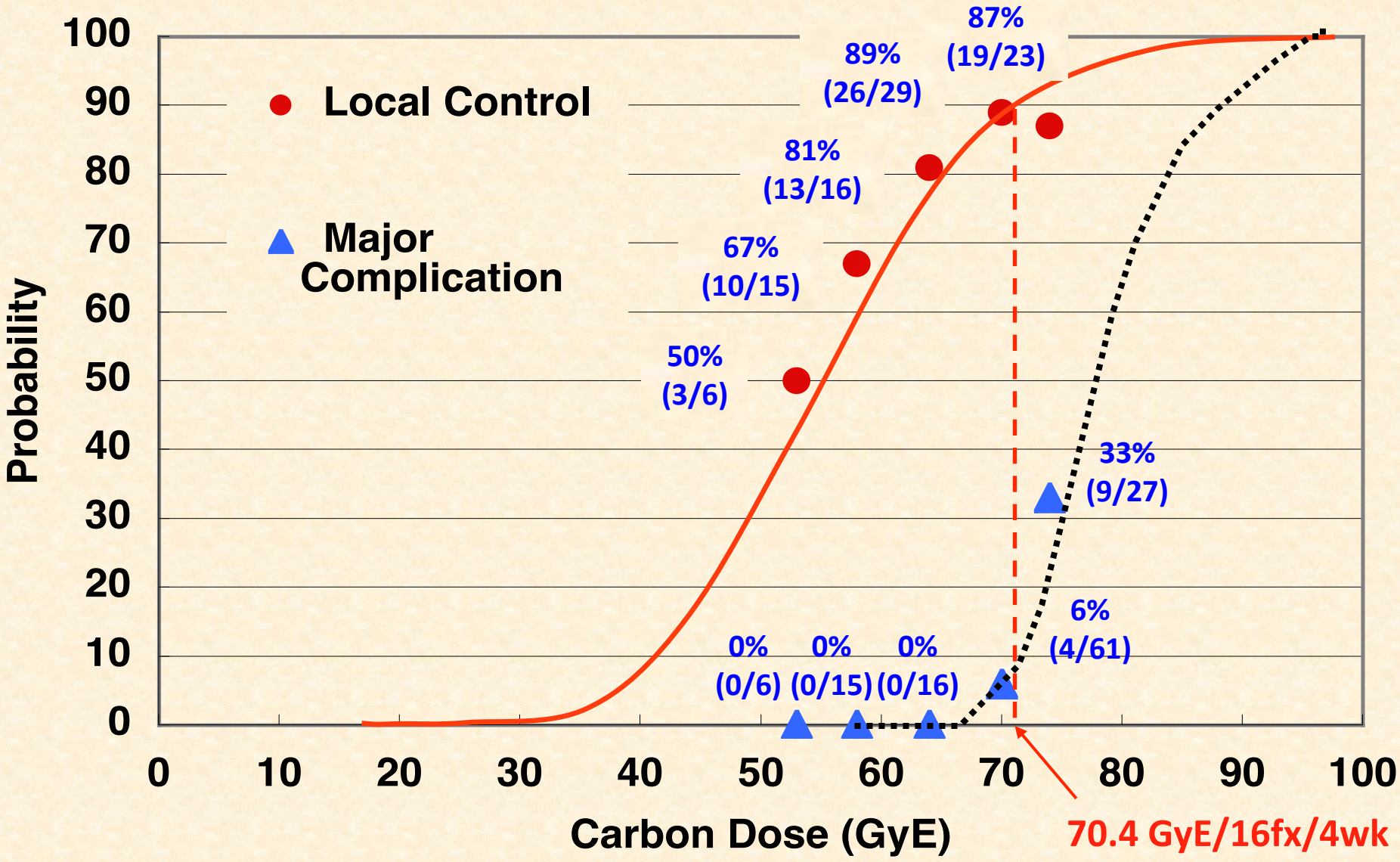
Ionization density increases with depth, therefore the RBE increases as carbon ions travel deeper in the body and Peak/Plateu ratio (a/b) of RBE for carbon ion beam is largest.



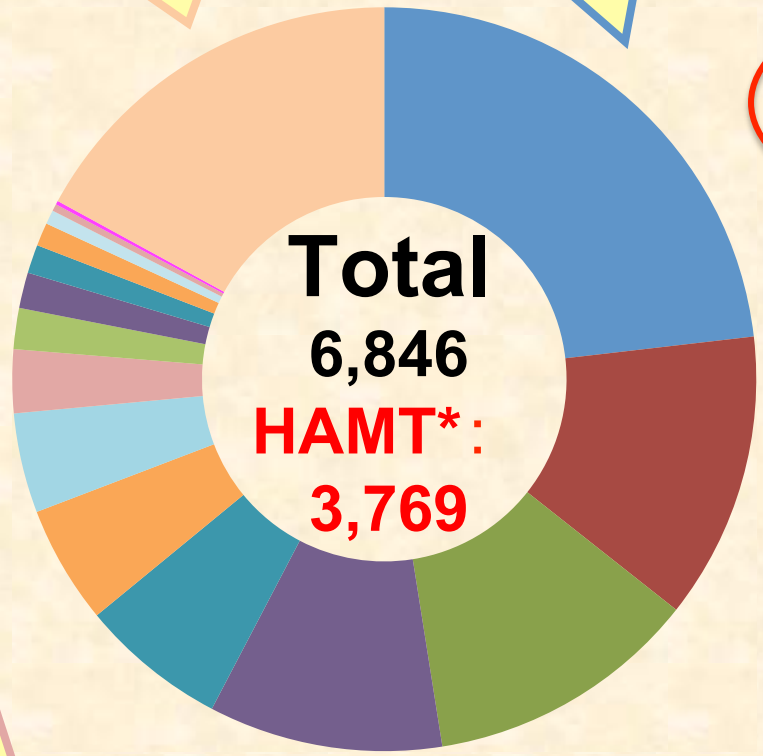
Local Control, Complications and Survival in Neutron Therapy for Bone/Soft Tissue Sarcomas

Author	Site	No.	Cont-rolled	Compli-cation	Survival
Caterall (1979)	Soft	28	75%	32%	-
Ornitz (1980)	B&S	20	65%	-	-
Salinas (1980)	B&S	34	62%	12%	59%(5-62mo)
Battermann(1981)	B&S	22	36%	27%	-
Cohen (1984)	B&S	51	47%	38%	39% (>2yr)
Schmitt (1983)	Soft	60	50%	-	-
(1982)	Bone	24	50%	33%	-
Wambersie (1984)	Soft	22	18%	18%	-
Duncan (1986)	B&S	30	38%	50%	-
Schwarz (1998)	Soft	1171	50%	-	-

Carbon-ion Therapy in Bone & Soft Tissue Sarcomas
Local Control and Morbidity by Dose



Patient Distribution enrolled in Carbon Ion Therapy at NIRS (June 1994～July 2012)



Scanning
11(0.2%)

Miscellaneous
1167(17.0%)
HAMT :531

Prostate
1586(23.2%)
HAMT :1254

HAMT*:Highly Advanced Medical Technology

Lacrimal gland
21(0.3%)

Bone & Soft tissue
854 (12.5%)
HAMT :642

Lymph node
42(0.6%)
HAMT :35

Head & Neck
812(11.9%)
HAMT :489

Esophagus
69(1.0%)

Skullbase
85(1.2%)
HAMT :56

Lung
696(10.2%)
HAMT :117

CNS
106(1.5%)

Liver
437(6.4%)
HAMT :212

Eye
122(1.8%)
HAMT :80

Gynecological
189(2.8%)
HAMT : 6

Pancreas
297(4.3%)
HAMT :60

Rectum
352(5.1%)
HAMT :287

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3. **Bone sarcoma**
    1) **Sacral chordoma**
    2) **Osteosarcoma**
    3) **Chondrosarcoma**
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Clinical Study on Unresectable Bone and Soft Tissue Sarcomas

Phase I/II Dose Evaluation Study
June 1996 – Feb 2000 n=59

J Clin oncol(20) 4466-4471.2002

- Efficacy depended on total irradiated dose. (52.8GyE/-73.6GyE/16Fr)
- G3 acute skin reactions were observed with the total dose of 73.6GyE/16Fr (= dose constraint)

Phase II Fixed Dose Study
April 2000 – Feb 2011 n=520

- 70.4GyE/16Fr was basic effective dose.
- Better beam delivery to avoid severe skin reactions.

J Clin oncol(26)562s.2008

Advanced cases including palliations
April 2005-Feb 2011 n=284

Evaluation

495 pts (514 lesions)

Followed for 6 months or more

NIRS

Eligibility in B & STS Phase I/II & II study

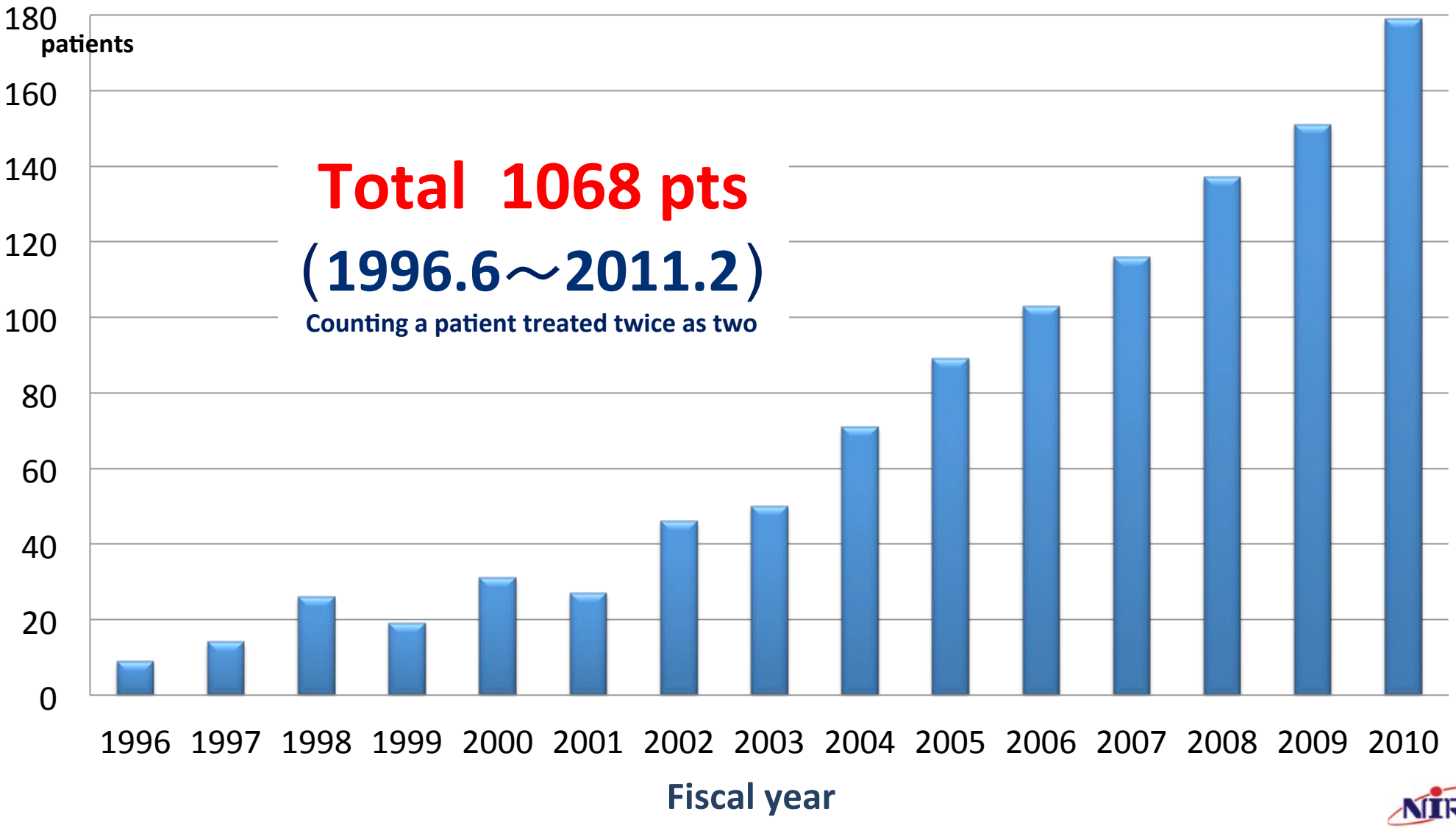
- Histologically confirmed* bone or soft tissue sarcomas
- Unresectable or declines surgery
- Gross measurable lesion
- Lesion size is <15cm in maximum diameter
- KPS 60~100%
- No prior radiotherapy to the lesion
- Signs the informed consent statement
- no systemic metastases

For phase II : Radiation associated sarcoma is eligible

: Tumor thrombus excluded

*Central pathological review was carried out

Yearly Number of Pts with B&S Sarcoma treated with Carbon Ion Radiotherapy (C-ion RT)



Bone & Soft Tissue Sarcomas

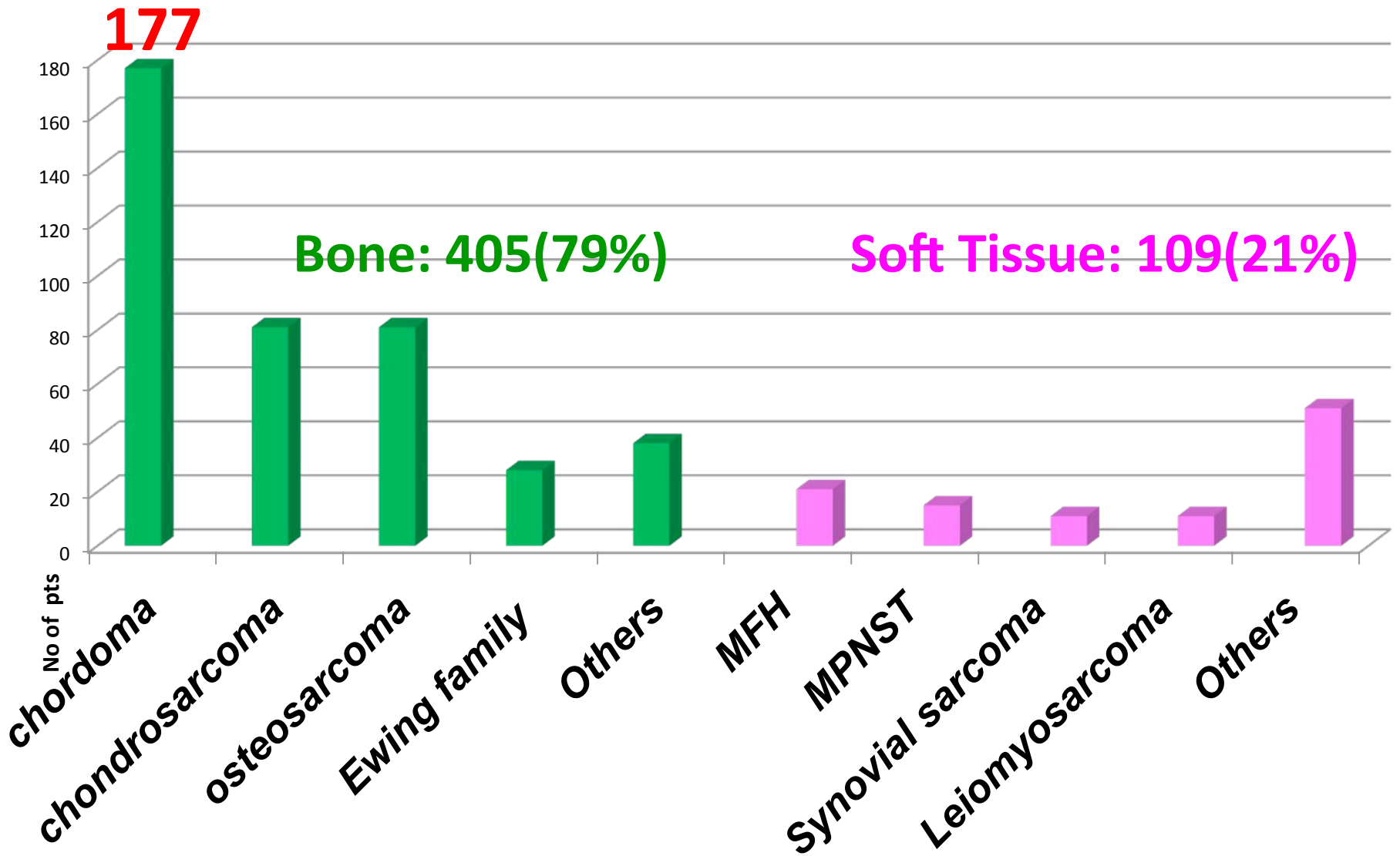
April 2000 - Feb 2011 : n=495 pts/ 514 lesions

Age :	**Median**	**58(11-87)**
Sex :	**Male**	**288 (58%)**
	Female	**207 (42%)**
Tumor Site :	**Pelvis**	**388 (75%)**
	Spine/Paraspine	**96 (19%)**
	Extremities/ Others	**30 (6%)**
Histology :	**Bone**	**405 (79%)**
	Soft Tissue	**109 (21%)**

The current protocol is mainly for unresectable sarcomas using 70.4GyE/ 16Fr /4 weeks

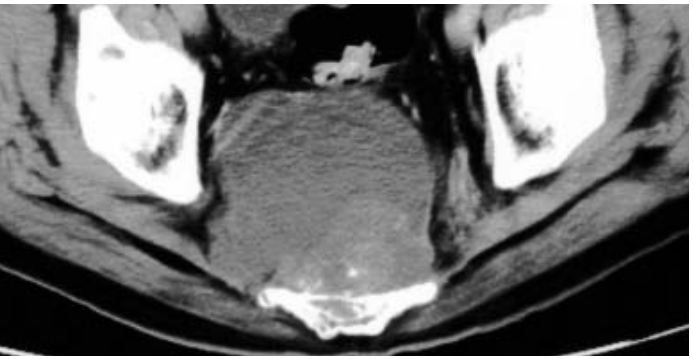
Bone & Soft Tissue Sarcomas

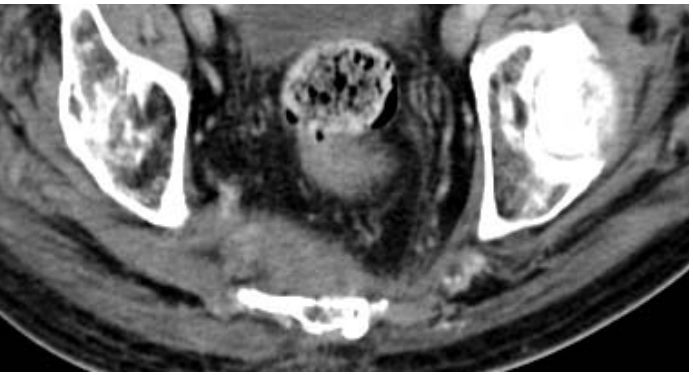
April 2000 - Feb 2011 : n=495 pts/ 514 lesions



Sacral Chordoma

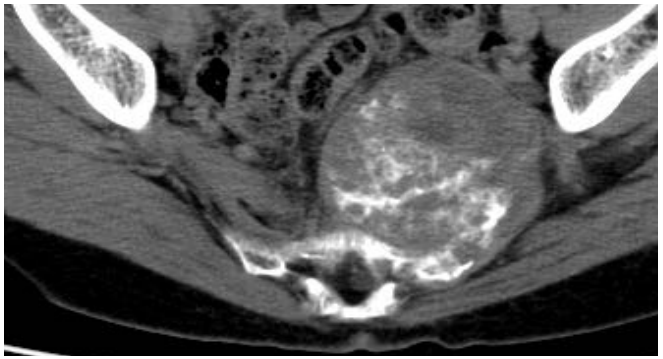
Case 1. 81 y.o.M.

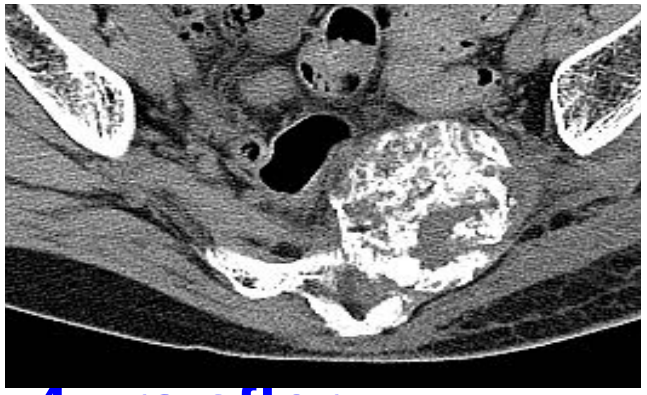




3.5 yrs after

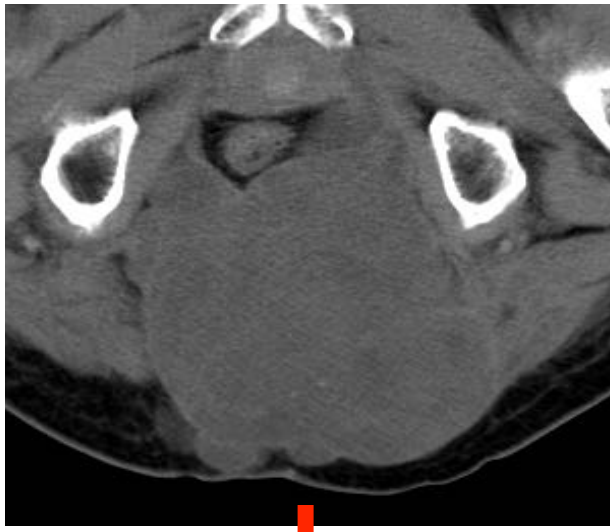
Case 2. 57 y.o.F.

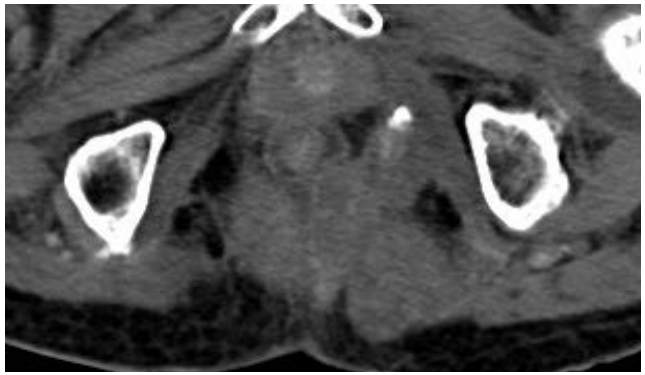




4 yrs after

Case 3. 83 y.o. M.





4.5 yrs after

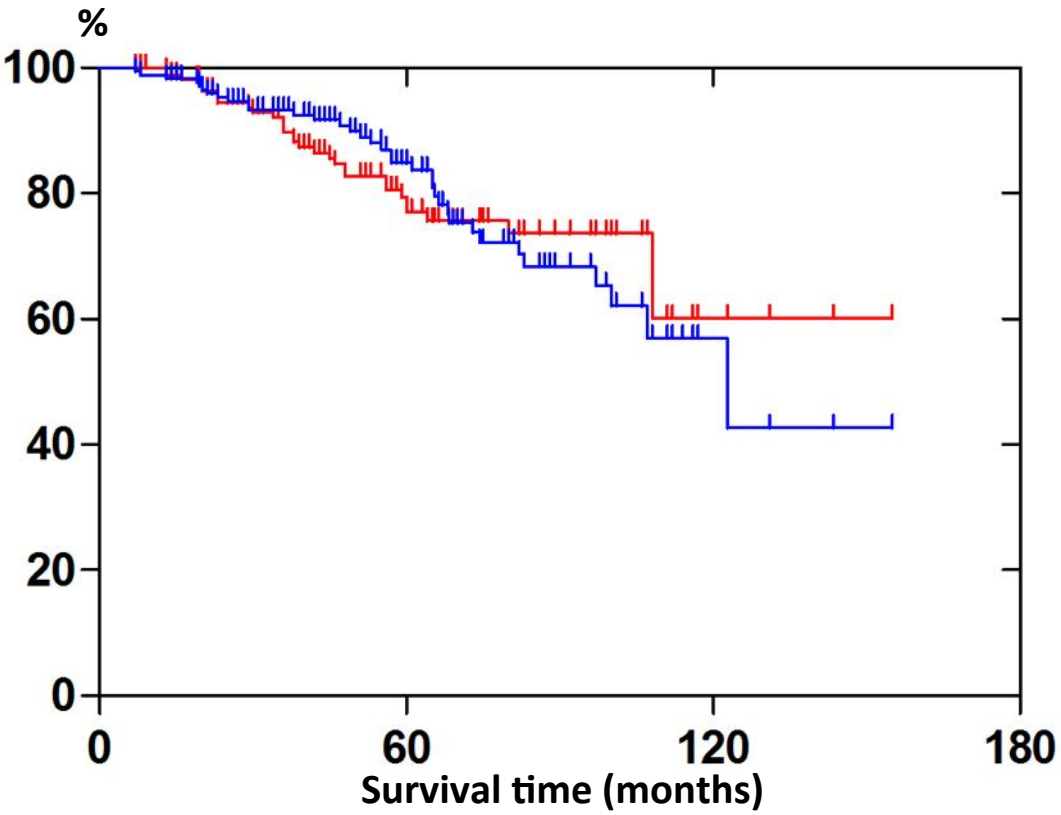
Results of Treatment in Sacral Chordoma

	Total No.	No. per year	Method	Local Control	Survival	
					5-Yr	10-Yr
USA: MGH [1)]	21	1.1	Surgery	77 %	-	50 %
Sweden: SUH [2)]	39	1.1	Surgery	44 %	84 %	64 %
USA: MGH [3)]	27	1.4	Surgery	72 %	82 %	62 %
USA: LBNL [4)]	14	1.2	Surgery + He-ion	55 %	85 %	22 %
USA: Mayo Clinic [5)]	52	2.5	Surgery	56 %	74 %	52 %
NIRS	183	12 (Max>25)	Carbon alone	77 %	85 %	74 %

1) J Bone Joint Surg. 1998 2) Cancer.2000 3)IJROBP.2006 4) IJROBP.1993 5) J Bone Joint Surg. 2005

Spinal Chordoma

1996.6-2011.2 n=183 pts (phase I/II and II study)

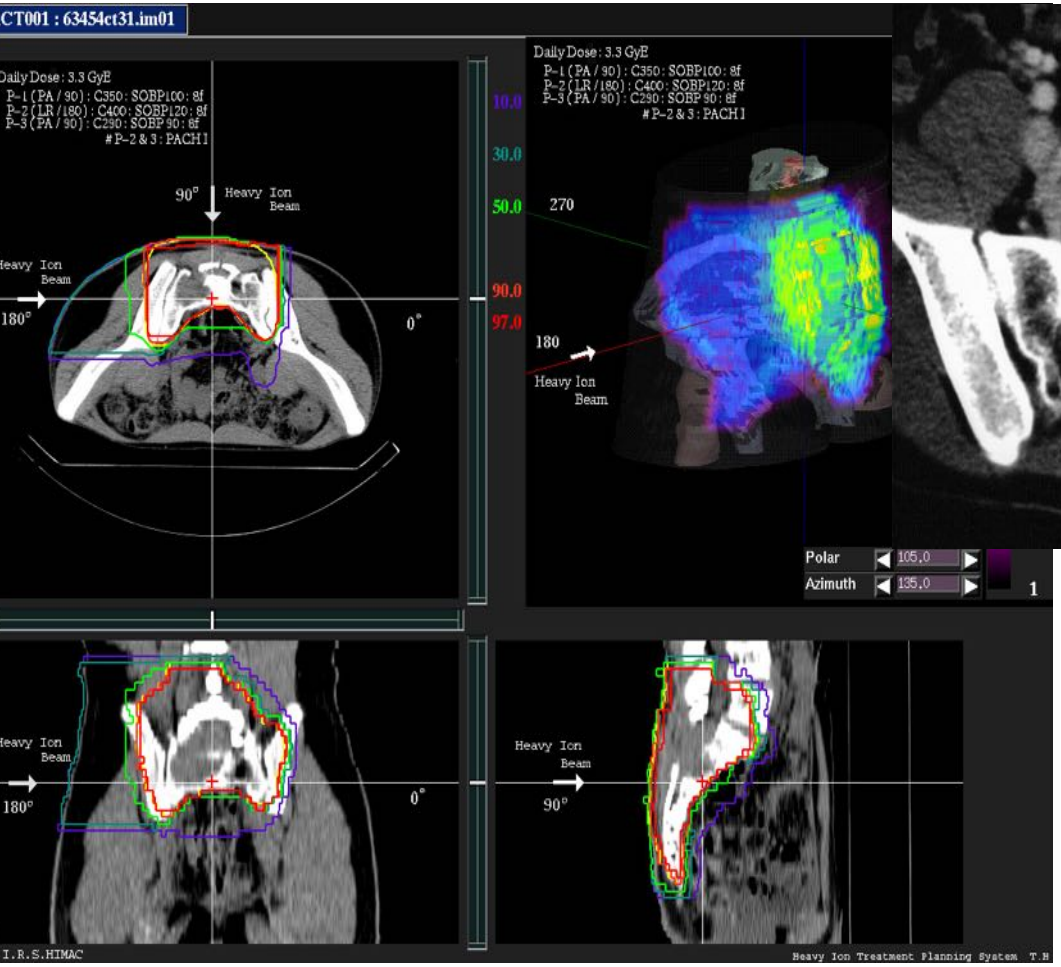


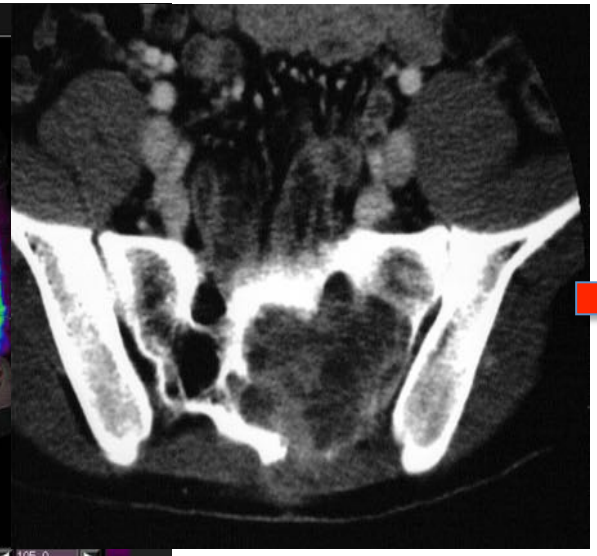
Follow-up period : 68 mths (7-155)
Median Age : 66 yo (26-87)
Median CTV : 330 cm
(Sacral chordoma : Median 636 cm^3)
Ambulatory was remained in 97%
Sciatic nerve dysfunction: 15pts

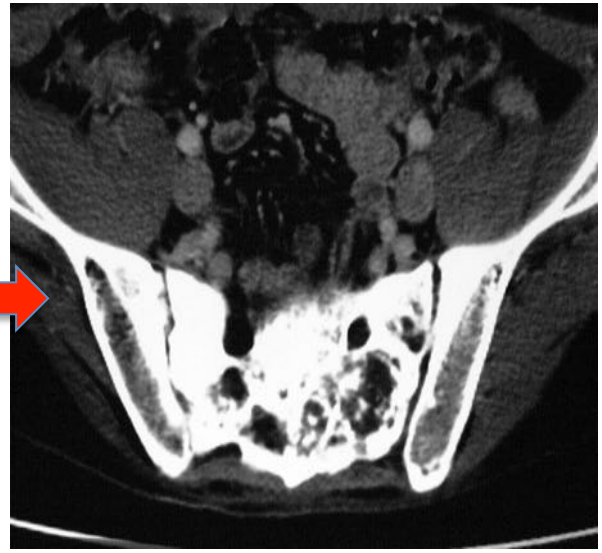
	5-year(%)
Local Control	77
Overall Survival	85

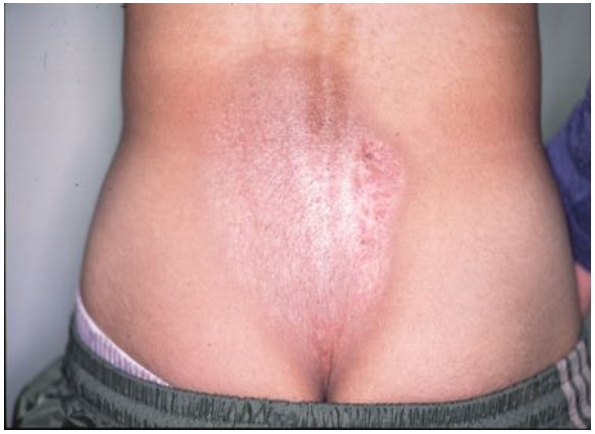
Osteosarcoma of the Trunk

Re-calcification after treatment





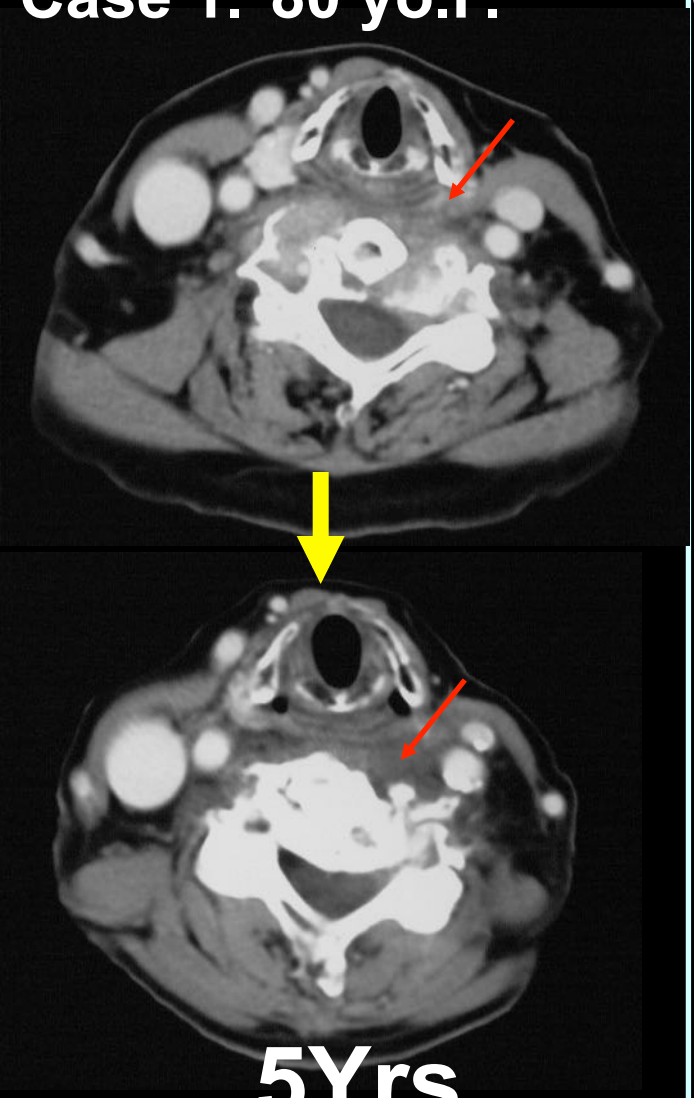




Osteosarcoma

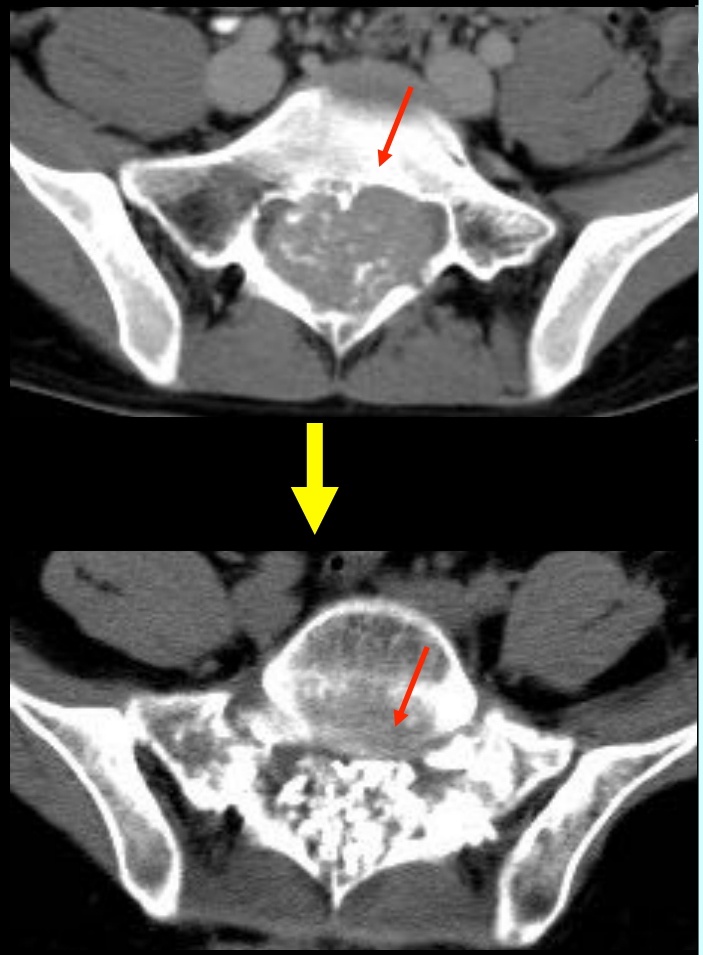
70.4 GyE/ 16 fx/4 wks (4.4GyE x16)

Case 1. 80 yo.F.



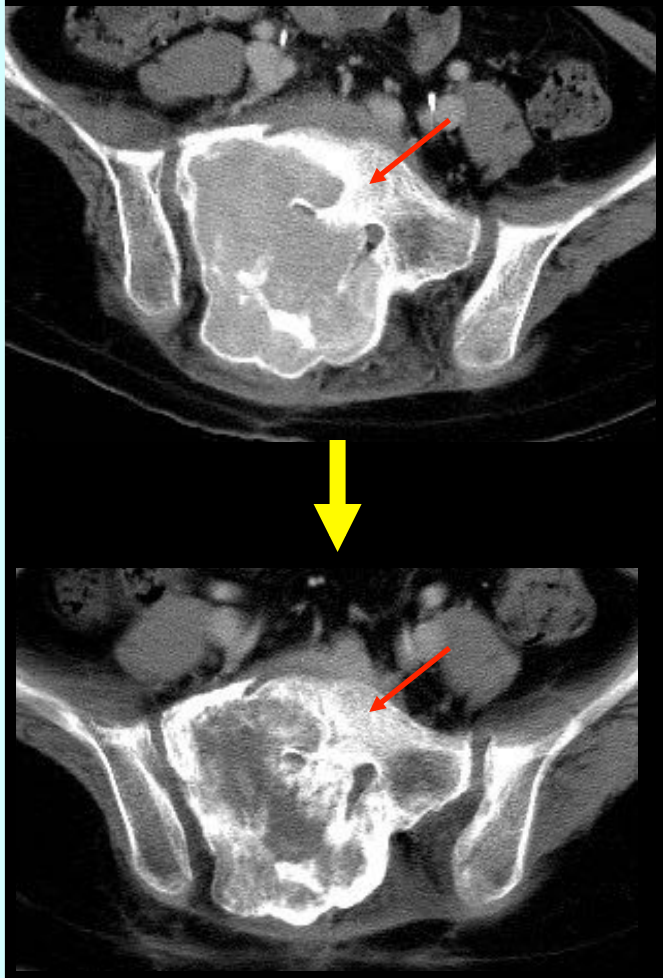
5Yrs

Case 2. 17 yo.M.



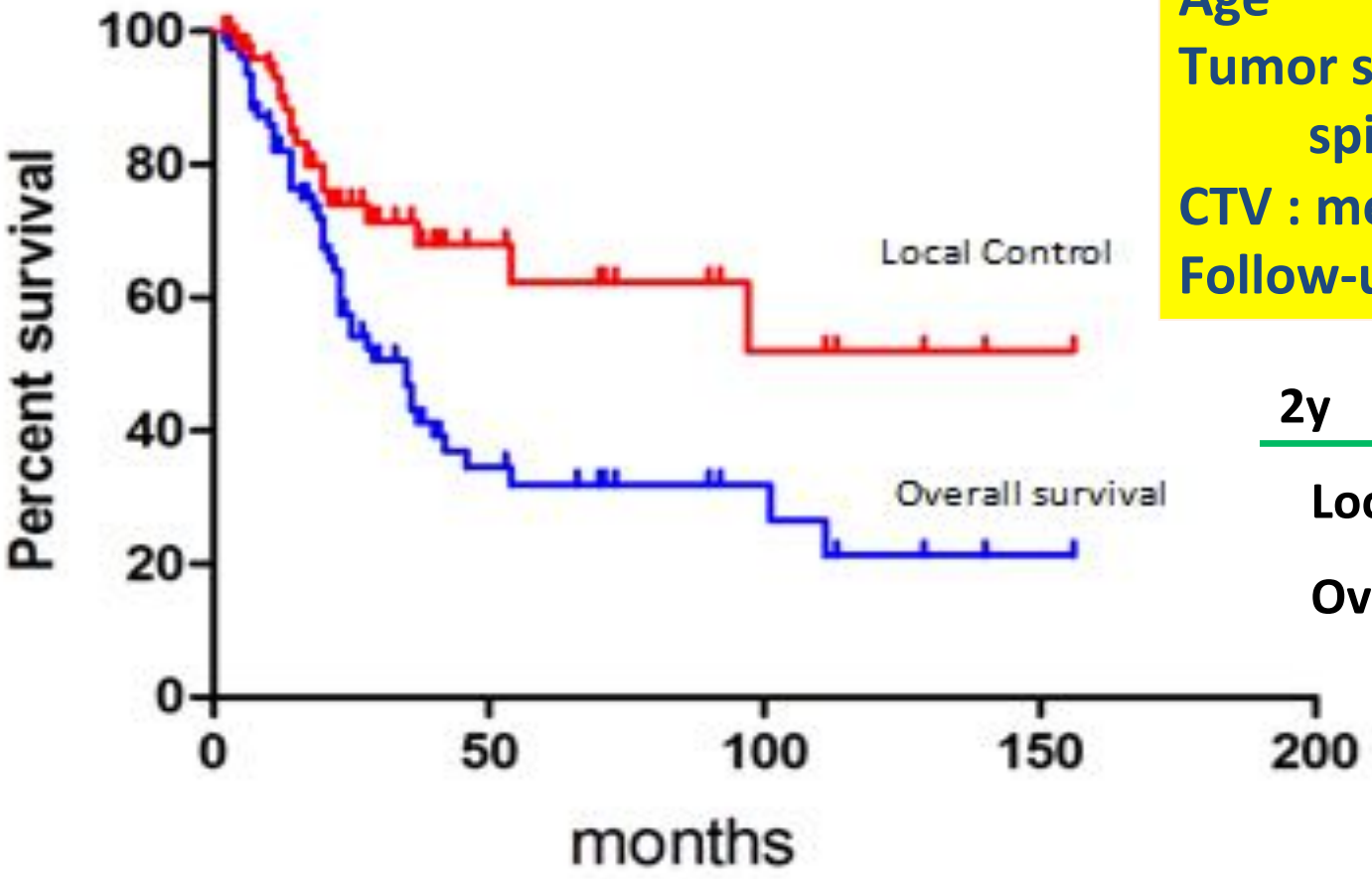
4Yrs

Case 3. 14 yo. M.



2Yrs

Osteosarcoma of the Trunk
1996.6-2009.6 n=78 pts



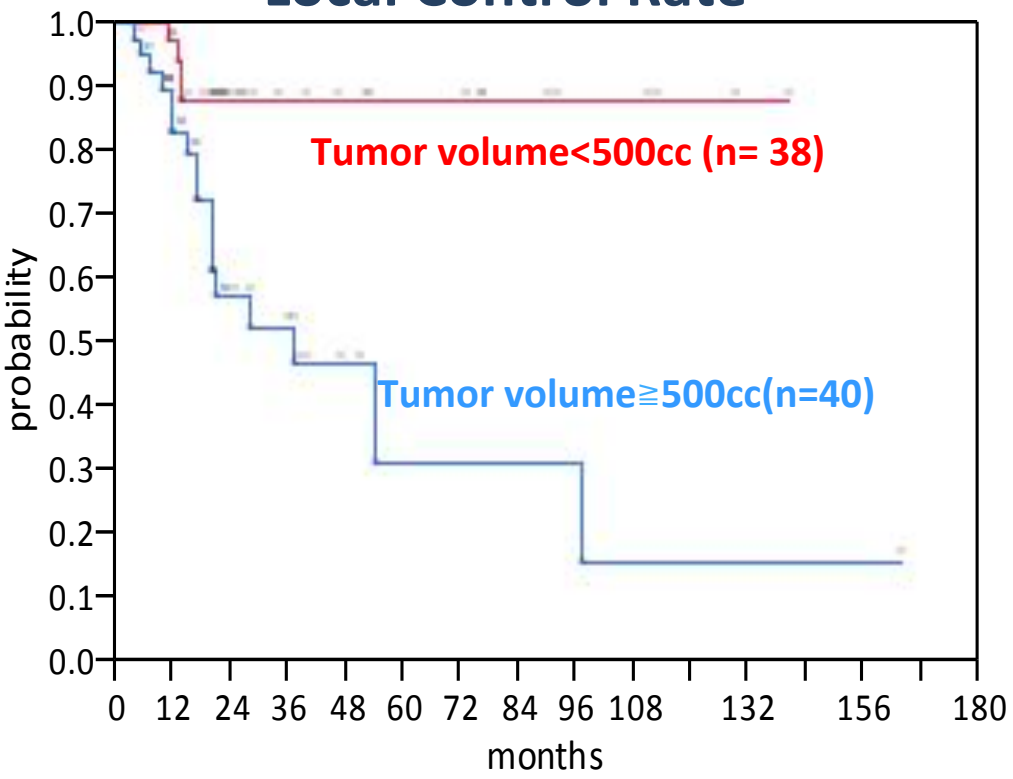
Age :Median 42 yo (11-83)
Tumor site: pelvis 61,
spine/paraspine 15, others 2
CTV : median 510cc (60-2290)
Follow-up period: mean 70 months

	2y	5y
Local Control	73%	61%
Overall Survival	57%	
	32%	

Osteosarcoma of the Trunk: Result By Tumor Volume

A smaller tumor volume provided a better result.

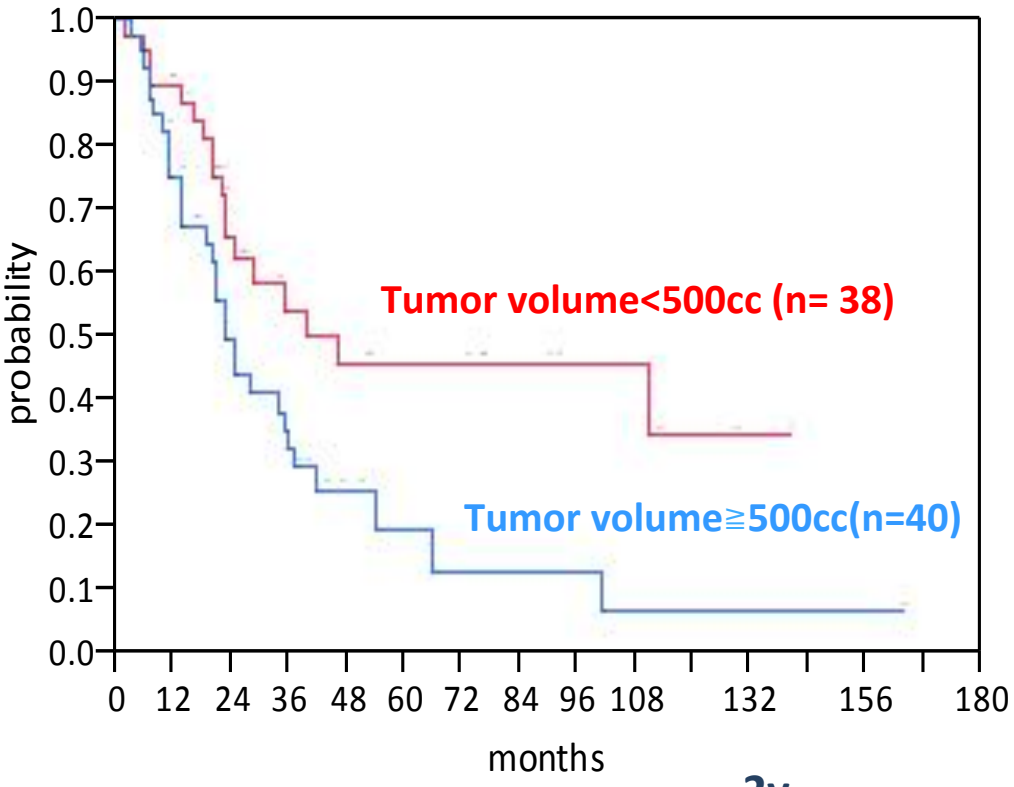
Local Control Rate



	2y	5y
< 500cc	87%	87%
≧ 500cc	57%	31%

Logrank p=0.0006

Overall Survival Rate



	2y	5y
< 500cc	65%	46%
≧ 500cc	50%	19%

Logrank p=0.015

Osteosarcoma of the trunk

Institutes	Treatment	No of Pts	Site	5-yr Overall Survival (%)		
				All case	Resectable	Unresectable
MGH [1,2]	Surgery	26	S	31%	-	-
	Surgery +Proton/photon	55	V	67%	-	-
Mayo Clinic[3]	Surgery	43	P	38%	38%	-
Inst Orthop Rizzoli [4]	Surgery	60	P	15%	30%	0%
COSS [5,6]	Surgery	67	P	27%	34%	0%
	Surgery	22	S	30%	40%	0%
NCBT [7]	Surgery	40	P	21%	26%	-
MSKCC [8]	Surgery	40	P	34%	41%	10% (1/10)
NIRS [9,10]	Carbon ions	92	P+S	35%	-	35%
		45	(<500cc)	46%		46%

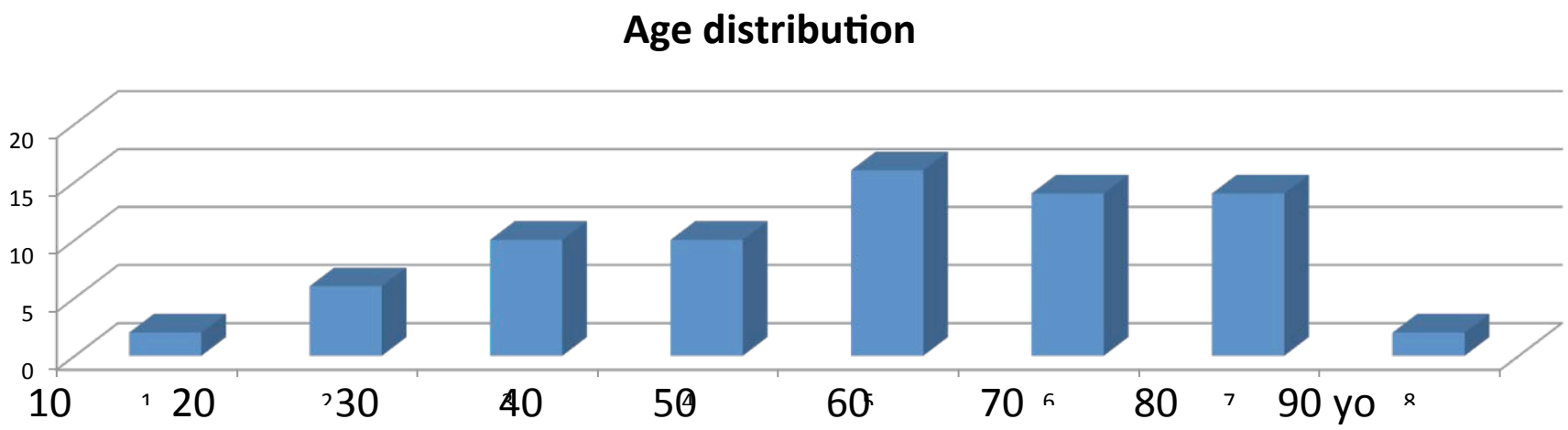
S, Spine; P, pelvis; V, various

1. Schoenfeld AJ, et al. *Spine J* 2010; 10: 708–14. **2.** Ciernik IF, et al. *Cancer* 2011; 117(19): 4522-30.
3. Fuchs B, et al. *Clin OrthopRelat Res* 2009; 467: 510–8. **4.** Donati D, et al. *Eur J Surg Oncol* 2004; 30: 332–40.
5. Ozaki T, et al. *J Clin Oncol* 2003; 21: 334–41. **6.** Ozaki T, et al. *Cancer* 2002; 94: 1069–77.
7. Ham SJ, et al. *Eur J Surg Oncol* 2000; 26: 53–60. **8.** Kawai A, et al. *Clin Orthop* 1998; 348: 196–207.
9. Imai R, et al. Proceedings of NIRS-ETOILE 2nd Joint Symposium on Carbon Ion Radiotherapy 2011; NIRS-M-243: 38-45.
10. Matsunobu A, et al. *Cancer* 2012, in press.

Chondrosarcoma

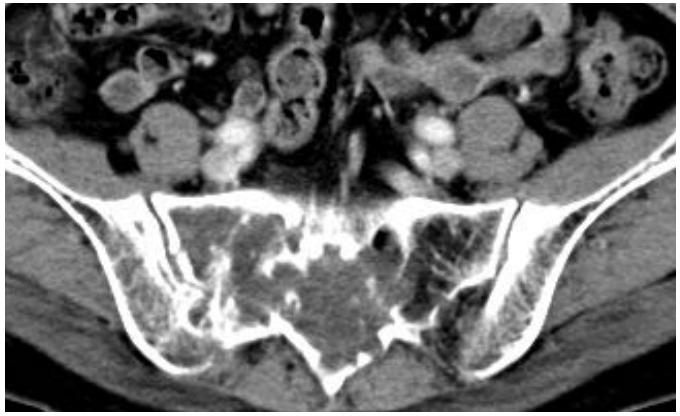
1996.6 –2009.8 n=71 pts

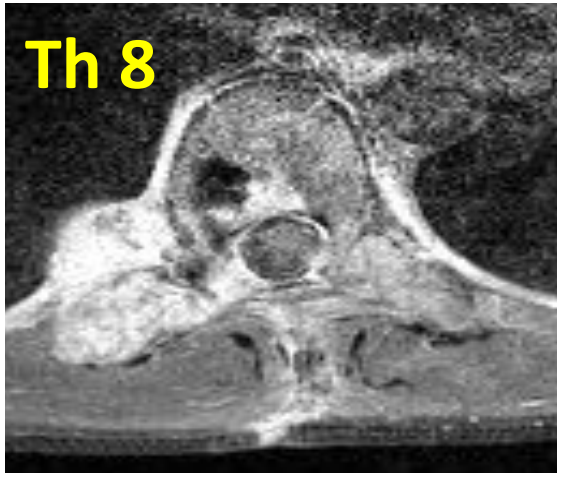
- Sex : M:F = 40 :31
- Age : median:56 yo (17 – 82)
- Tumor Volume : median:488 ml (25～2900 cc)
- Total Dose(GyE) : 70.4GyE was applied to 84% pts
- Histology : G2 or worse = 87% pts

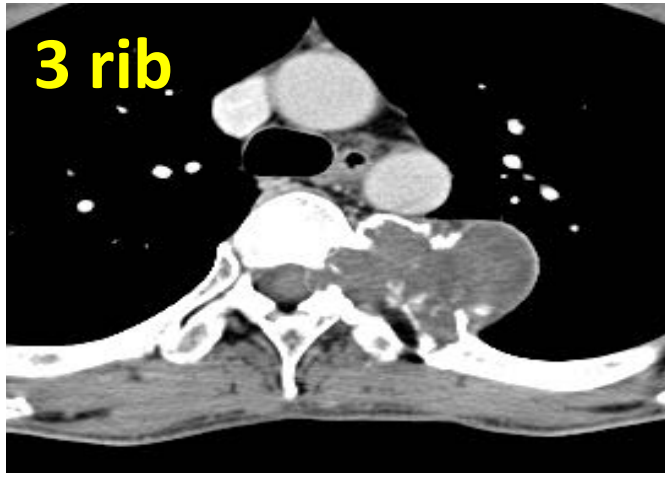


Chondrosarcoma

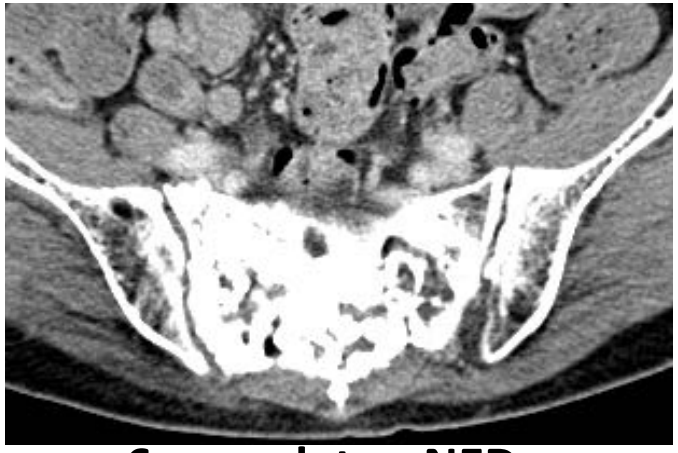
Prior CIRT



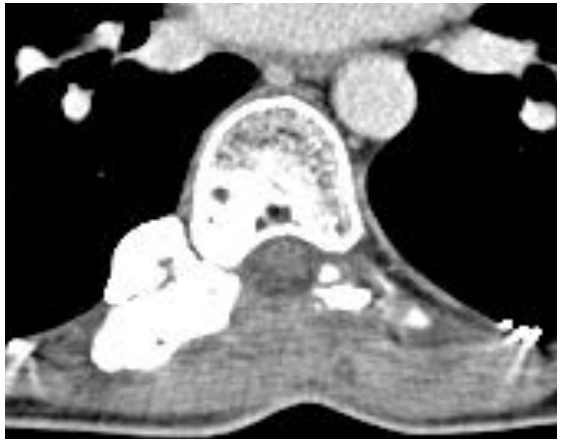




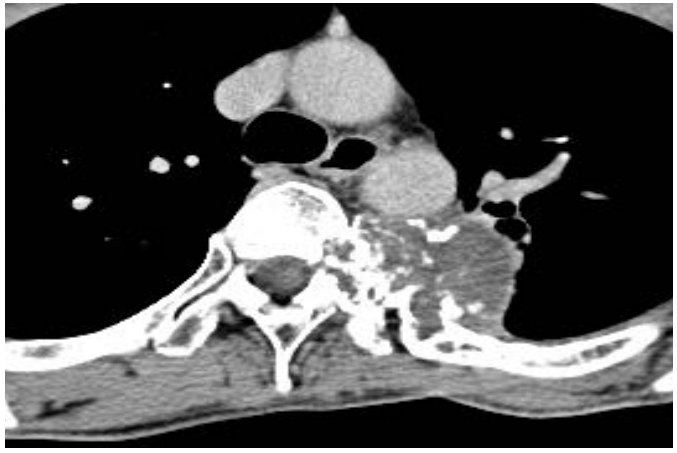
After CIRT



6 years later NED
Ambulatory with cane .
Incontinence using pads
workable



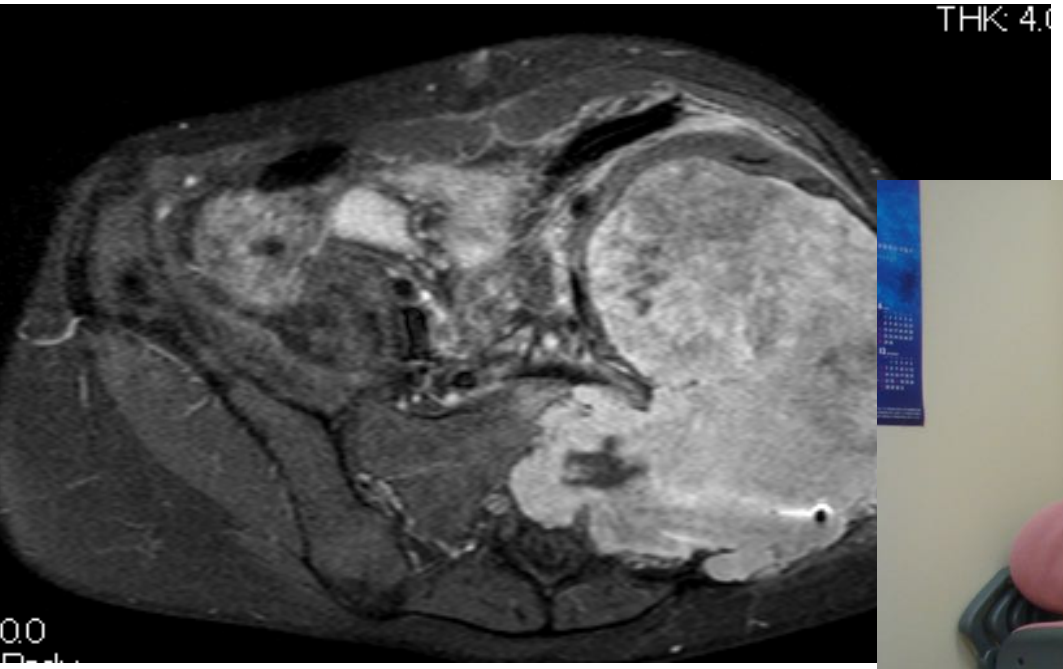
5 years later NED
No symptom
workable

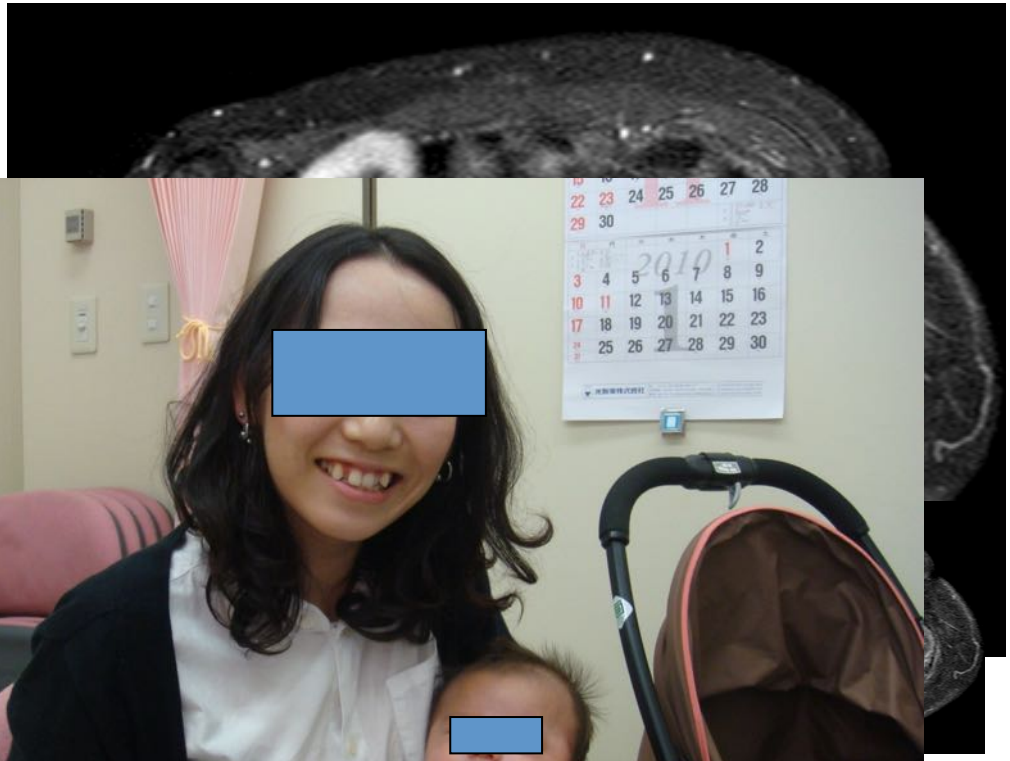


5 years later NED
No symptom
workable

Chondrosarcoma 29yr F

(Spacer in place, 64GyE/16Fx)





2007.9

Before

Contents

1. Characteristics of C-ion RT
2. Unresectable bone & soft tissue sarcoma
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    2) **Preliminary results**
    3) **Update results**
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Soft Tissue Sarcomas treated with C-ions at NIRS

1996.6 ～ 2012.2

Total No.: 139

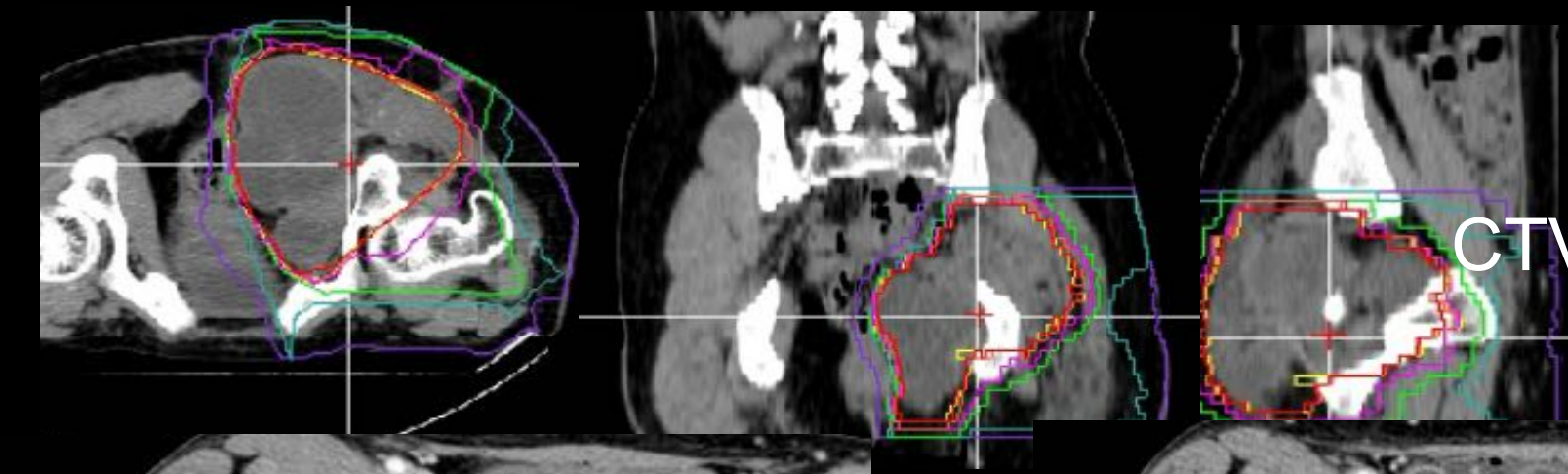
Age：	**14-87 y/o**	**（Median 55）**
Gender：	**M:F=80：59**	
Previous Tx：	**Fresh case**	**86 (62%)**
	Post-ope rec or meta	**53 (38%)**
Tumor size：	**13-1871cm^3 (Median 335cm^3)**	

Soft Tissue Sarcomas treated with C-ions at NIRS (n=139)

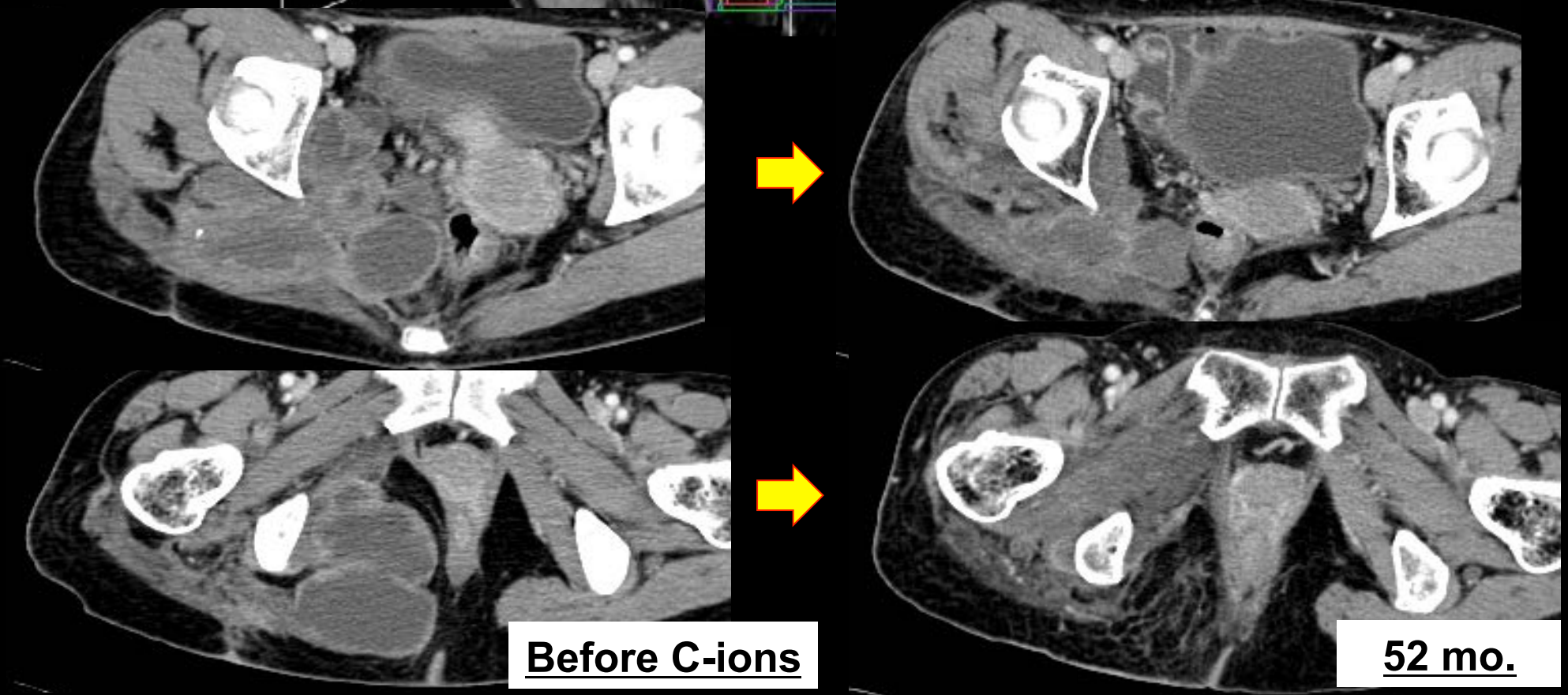
Histo-pathology	No.
MFH	30
MPNST	14
Liposarcoma	14
Synovial sarc	10
Others	71
Total	139

Sites	No.
Retroperitoneal& Paracervical	56
Pelvis	54
Extremity	16
Others	13
Total	139

49y/o F Rt Gluteal tumor (M P N ST)



CTV : 708 cm^3



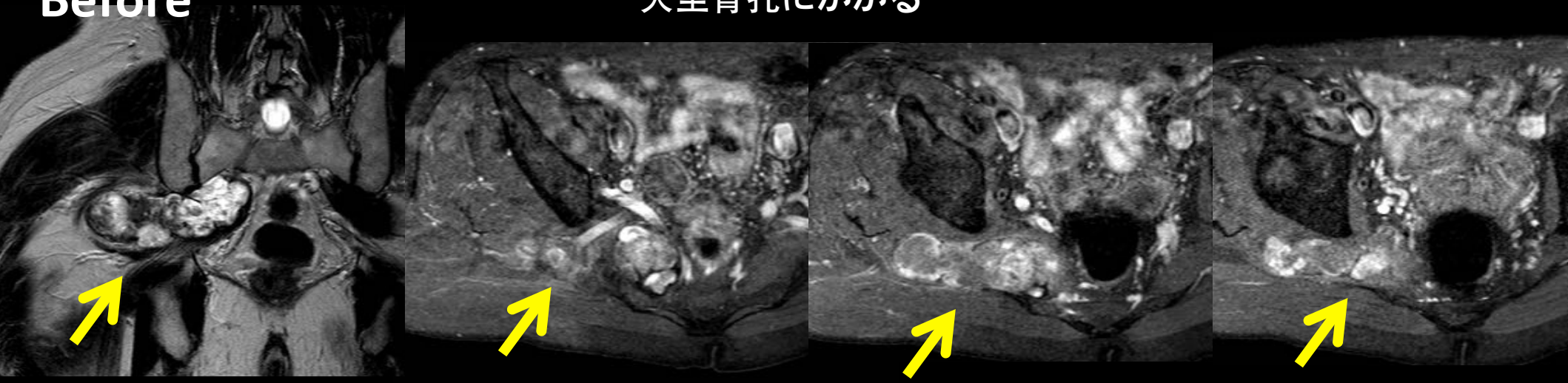
Before C-ions

52 mo.

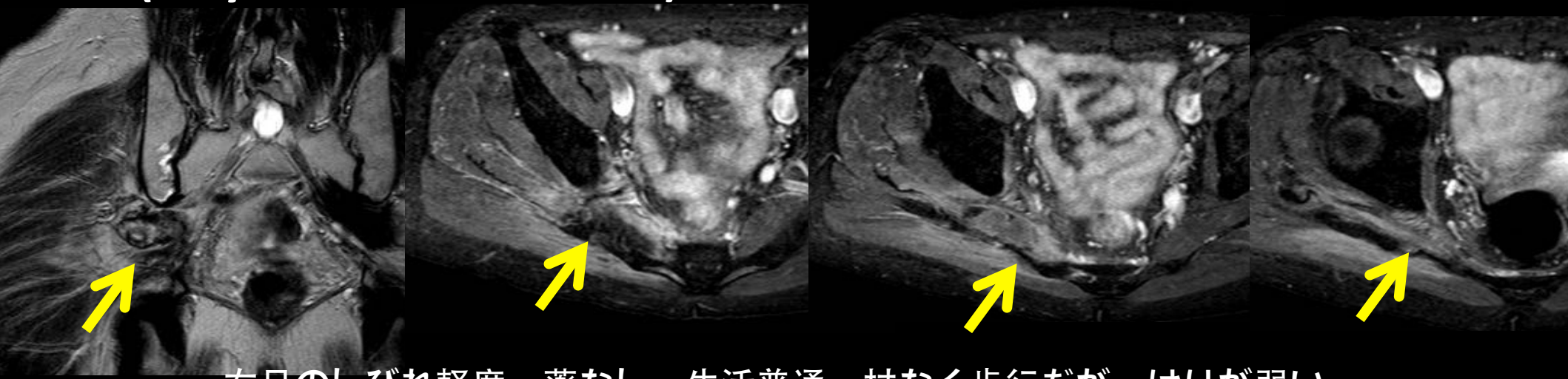
57y/o M　　myxoid chondrosarcoma of rt. buttock

Before

大坐骨孔にかかる



CR (4 years after c-ion RT)

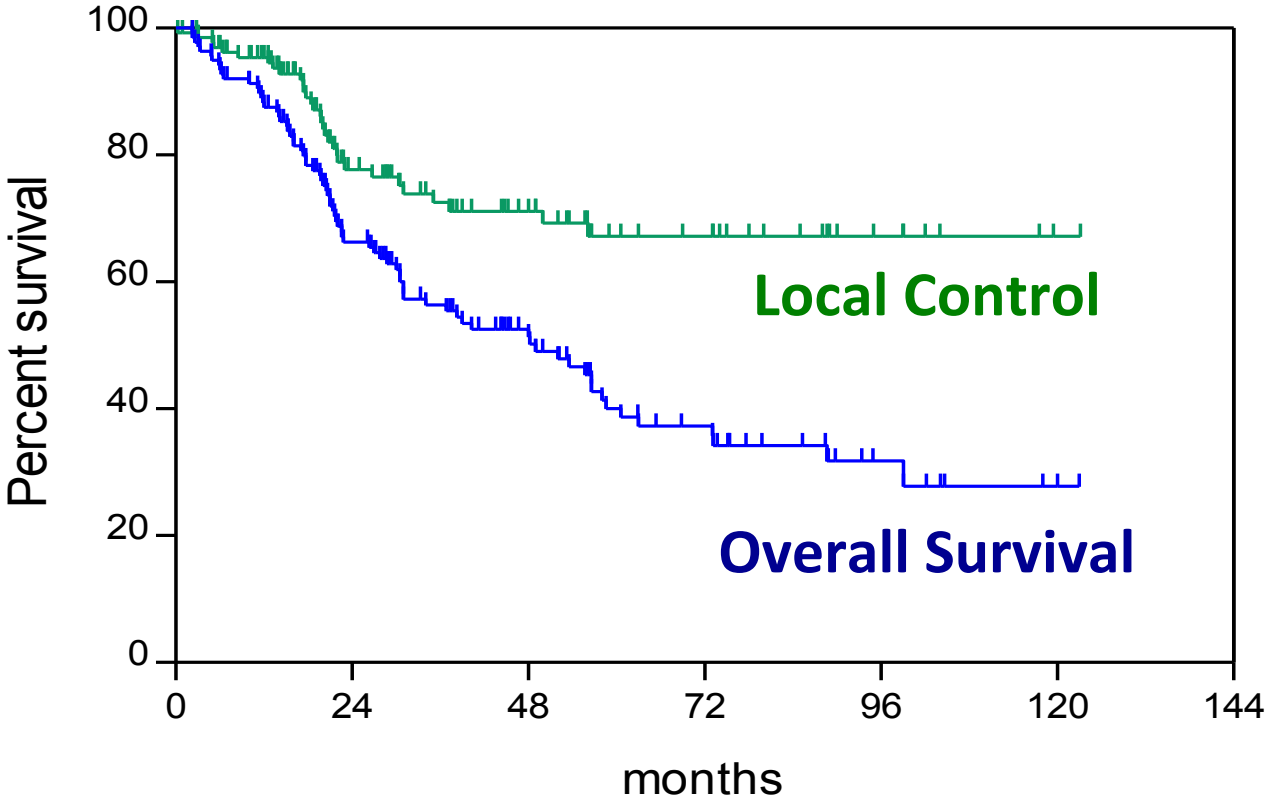


右足のしびれ軽度。薬なし、生活普通、杖なく歩行だが、けりが弱い。

Results of C-ion RT in Soft Tissue Sarcomas

1996.6 ～ 2012.2 n=139

	2-yr	5-yr	10-yr
Local Control	77%	67%	67%
Overall Survival	66%	40%	28%



Toxicities in Soft Tissue Sarcomas in a total of 139 patients

- **≧G3 Dermatitis : 1.5% (2/139pts)**
- **≧G2 Peripheral Neuropathy : 11% (10/91pts)**
- **≧G2 Myelopathy : 5% (3/56pts)**

Soft Tissue Sarcomas of the Extremities

ARTICLE IN PRESS

Radiother & Oncol, 2012

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Original article

Carbon ion radiotherapy for localized primary sarcoma of the extremities: Results of a phase I/II trial

Shinji Sugahara [a,b,*], Tadashi Kamada [a], Reiko Imai [a], Hiroshi Tsuji [a], Noriaki Kameda [c], Tohru Okada [a], Hirohiko Tsujii [a], Shinichirou Tatezaki [d], For the Working Group for the Bone and Soft Tissue Sarcomas

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ABSTRACT

Purpose: To determine the effectiveness of carbon ion radiotherapy (CIRT) for localized primary sarcomas of the extremities in a prospective study.
Patients and materials: From April 2000 to May 2010, 17 (male/female: 12/5) patients with localized primary sarcoma of the extremities received CIRT. The median age was 53 years (range: 14–87 years). Nine patients had primary diseases and eight had recurrent diseases. Of the 17 patients, eight refused amputation, and the remaining nine refused surgical resection. Tumors were located in the upper limbs in four patients and lower limbs in 13. Histological diagnosis was osteosarcoma in three patients, liposarcoma in two, synovial sarcoma in two, rhabdomyosarcoma in two, pleomorphic sarcoma in two, and miscellaneous in six. The CIRT dose to the limb was 52.8 GyE for one patient, 64 GyE for three, 70.4 GyE for 13 in 16 fixed fractions over 4 weeks. Records were reviewed and outcomes including radiologic response, local control (progression-free), and survival were analyzed.
Results: The median follow-up was 37 months (range: 11–97 months). Radiological response rate was 65% (PR in 11, SD in 5, and PD in 1). The local control rate at 5 years was 76%. The overall survival rate at 5 years was 56%. Of the 17 patients, 10 survived without disease progression. Four patients had local

Soft Tissue Sarcomas of the Extremities

1996.6 ～ 2012.2 , n=17

Age： 14-87 y/o （Median 73）
Gender： M:F=10:7
Previous Tx： Fresh case 9
Post-ope rec or meta 8
Tumor size： 59-1871cm^3 (Median 301cm^3)

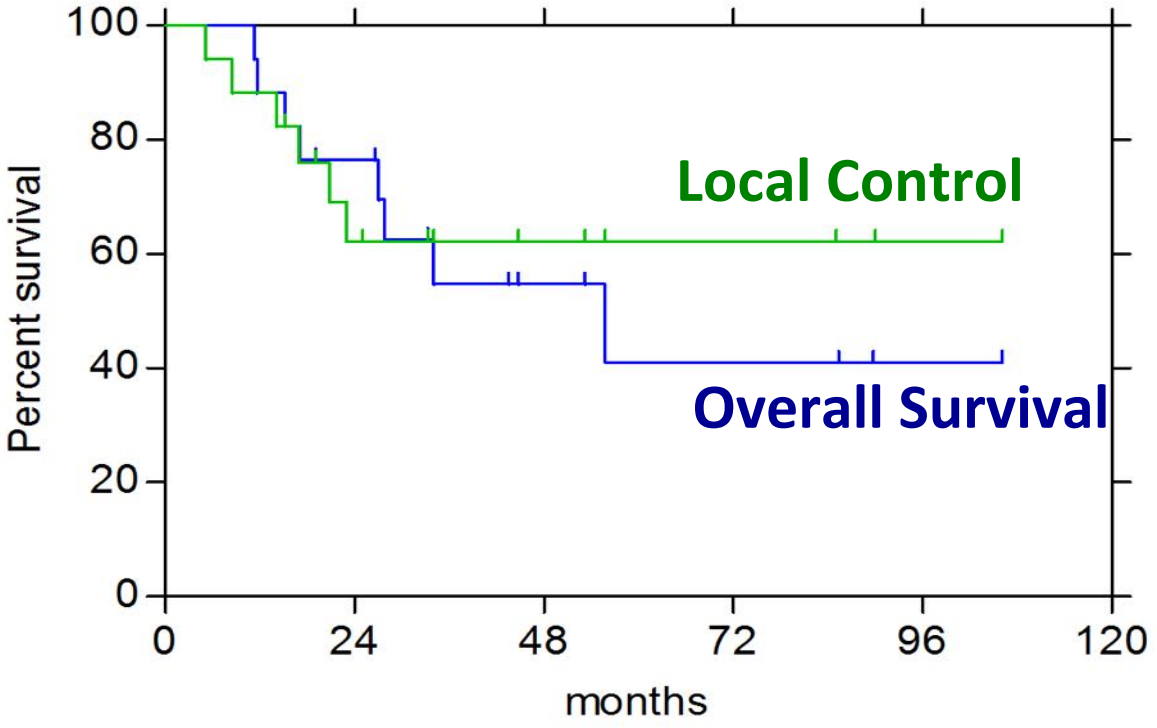
Histo-pathology	No.
MFH	4
Liposarcoma	3
Synovial	2
Fibrosarcoma	2
Rhabdomyosarcoma	2
Others	4

Sites	No.
Lower leg	6
Upper leg	5
Foot	1
Hand	1
Forearm	2
Upper arm	2

Sugahara, et al: Radiother Oncol, on line , 2012.

Soft Tissue Sarcomas of the Extremities
1996.6 ～2012.2　n=17

Age (Median): 73 (14-87)
Locally no recurrence: 11
Surviving in 9pats
Surviving periods: 19~106mon. (MST 56mo.



5-yr LC 62%
5-yr Survival 41%

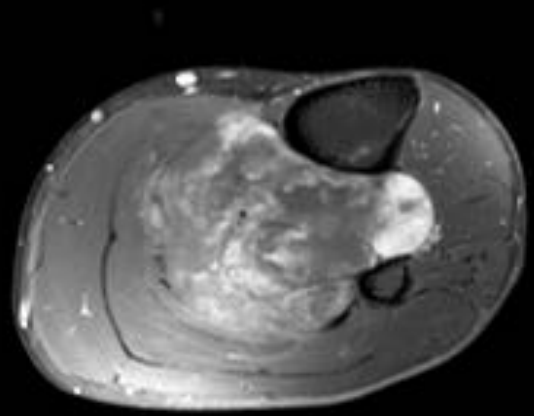
Sugahara, et al: Radiother Oncol, on line , 2012.

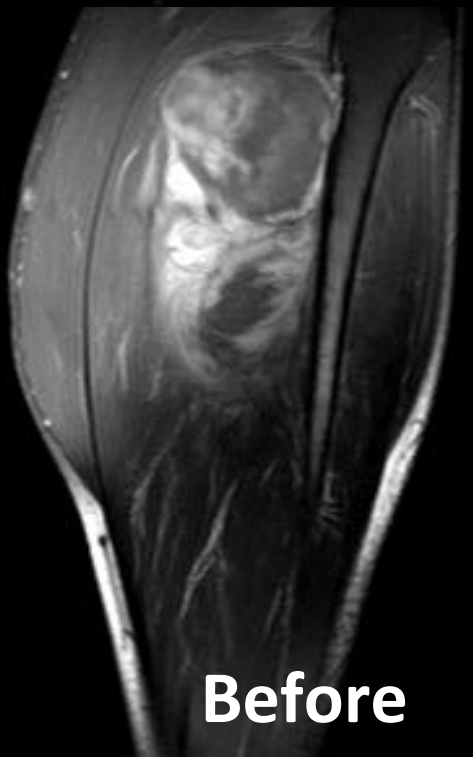
Toxicities in Soft Tissue Sarcomas of the Extremities

- **≧G3 Dermatitis : 0%**
- **Bone fracture : 0%**
- **No recurrence (Leg): 100% (7/7)**
- **≧G2 Myelopathy : 6% (1/17pts)**

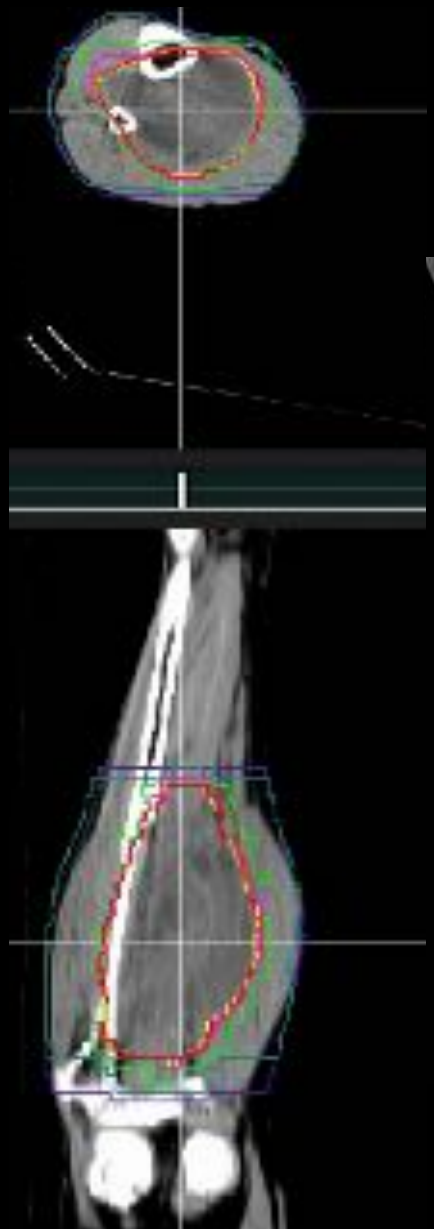
Sugahara, et al: Radiother Oncol, on line , 2012.

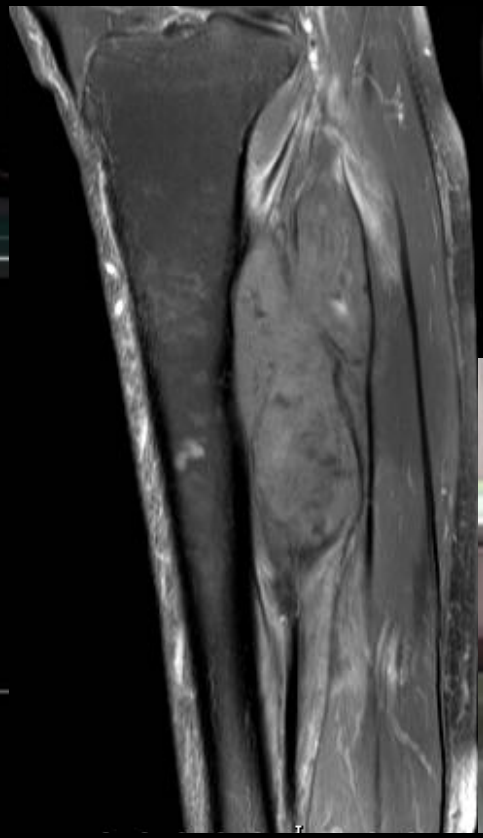
49M Liposarcoma of Rt Lower Leg

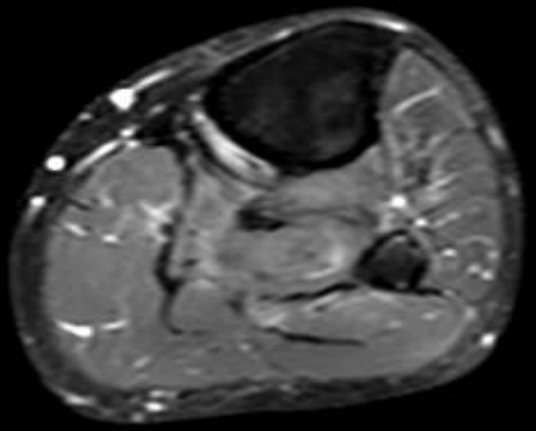




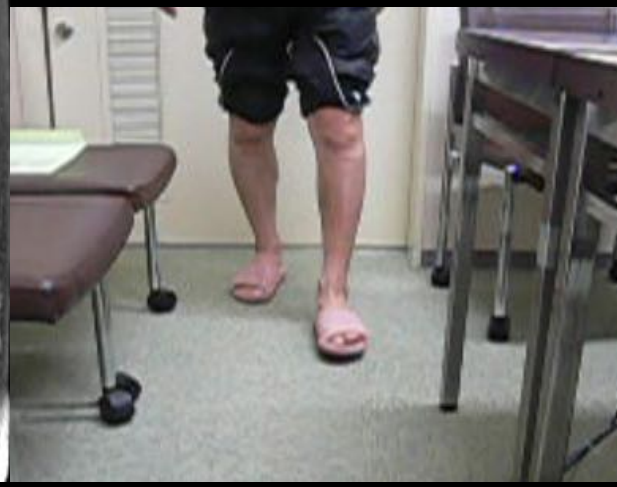
Before







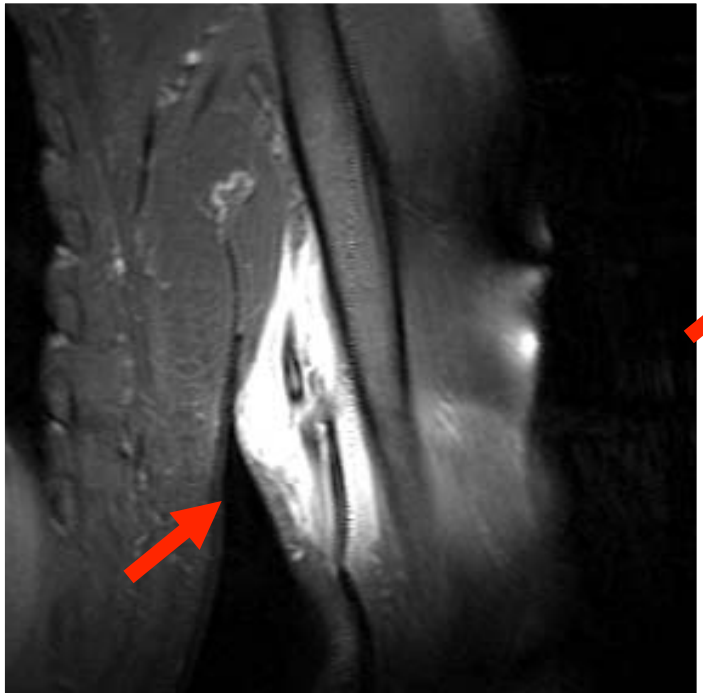
8 years

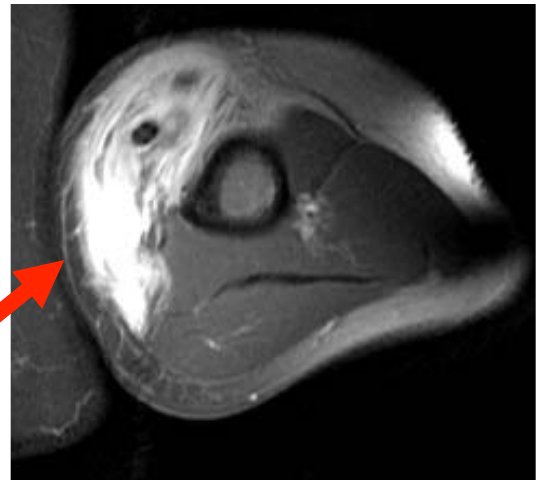


Sugahara, et al: Radiother Oncol, on line , 2012.

MFH

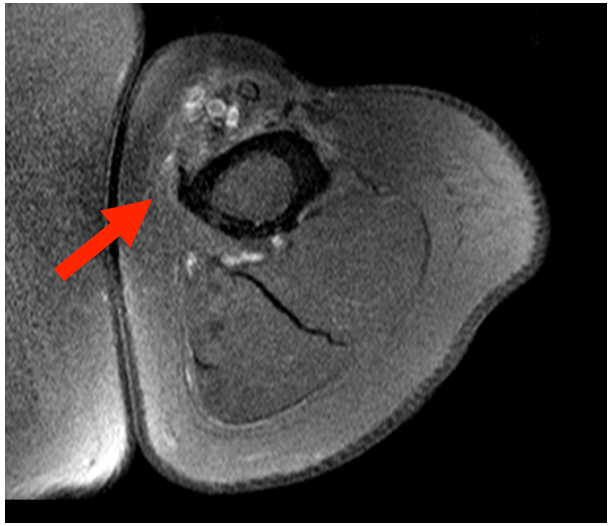
Figure 6.
Malignant fibrous histiocytoma of the left arm received 70.4 GyE in 16 fractions over 4 weeks carbon ion radiotherapy. Complete tumor regression, however and G3 neuropathy were observed at 106 months after treatment.



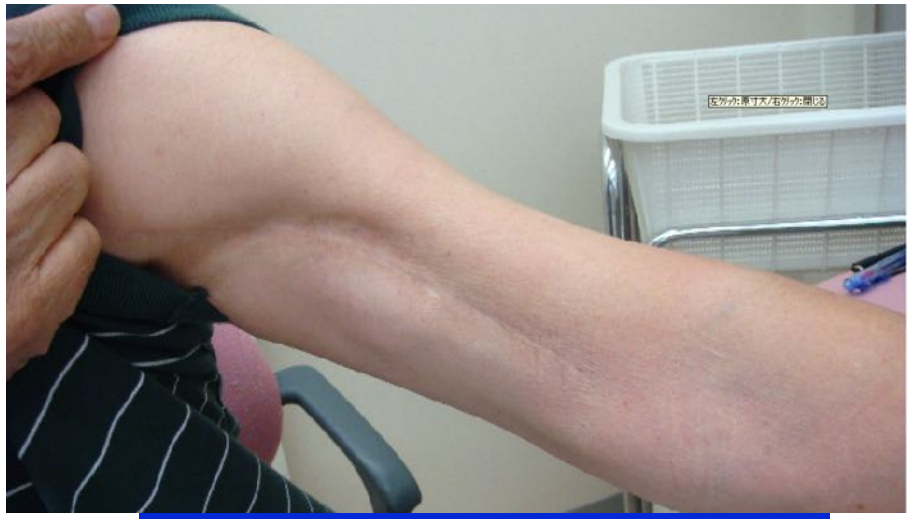


Gd(+) MRI

Before



Gd(+) MRI



6 years after C-ion RT

Retroperitoneal and Paracervical Sarcomas

Retroperitoneal Soft Tissue Sarcoma (RP-STS)

- **The RP space is the site of origin for 15% to 20% of STSs.**
- **Complete surgical resection is possible in less than 70% of the primary disease.**
- **Randomized trials have demonstrated that the addition of radiation to surgery unequivocally improves local tumor control for patients with extremity and superficial trunk STSs.**

  → This finding has led to considerable interest in the use of surgery plus radiation for patients with RP-STSs.
- **However, the efficacy of postoperative external-beam irradiation is limited by the inability to deliver adequate doses of irradiation on account of the dose tolerance limits of small bowel, spinal cord, stomach, kidney, and liver.**

→ Need of IORT or Ion Beam Therapy

Retroperitoneal Soft Tissue Sarcoma (RP-STS)
- Role of Radiotherapy -

- **In RP-STS, only 40–80% of the patients are resectable and microscopic or even gross residual disease is often present postoperatively.**
- **Surgery alone results in 5-year local control rates <50%.**
- **The local control rate with surgery and radiation (≥60Gy) is more than double that seen with surgery alone.**
- **Although uncertainty exists, one could speculate that improved local control could affect OS by improved LC, as well as a reduced risk of DM.**

Percent 10-year actuarial outcomes according to primary site

Survival endpoint	Retroperitoneum (n = 83)	Other (n = 1,452)	*p* value
Disease-specific	44	70	<0.001
Distant metastasis-free	67	68	0.7
Local control	40	83	<0.001

Ballo MT, et al: IJROBP 67: 158-163, 2007

Prognostic factors independently associated with outcomes for patients with RP-STS

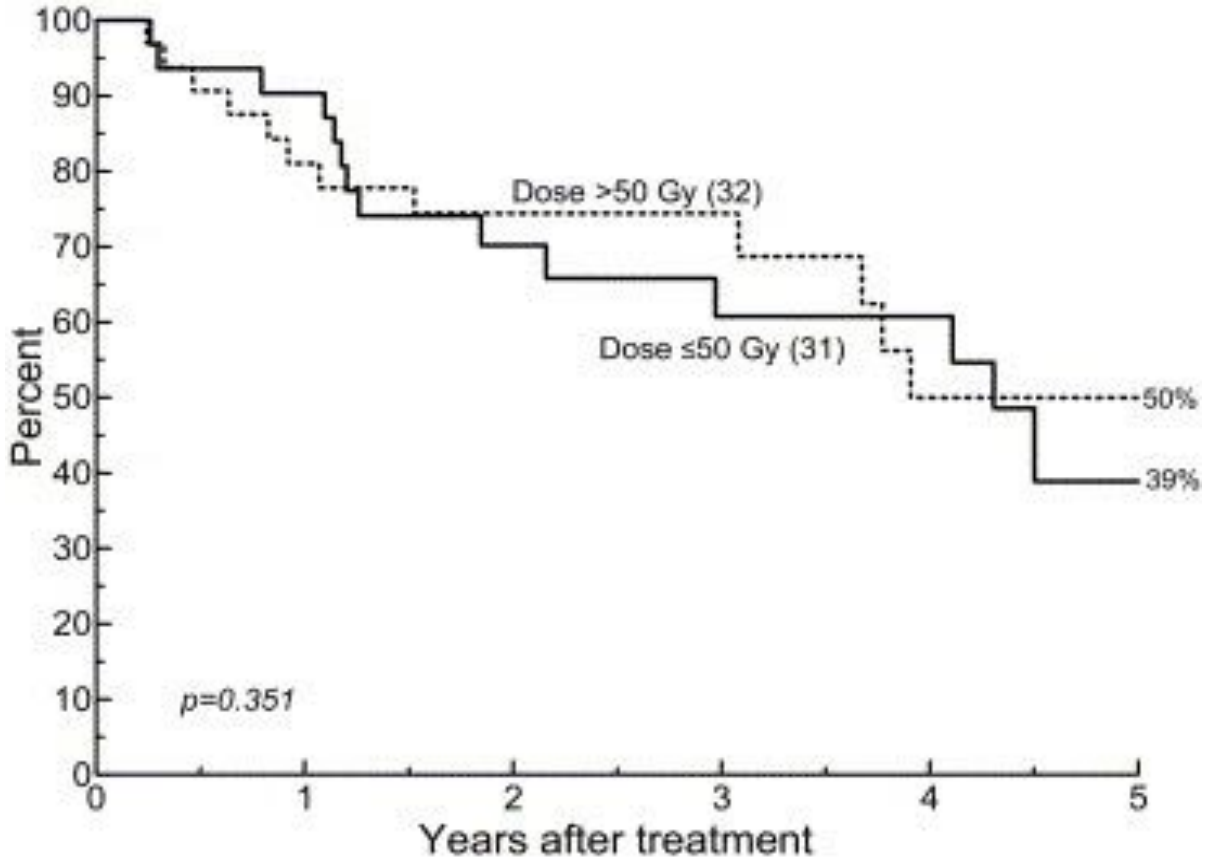
Survival endpoint	Factor	% at 5 years	*p* value*
Disease-specific survival	Low-grade	92	0.006
	Intermediate-grade	51	
	High-grade	41	
Distant metastasis-free survival	Low-grade	92	0.04
	Intermediate-grade	78	
	High-grade	57	
Local control	Negative resection margin	62	0.01
	Positive resection margin	33	
	Primary disease presentation	58	0.002
	Recurrent disease presentation	27	
	Age ≦65 y	54	0.05
	Age >65 y	30	

* Multivariate analysis.

Ballo MT, et al: IJROBP 67: 158-163, 2007

Kaplan-Meier local control curve according to external-beam radiation therapy dose.

- **The local control rate with surgery and adjuvant radiation is more than double that seen with surgery alone.**
- **However, analyzing local control according to EBRT dose (≤50 Gy or >50 Gy) revealed no improvement with higher doses.**



Ballo MT, et al: IJROBP 67: 158-163, 2007

Prognostic factors by multivariate analysis in RP-STS

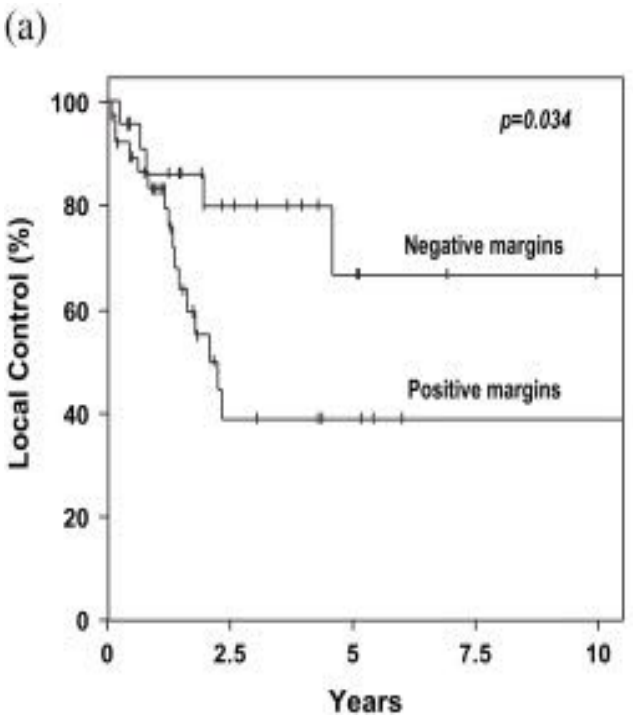
Variable	HR	95% CI	*p*
Local control (n = 63)			
Male gender	7.94	2.28-27.8	0.001
Positive or undetermined margins	4.78	1.49-15.3	0.009
RT dose (continuous)	0.78	0.69-0.88	<0.0001
Overall survival (n = 88)			
Male gender	2.06	1.15-3.68	0.015
High or intermediate grade	2.84	1.25-6.45	0.013
Surgery			
Complete resection	1.00	-	
Partial resection	1.39	0.65-2.94	0.390
Unresectable	3.53	1.69-7.37	0.0008

Abbreviations: HR = hazard ratio; CI = confidence interval; AI = Adriamycin/ifosfamide; IdUrd = iododeoxyuridine; GT = gemcitabine/Taxotere.

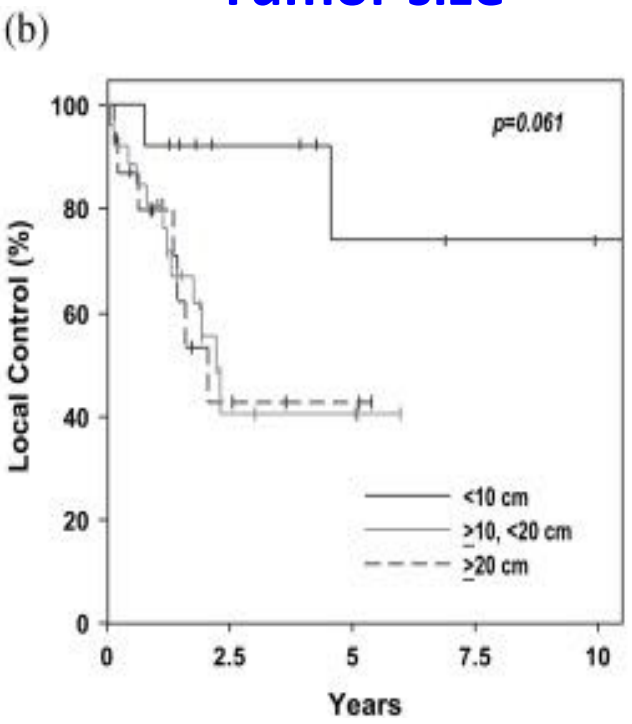
Feng M, et al. (2007) IJROBP 69;103 – 110.

Local control by tumor margin status, tumor size, and median radiation dose.

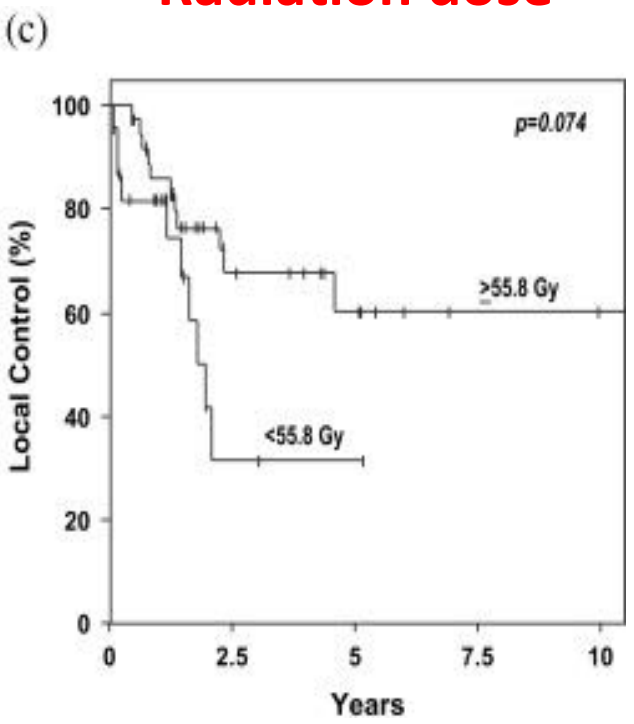
Surgical margin



Tumor size



Radiation dose



Feng M, et al. (2007) IJROBP 69;103 – 110.

Treatment outcomes of IORT-treated patients with RP-STS

Parameters		Alektiar et al. (2000)	Petersen et al. (2002)	Gieschen et al. (2001)	Sindelar et al. (1993)	Krempien (2006)
Treatment	Surgery	yes	yes	yes	yes	yes
	IORT	15Gy	15Gy	15Gy	20Gy	15Gy
	EBRT	45~50.4Gy	45Gy	45Gy	40~55Gy	45Gy
No. of patients		32	87	37	35	67
Median follow-up		33mo.	42mo.	38mo.	96mo.	30mo.
Prior treatment (%)						
Untreated		12	43	29	-	39
Recurrent		20	44	8	-	61
Macroscopic total resection (%)		94	88	-	-	82
5-yr local control (%)		62	59	59	37	40
5-yr DMFS (%)		82	57	54	NR	50
5-yr Survival (%)		45	47	50	42	62
5-yr DFS (%)		55	31	38	36	28

Abbreviations: DFS disease-free survival; DMFS distant metastasis–free survival; NR not reported.

Preliminary results of C-ion RT alone in unresectable RPS at NIRS

Serizawa et al: IJROBP 75: 1105–1110, 2009

Int. J. Radiation Oncology Biol. Phys., Vol. 75, No. 4, pp. 1105–1110, 2009

0360-3016/09/$–see front matter

ELSEVIER

doi:10.1016/j.ijrobp.2008.12.019

CLINICAL INVESTIGATION **Sarcoma**

CARBON ION RADIOTHERAPY FOR UNRESECTABLE RETROPERITONEAL SARCOMAS

ITSUKO SERIZAWA, M.D.,* KENJI KAGEI, M.D., PH.D.,* TADASHI KAMADA, M.D., PH.D.,* REIKO IMAI, M.D., PH.D.,* SHINJI SUGAHARA, M.D., PH.D.,* TOHRU OKADA, M.D.,* HIROSHI TSUJI, M.D., PH.D.,* HISAO ITO, M.D., PH.D.,† AND HIROHIKO TSUJII, M.D., PH.D.*

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Purpose: To evaluate the applicability of carbon ion radiotherapy (CIRT) for unresectable retroperitoneal sarcomas with regard to normal tissue morbidity and local tumor control.
Methods and Materials: From May 1997 to February 2006, 24 patients (17 male and 7 female) with unresectable retroperitoneal sarcoma received CIRT. Age ranged from 16 to 77 years (median, 48.6 years). Of the patients, 16 had primary disease and 8 recurrent disease. Histologic diagnoses were as follows: malignant fibrous histiocytoma in 6, liposarcoma in 3, malignant peripheral nerve sheath tumor in 3, Ewing/primitive neuroectodermal tumor (PNET) in 2, and miscellaneous in 10 patients. The histologic grades were as follows: Grade 3 in 15, Grade 2-3 in 2, Grade 2 in 3, and unknown in 4. Clinical target volumes ranged between 57 cm^3 and 1,194 cm^3 (median 525 cm^3). The delivered carbon ion dose ranged from 52.8 to 73.6 GyE in 16 fixed fractions over 4 weeks.
Results: The median follow-up was 36 months (range, 6–143 months). The overall survival rates at 2 and 5 years were 75% and 50%, respectively. The local control rates at 2 and 5 years were 77% and 69%. No complications of the gastrointestinal tract were encountered. No other toxicity greater than Grade 2 was observed.
Conclusions: Use of CIRT is suggested to be effective and safe for retroperitoneal sarcomas. The results obtained with CIRT were a good overall survival rate and local control, notwithstanding the fact that most patients were not eligible for surgical resection and had high-grade sarcomas. © 2009 Elsevier Inc.

Retroperitoneal, Sarcoma, Carbon ion radiotherapy, Particle radiotherapy, Bone and soft tissue sarcomas.

INTRODUCTION

radiation doses are difficult to deliver, and toxicity can be significant. Various institutions have advocated preoperative

Histologic subtype	n
MFH	6
Liposarcoma	3
MPNST	3
Ewing/PNET	2
Other	10
Histological grade	
G3 (high grade)	15
G2–3 (high grade)	2
G2 (intermediate)	3
G1 (low grade)	0
Unknown	4
Total	24

Table 2. Toxicity in study patients

Acute reaction	G1 n	G2 n	G3 n	G4 n
Skin	20	4	0	0
Gastrointestinal	0	0	0	0
Late reaction	**G1 n**	**G2 n**	**G3 n**	**G4 n**
Skin	22	1	0	0
Gastrointestinal	0	0	0	0
Neurologic	0	5	0	0

Serizawa et al: IJROBP 75: 1105–1110, 2009

Table 4. Complications in studies reported

First author, year	Treatment protocol	n	2-y LC (%)	Acute ≧G2(%)		Late I ≧G2(%)		Death(%)
				GI	NT	GI	NT	
Gilbeau, 2002 (17)	Op+EBRT± IORT	45	70	77	0	9	19	0
Fein, 1995 (20)	Op+EBRT	19	72	5	0	0	0	0
Jones, 2002 (21)	Op+EBRT± BT	41	80	15	0	10	2	7
Peterson, 2002 (22)	Op+EBRT + IORT	87	84	14	10	-	-	0
Tzeng, 2006 (23)	Op+IMRT	14	80	6	0	6	0	0
Current study (2009)	C-ions alone	24	77	0	0	0	21*	0

*** Neurotoxicity: 3 of the 5 patients had neurologic disabilities before CIRT**

17. Gilbeau L, Kantor G, Stoeckle E, et al.(2002). "Surgical resection and radiotherapy for primary retroperitoneal soft tissue sarcoma." *Radiother Oncol* ;65:137–143.
20. Fein DA, Corn BW, Lanciano RM, et al.(1995). "Management of retroperitoneal sarcomas: Does dose escalation impact on locoregional control?" *Int J Radiat Oncol Biol Phys* ;31:129–134.
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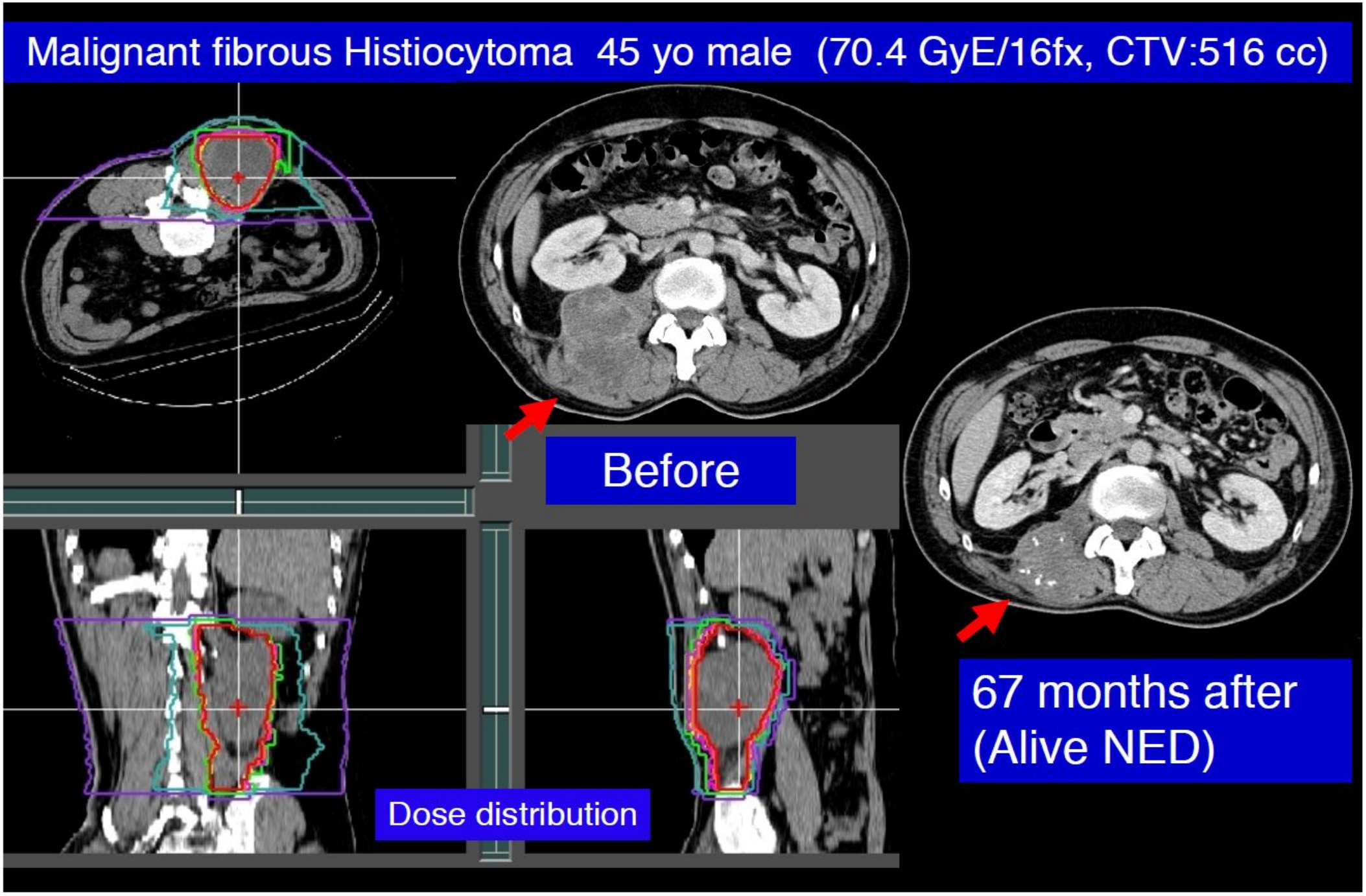
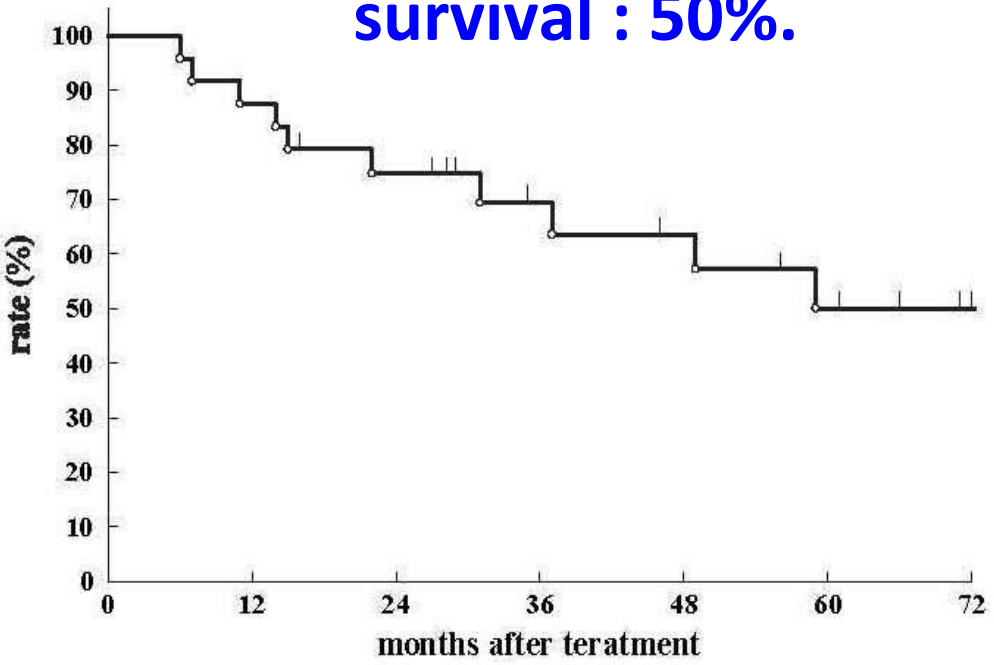
22. Petersen IA, Haddock MG, Donohue JH, et al.(2002). "Use of intraoperative electron beam radiotherapy in the management of retroperitoneal soft tissue sarcomas." *Int J Radiat Oncol Biol Phys* ;52:469–475.
23. Tzeng CW, Fiveash JB, Popple RA, et al.(2006). "Preoperative radiation therapy with selective dose escalation to the margin at risk for retroperitoneal sarcoma." *Cancer* ;107:371–379.

Serizawa et al: IJROBP 75: 1105–1110, 2009

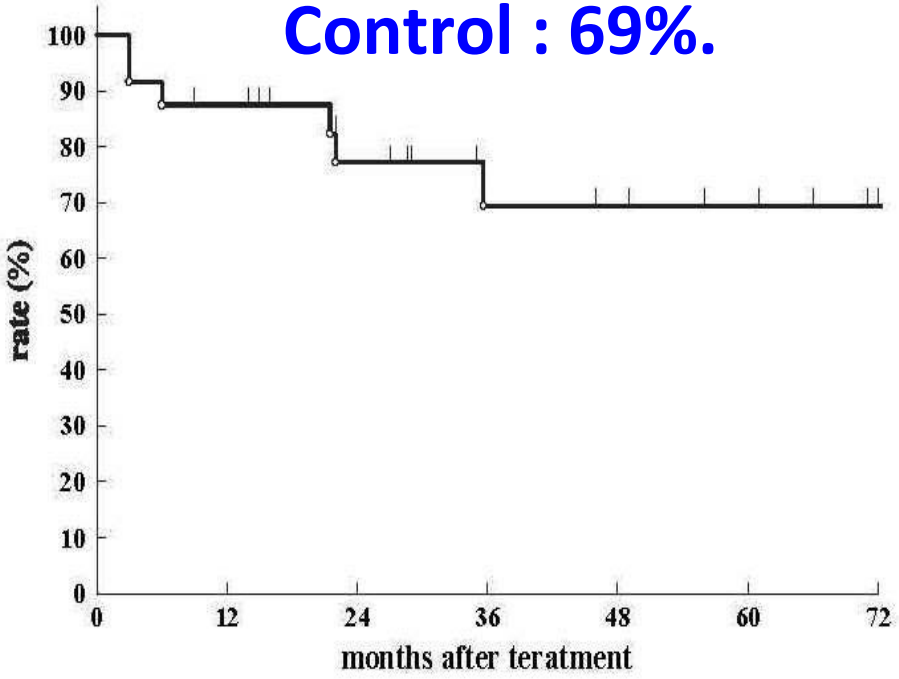

Malignant fibrous Histiocytoma 45 yo male (70.4 GyE/16fx, CTV:516 cc)
Before
67 months after
(Alive NED)
Dose distribution

Results of C-ion RT in RP-STS at NIRS
N=24

The 5-yr overall survival : 50%.



The 5-yr Local Control : 69%.



Serizawa et al: IJROBP 75: 1105–1110, 2009

Table 3. Overall survival (OS) and local control (LC) in various studies

First author, year	Treatment	n	Resec-tion (%)	Complete resection (%)	Microsco-pically positive margin (%)	5-y OS (%)	5-y LC (%)
Catton, 1994 (2)	Op+EBRT	104	43			36	28
Stoeckle, 2001 (14)	Op+EBRT	145	65			49	41
Van Dalen, 2001 (15)	Op	142		54	ND	ND	32
Lewis, 1998 (4)	Op+EBRT	278	67	49	18	54	59
Gronch, 2004 (16)	Op+EBRT+IORT	167	88			53	54
Gilbeau, 2002 (17)	Op+EBRT	45		38	58	60	40
Krempien, 2006 (18)	Op+IORT EBRT	67		31	51	64	40
Youssef, 2002 (19)	Op+EBRT BT	60		45	30	56	71
Current study (2009)	C-ion RT alone	24				50	69

Abbreviations: BT = brachytherapy; CIRT = carbon ion radiotherapy; EBRT = external beam radiation therapy; IORT = intraoperative; radiation therapy; ND = no description; Op = operation.

Serizawa et al: IJROBP 75: 1105–1110, 2009

Update Results of C-ion RT alone for RP and paracervical STS at NIRS

Soft Tissue Sarcomas of Retroperitoneal and Paracervical region at NIRS (1996.6 ～ 2012.2 , n=56)

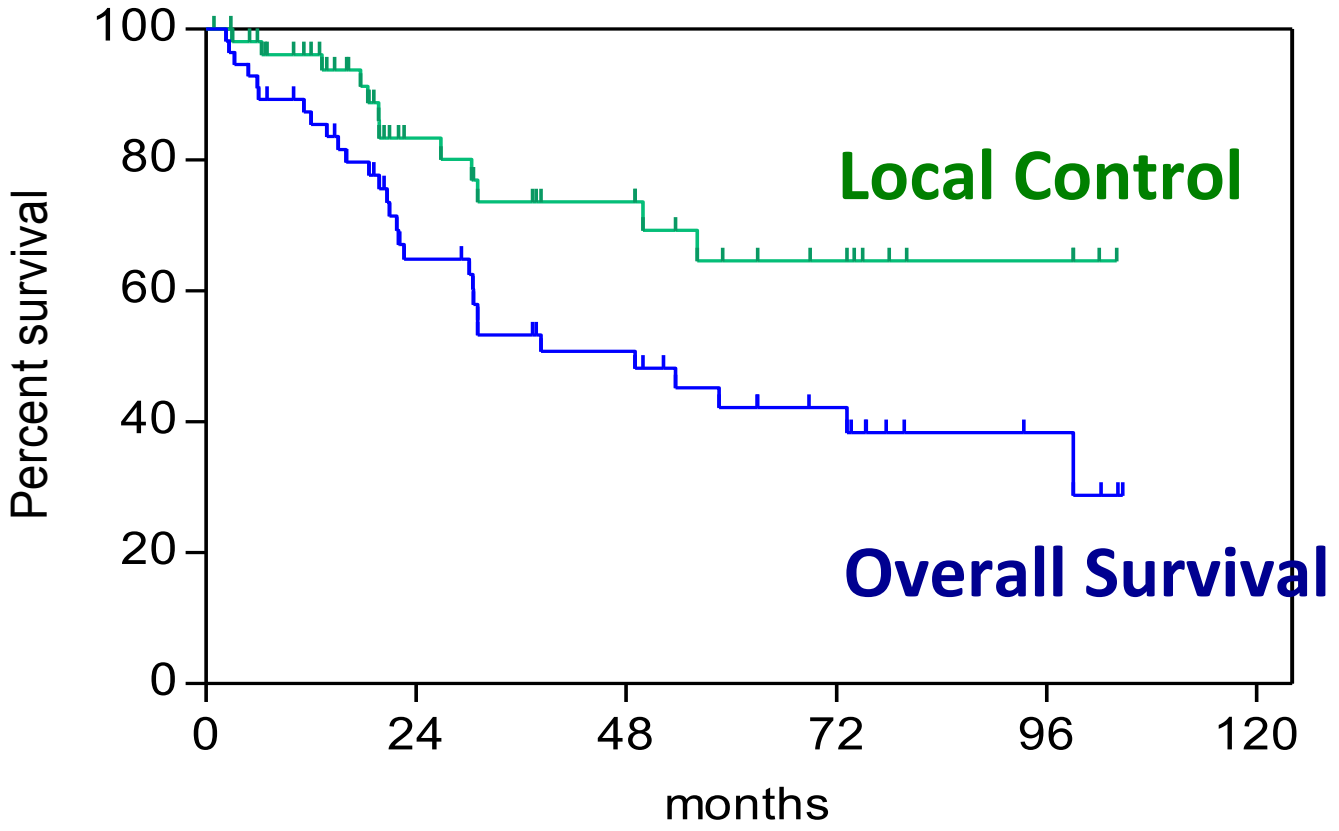
Age： 14-78 y/o （Median 58）
Gender： M:F=29:27
Previous Tx： Fresh case 36
Post-ope rec or meta 20

Histo-pathology	No.
MFH	14
Liposarcoma	6
MPNST	5
Synovial sarcoma	4
Rhabdomyosarcoma	4
Others	23

Retroperitoneal and Paracervical Sarcomas

1996.6 ～ 2012.2 n=56

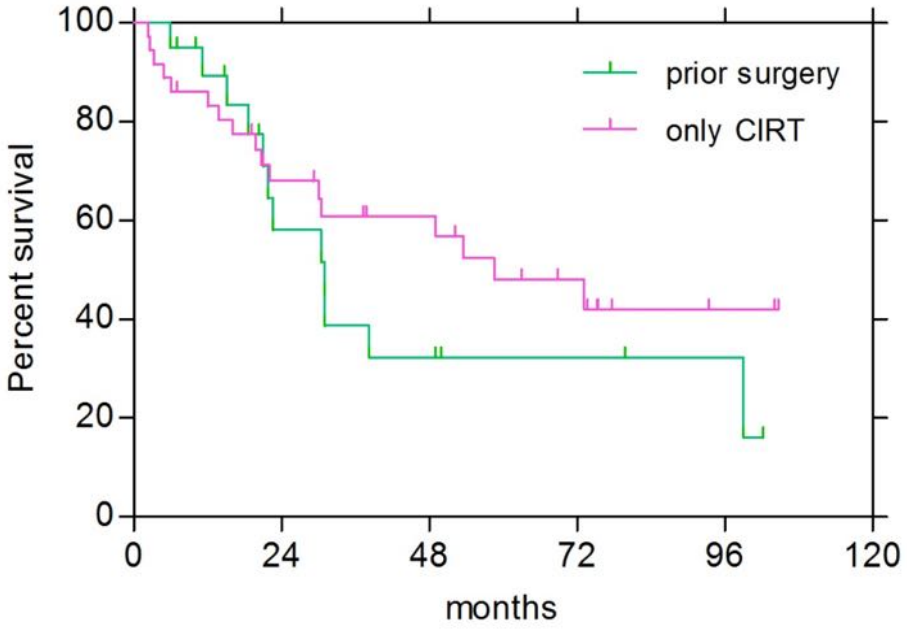
	24mo.	60mo.
Local Control	**83%**	**65%**
Overall Survival	**65%**	**42%**



Retroperitoneal and Paracervical Sarcomas
- Post-ope Recurrence vs Fresh case -

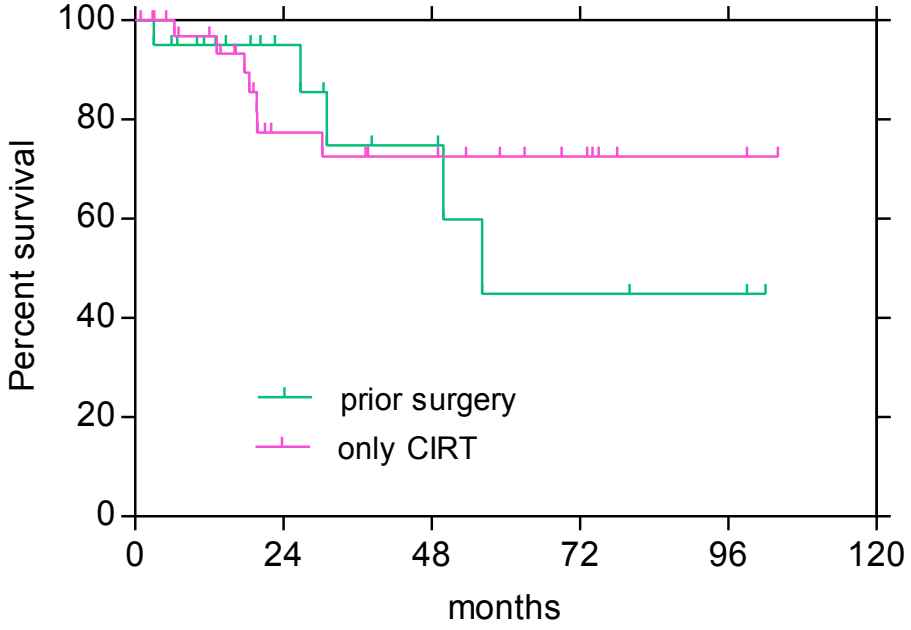
Post-ope (n=20) , Fresh (n=36)

Survival



	36m.	60m.
Post-ope	39%	32%
Fresh	60%	48%

Local Control



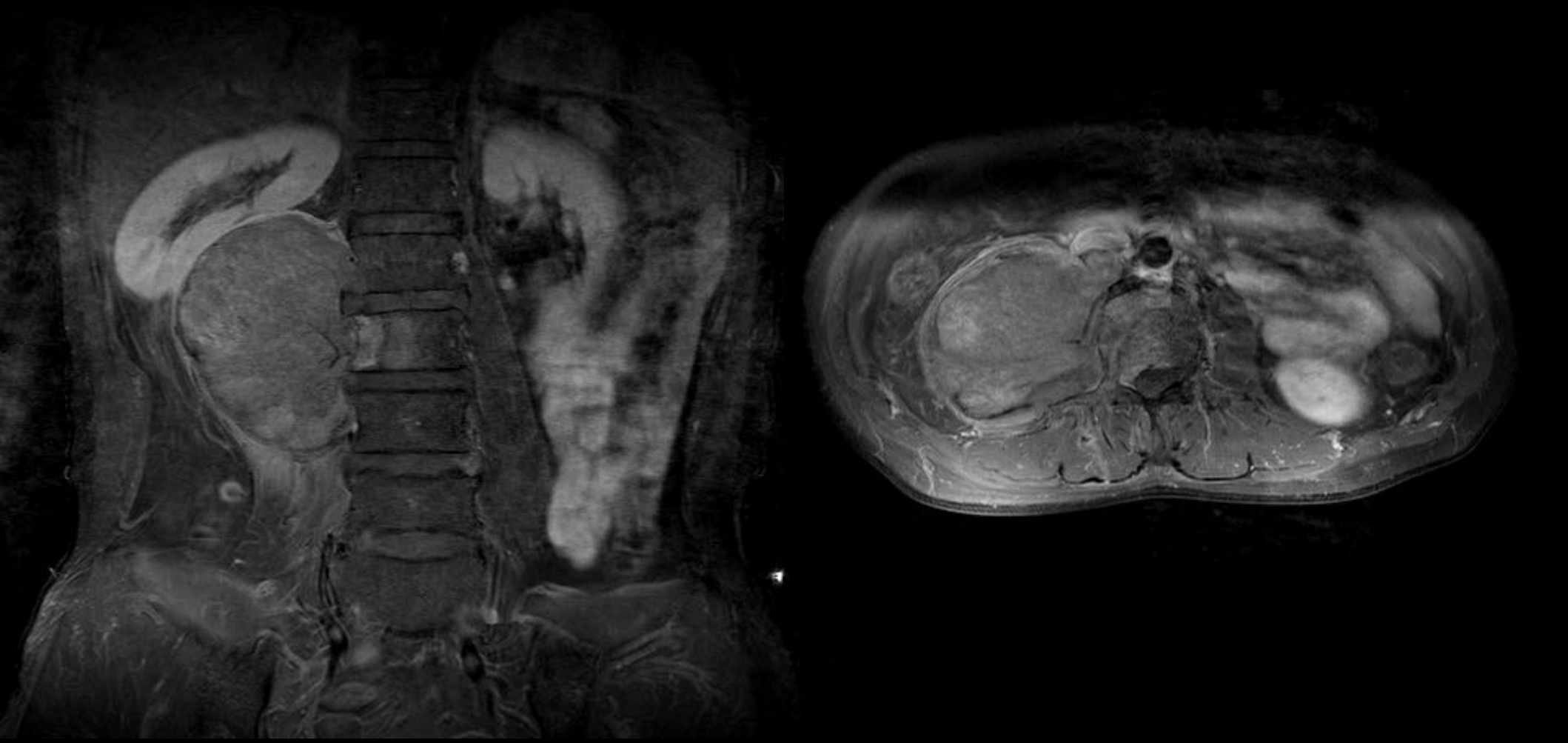
	36m.	60m.
Post-ope	75%	45%
Fresh	73%	73%

Toxicities in Retroperitoneal and Paracervical Sarcomas

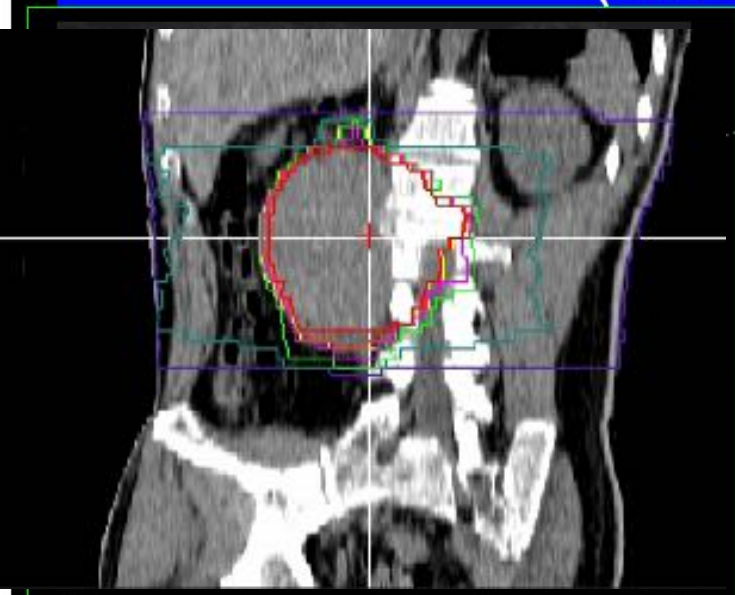
- **≧G3 Dermatitis 0%**
- **≧G2 Myelopathy 5% (3/56pts)**
- **≧G3 Intestinal 0%**
- **Hydronephrosis 25%**

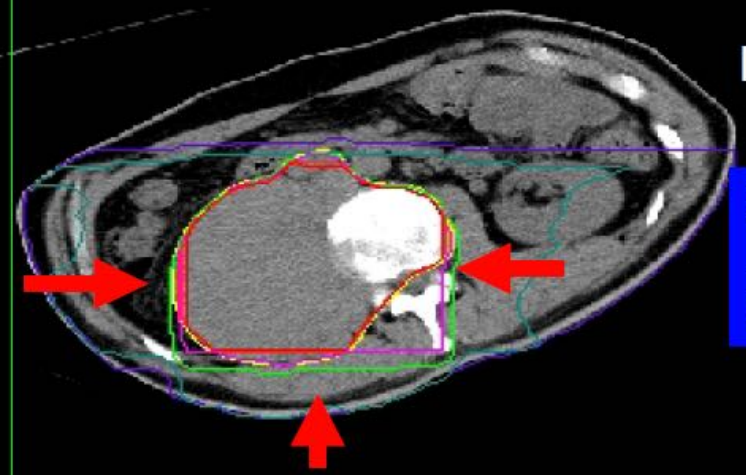
(Renal function: Normal)

(1) 9901-154 PNET/Ewing of the psoas 52M



Ewing/ PNET family tumor 52 yo male
(70.4GyE/16Fr, CTV : 728 cc)

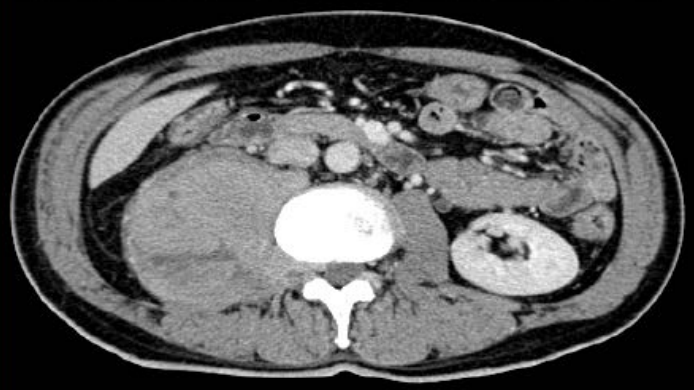


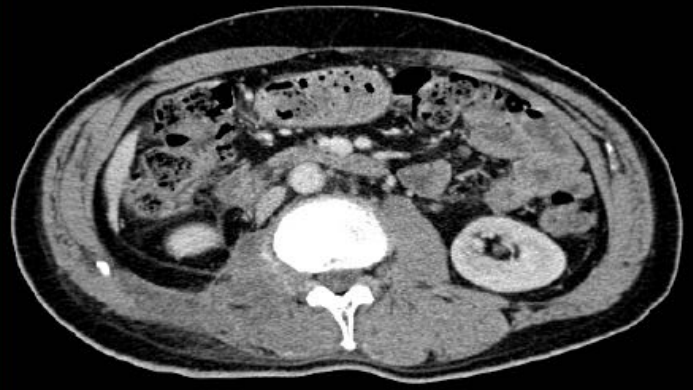


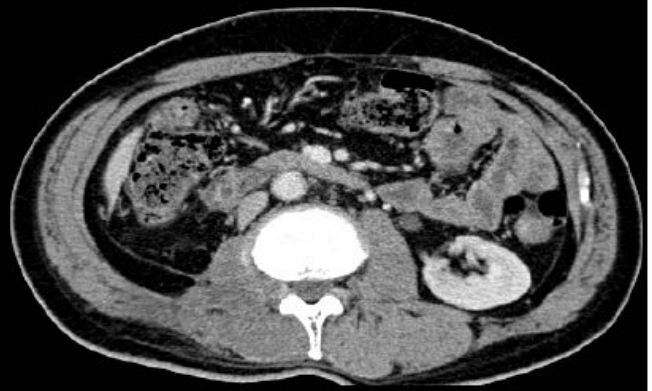
Dose distribution

60 MONTHS ALIVE, LOCALLY CONTROLLED WITH LUNG METS

Image upside down
(prone position at treatment)

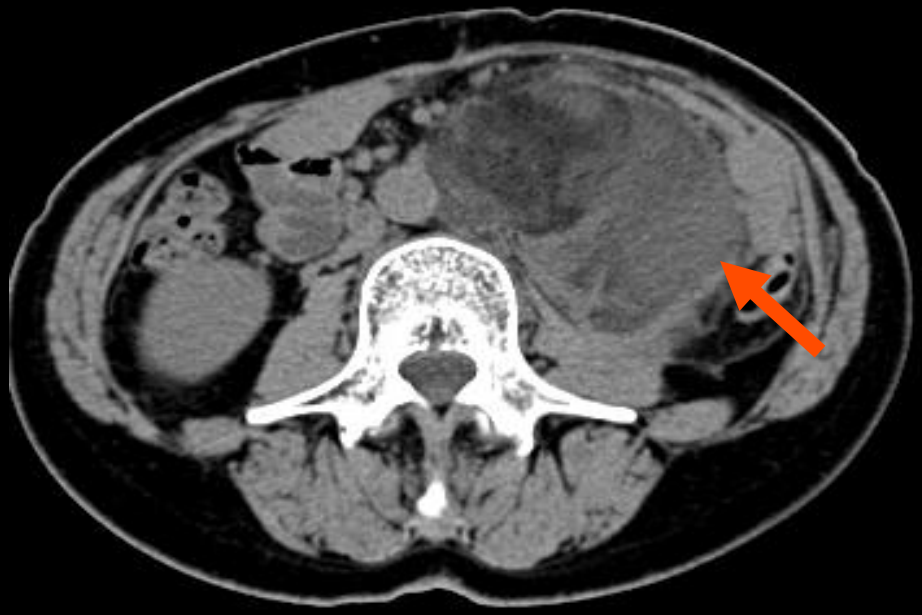


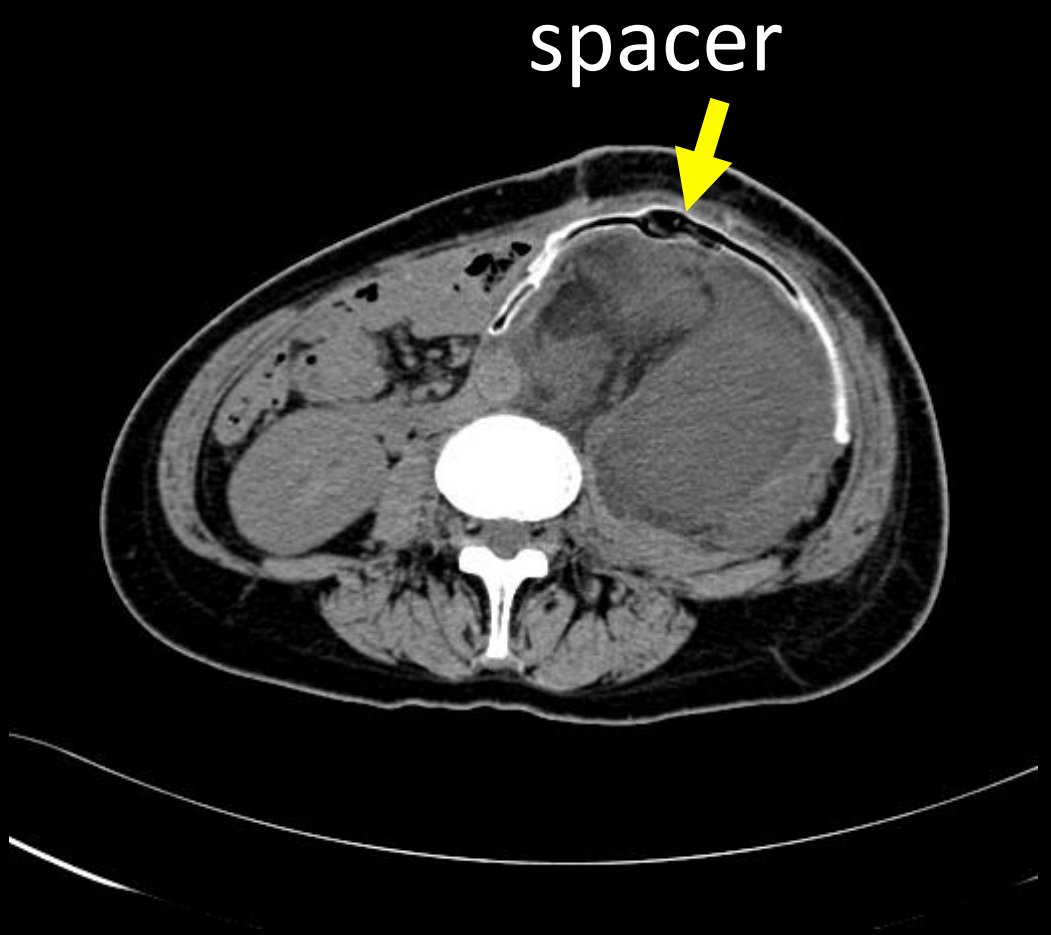




Before (after chemotherapy) -> 12 months -> 24 months

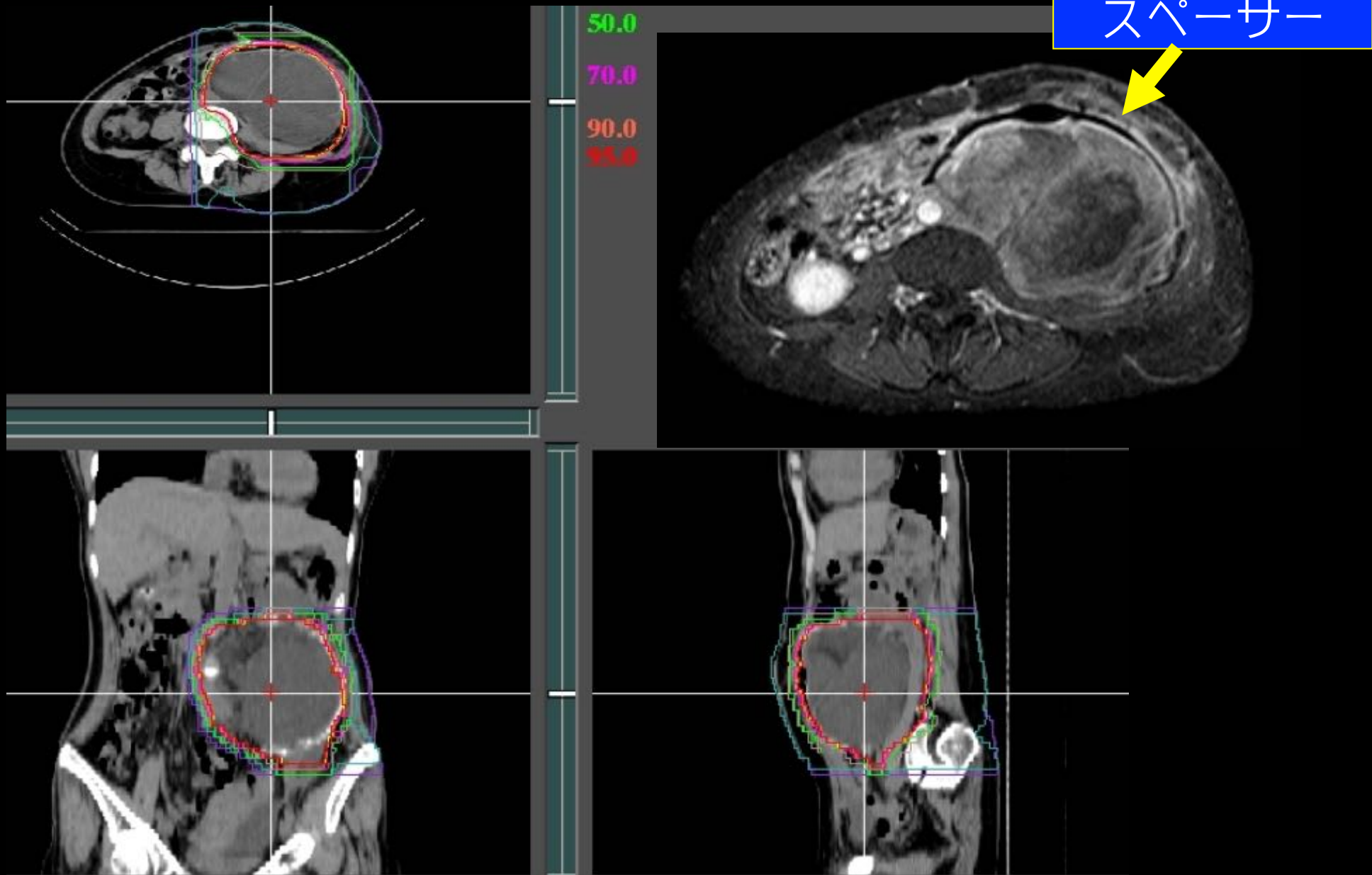
764361 9901 （2） -145 liposarcoma p/o rec 68F





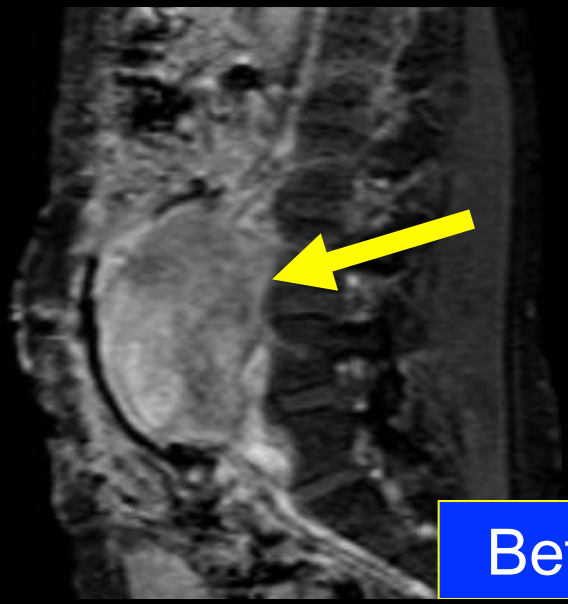
9901-(2)-145　liposarcoma of the retroperitoneum

p/o rec　54　F

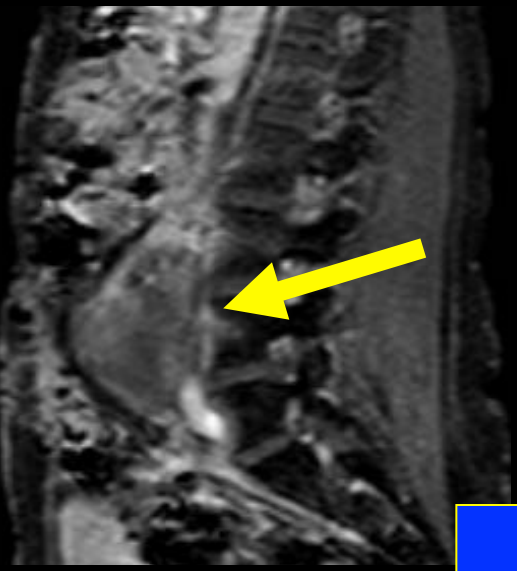


9901-(2)-145 liposarcoma of the retroperitoneum

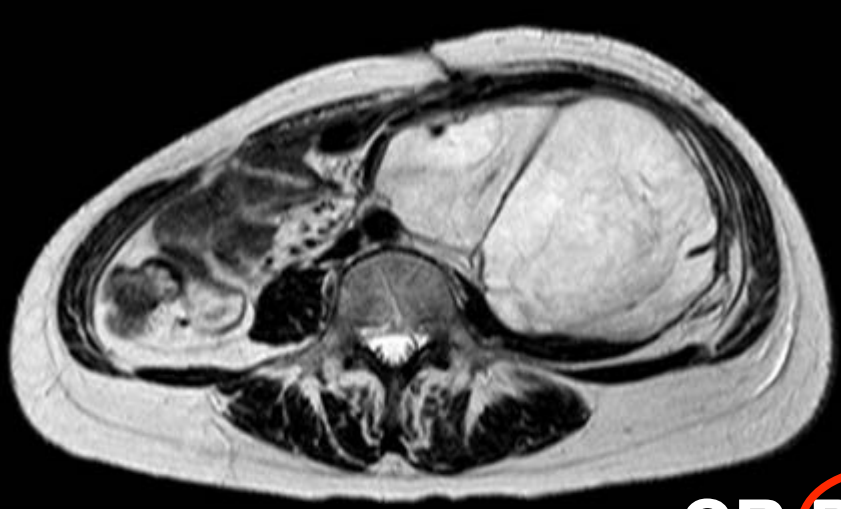
p/o rec 54 F

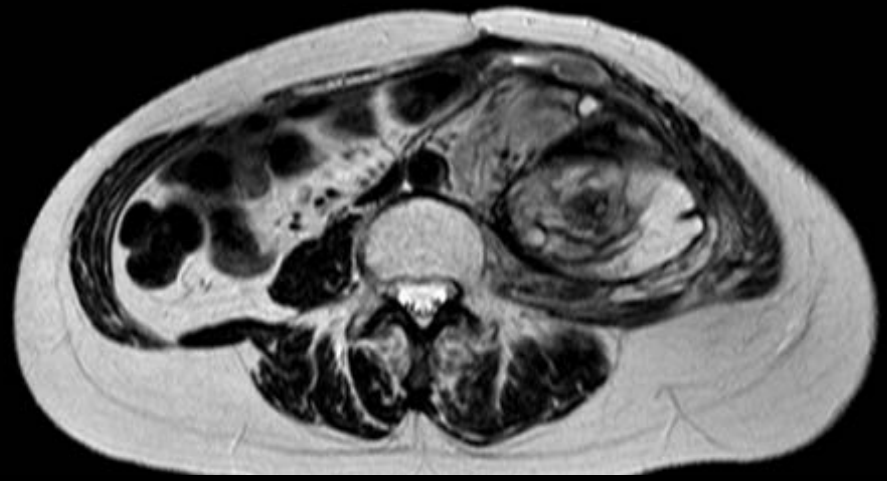


Before CIRT



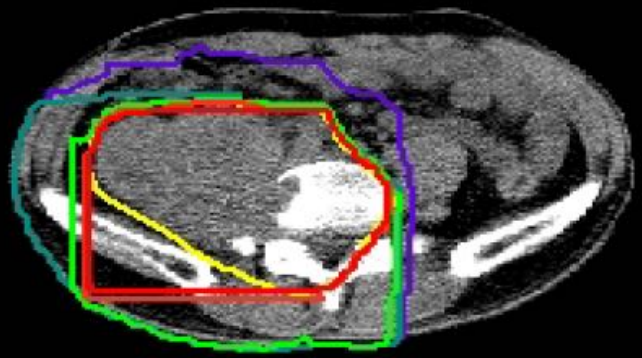
After CIRT



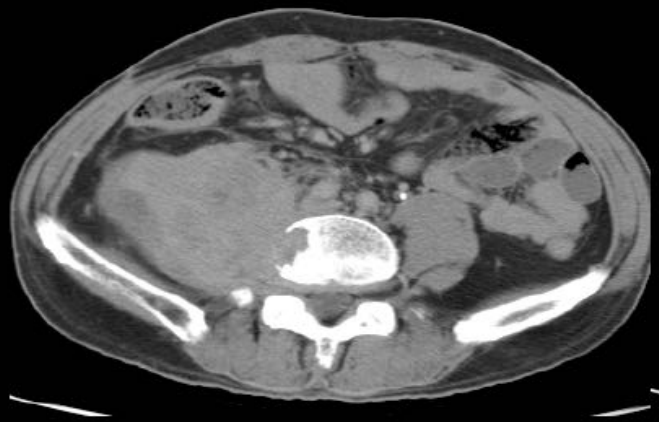


CR PR SD PD

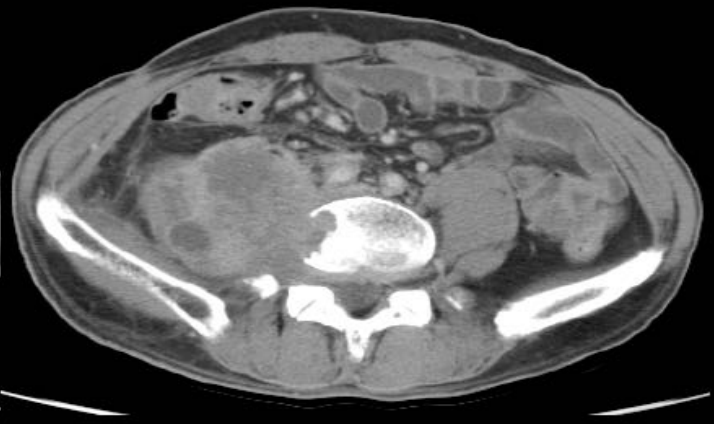
Rhabdomyosarcoma Grade 3 53 yo male
(73.6GyE/16Fx, CTV: 1034 cc)



Dose distribution

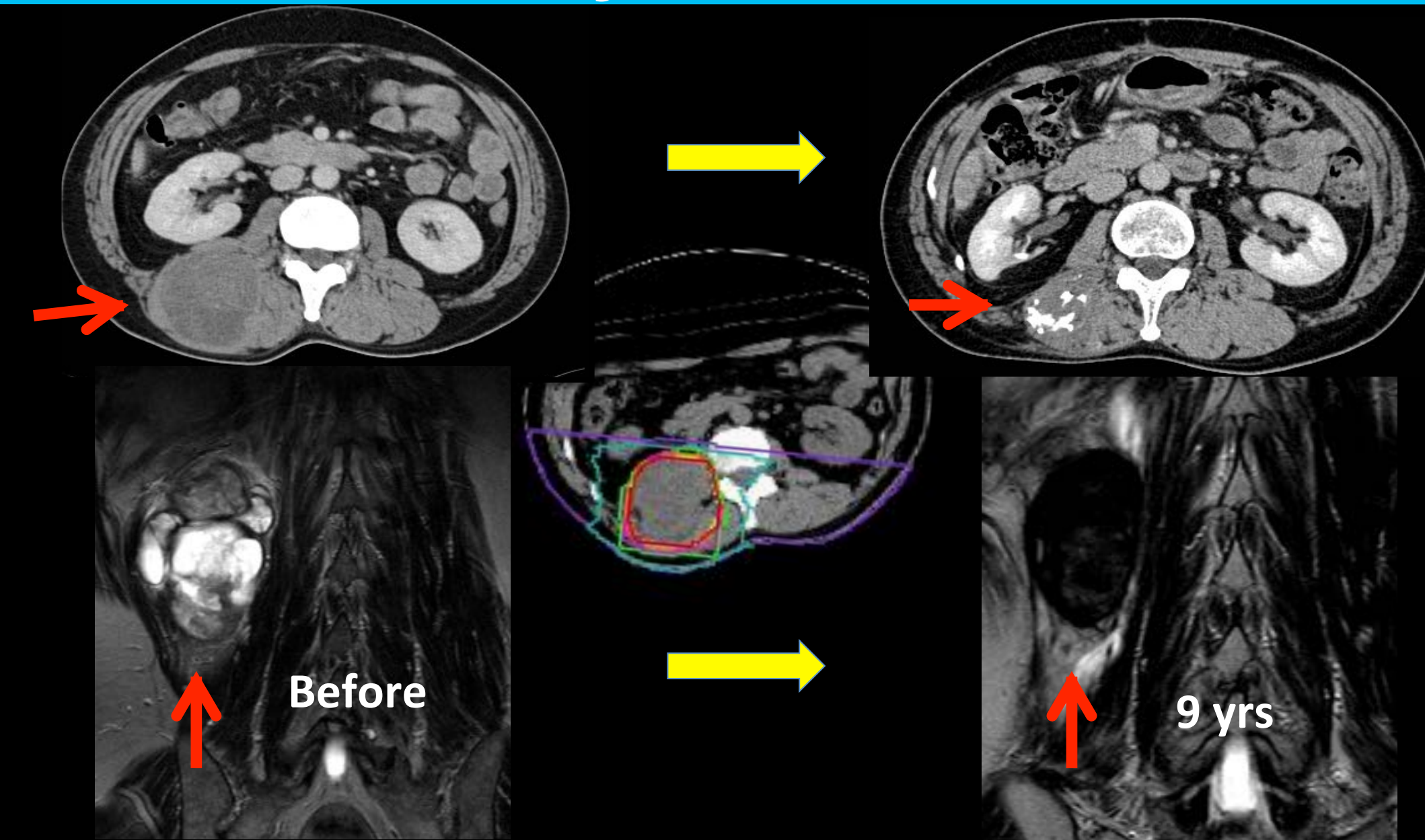


Pre Treatment

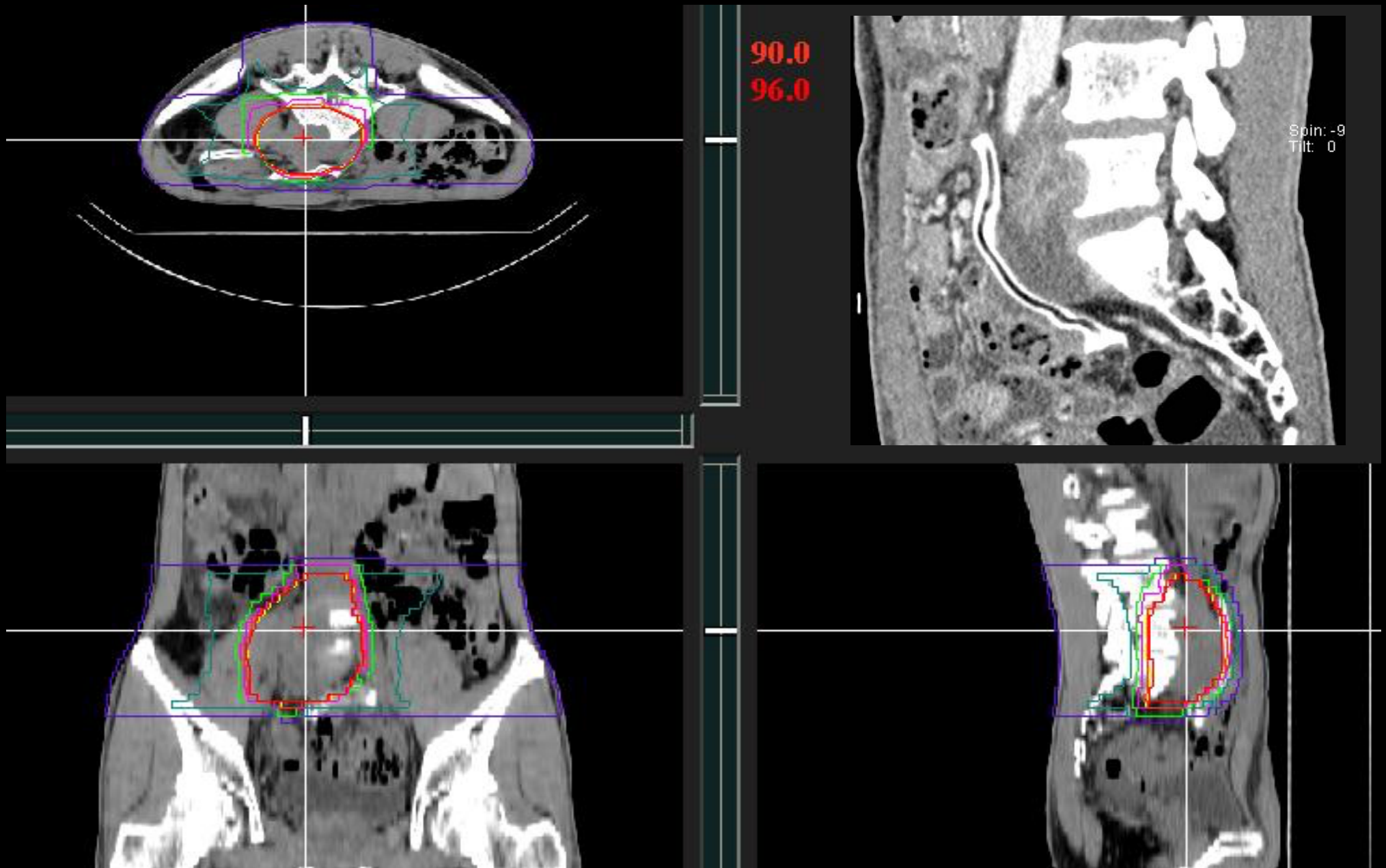


2 months later

44y/o, M MFH



9901-76 LMS of the retroperitoneum 42 M



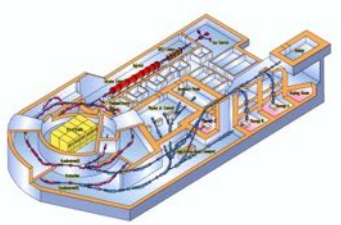
Actuarial local control rate according to treatment received in RP-STS

First author (reference)	Year	No. of patients	5-year LC (%)	
Complete (R0/R1) resection alone				
7 articles	1991-2003	9~201	8~47%	**<50%**
Complete (R0/R1) resection and radiation				
8 reports	1993~2005	13~60	38~71%	**>50%**
Complete (R0/R1) resection and radiation with IORT				
Sindelar (1993)	1993	15	60	
Alektiar (2000)	2000	32	62	
Geischen (2001)	2001	16	83	
Petersen (2002)	2002	87	59	
Krempien (2006)	2006	12	100	
Ballo (2007)	2005	18	51	
Carbon-ion RT alone				
NIRS	2012	56	65%	

LC local control; R0/R1 margin negative/positive; IORT intraoperative

Ballo MT, et al: IJROBP 67: 158-163, 2007

Summary:
Bone and Soft Tissue Sarcoma



- **During 1996 and 2012 at NIRS, C-ion RT was administered to 854 pats with B&S sarcomas including 56 pats with retroperitoneal and paracervical sarcomas, who were considered unfit to surgery, using 64~73.6GyE/16 fr/4wks.**
- **In these tumors, C-ion RT as a sole treatment has yielded comparable or even better results as compared to surgery, indicating that C-ion RT could replace surgery in elderly patients and in patients whose function would be greatly reduced if resected..**

Role of C-ion RT in RP-STS

The results obtained with C-ion RT at NIRS could have shown overall survival and local control rates comparable to surgery with/without radiation, notwithstanding the fact that most patients were not eligible for surgical resection and had high-grade sarcomas.


Thank You