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Proton Radiation Therapy for Osteosarcomas, Chondrogenic Tumors and Soft Tissue Sarcomas

Eugen B. Hug

Center for Proton Radiation Therapy

Paul Scherrer Institute

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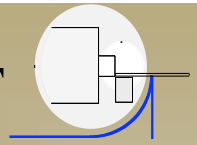

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Is there a place for Proton/Particle Radiotherapy in the treatment of Sarcomas ?

=

Is there still a need to improve outcome for a subgroup of Sarcoma patients?

Is it desirable to reduce side effects and improve functional outcome?

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Is there a need for (improved) RT?

Osteosarcoma of the pelvis: COSS-Group results
Ozaki et al., JCO, 21(2), 2003

- COSS = German/Austrian Coop. Osteosarc. Study Group
- 1,982 patients on sequential protocols 1979-1998

- 67 patients with pelvic, high gradeosteosarcoma
- Chemotherapy plus maximum possible surgery
- 11 patients with XRT

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Osteosarcoma of the pelvis: COSS-Group results

Ozaki et al., JCO, 21(2), 2003

Surgical Margin and Local Failure

Margin	No. of Patients	No. of Local Failures
Definitive operation		
Radical	2 (0)	1 (0)
Wide	23 (0)	11 (0)
Marginal	10 (0)	7 (0)
Intralesional	13 (4)	12 (3)
Unknown	2 (0)	0 (0)
No operation	17 (7)	16 (6)
Total	67 (11)	47 (9)
NOTE: Values in parentheses indicate radiotherapy.		

LF:

48 %

83 %

94 %

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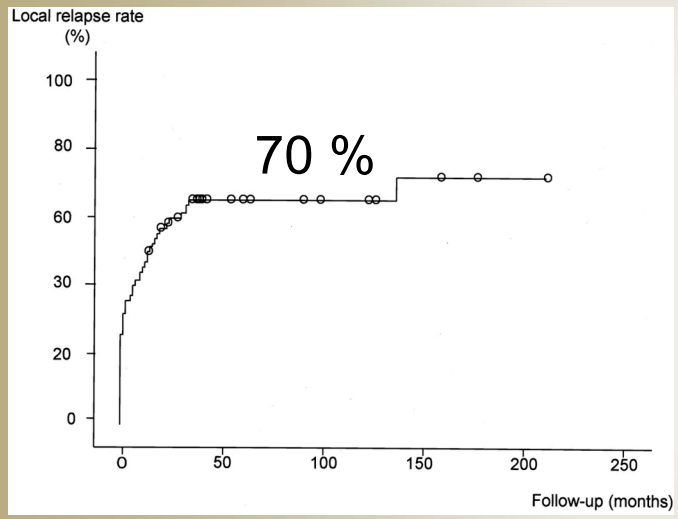
Osteosarcoma of the pelvis: COSS-Group results

Ozaki et al., JCO, 21(2), 2003

Cumulative local failure



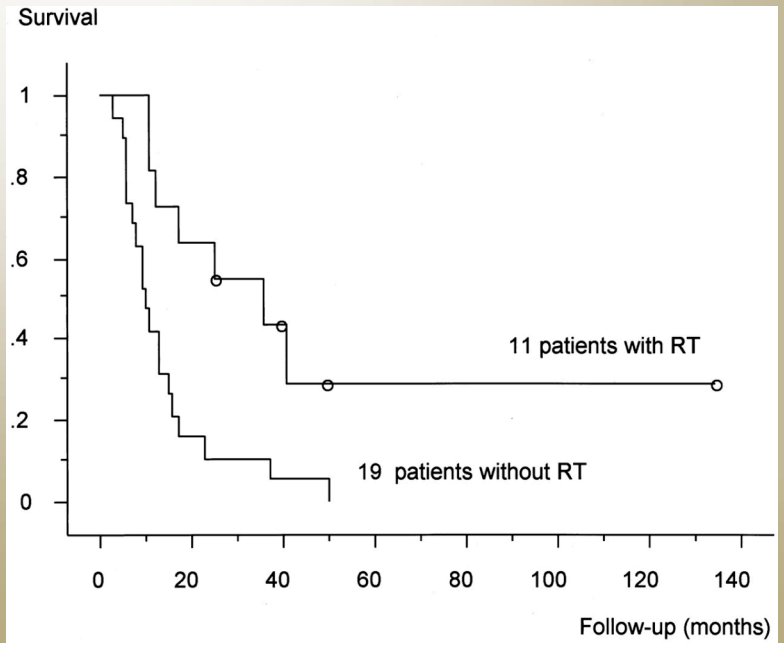
Impact of RT on Survival:

30 pts. Intralesional or no surgery:

RT p= 0.033

Multivariate analysis:

RT independently prognostic



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Photon - IMRT for paraspinal Chordomas and Rare Sarcomas

Terezakis et a., MSKCC, IJROBP 69(5), 2007

- 27 patients partially resected or unresected tumors
- treated 2001 – 2005
- IMRT photons
- 5/27 re-irradiation
- Histology:
  - 18 Sarcomas (6/18 chondrosarcomas)
  - 7 Chordomas
  - 2 Ependymomas

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Photon - IMRT for paraspinal Chordomas and Rare Sarcomas

Terezakis et a., MSKCC, IJROBP 69(5), 2007

Tx- Characteristics

Characteristic	Median	Interquartile range
Prescribed dose (cGy)	6,600	6,000–7,000
Fractions *(n)*	33	32–35
PTV (cm)	164	110–436
Maximal dose (cGy)	7,746	7,051–8,170
V_{95} (%)	94	92–97
Mean dose to spinal cord (cGy)	2,949	1,350–3,409
Maximal dose to spinal cord (cGy)	5,261	3,303–5,383
Previous radiation dose (cGy)	4,400	4,000–5,000

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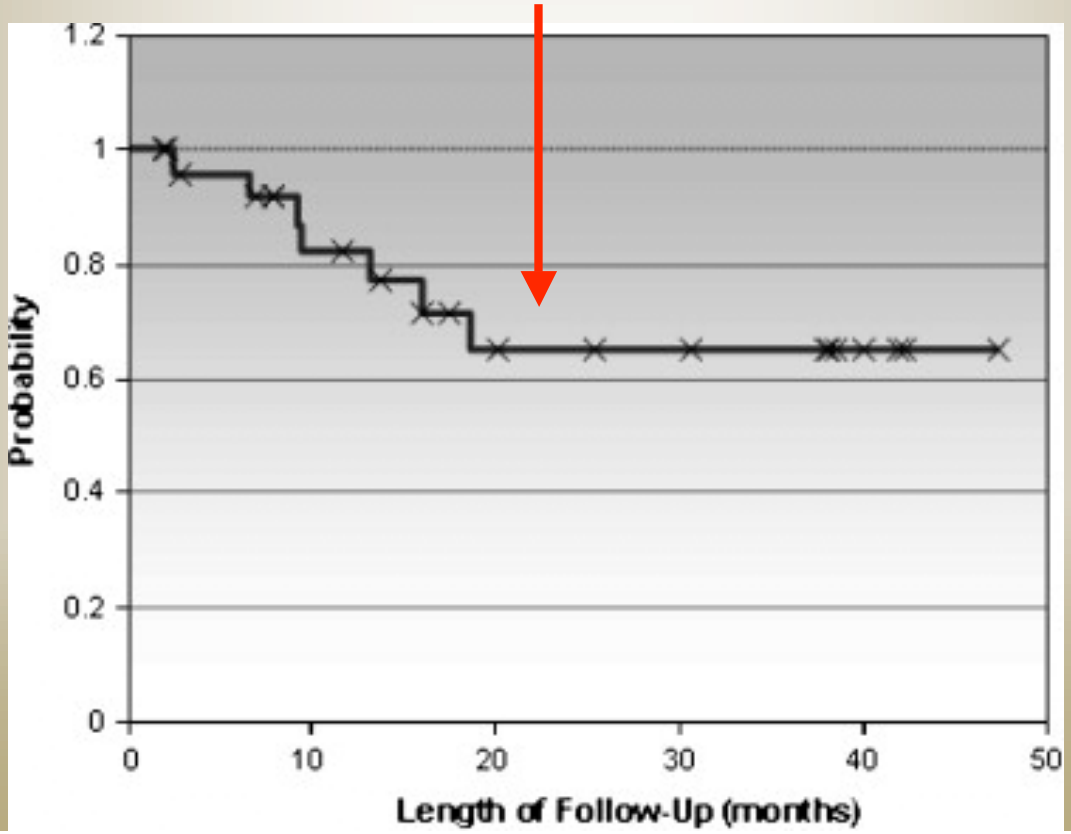
Photon - IMRT for paraspinal Chordomas and Rare Sarcomas

Terezakis et a., MSKCC, IJROBP 69(5), 2007

F/U period: range 2.1 – 47.3 months, median 17.4 months

Local control: 65% at 2 years only



Toxicity of photon RT for Soft Tissue Sarcomas

Mundt, Weichselbaum et al., U Chicago, IJROBP 1995

RT for extremity sarcomas

Dose Range (Gy)	Mild-Moderate	Severe	All
< 63	4/20 (20.0%)	0/20 (0%)	4/20 (20.0%)
≥ 63	10/39 (25.6%)	9/39 (23.1%)	19/39 (48.7%)
< 60	2/2	0/2	2/2
60–62.9	2/16 (12.5%)	0/16 (0%)	2/16 (12.5%)
63–65.9	4/22 (18.2%)	5/22 (22.7%)	9/22 (40.9%)
≥ 66	5/17 (29.4%)	5/17 (29.4%)	10/17 (58.8%)

Livi et al, U Florence, Am J Surg 2006

S + postop RT for extremity sarcomas

23 / 213 pts. With Severe Late Complications

	> 66 Gy	< 66 Gy
Bone fracture	**7**	**O**
Fibrosis	**5**	**0**
Per. Neuropathy	**3**	**0**
Wound complic.	**5**	**3**

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Is there a place for Proton/Particle Radiotherapy in the treatment of Soft Tissue Sarcomas ?

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Is there still a need to improve treatment for [illegible]ogroup of Sarc[illegible]nts?

Is it desira[illegible] reduce side effects and [illegible]prove functional outcome?

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Opportunity for Protons:

- Tumor subgroups with unsatisfactory local control:
  - Tumor size
  - Anatomic site
  - Status of tumor resection
- Reduction of Adverse Events
- Improvement of functional outcome
- Local control translates into survival

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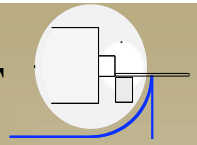

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There is a paucity of proton-literature specifically on Osteosarcoma and Soft Tissue Sarcomas

Essentially one has to anticipate Osteo- and STS outcomes data from extrapolating data from Chordomas and Chondrosarcomas

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Histologies

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- ***Osteogenic Tumors***
  - **Osteogenic Sarcoma**
  - (Ewing Sarcoma)
- ***Chondrogenic Tumors***
  - Chordomas
  - Chondrosarcomas
- ***Soft Tissue Sarcomas***
  - STS
  - Rhabdomyosarcoma

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MGH update: „Radiotherapy for Local Control of Osteosarcoma“

Delaney, Park et al., IJROBP 61(2), 2005

- Retrospective reivew of ***41 patients***
- RT 1980 – 2002
- Location: H&Skull Base 17 pts., extremity 8, spine 8, pelvis 7, trunk 1
- Chemo-Tx: 85%
- 23 patients (56%) combined photons/protons (H&Skull Base, Spine)
- 66% primary, 24% recurrent, 10% metastatic disease
- Dose: 10 – 80 Gy (median 66 Gy),

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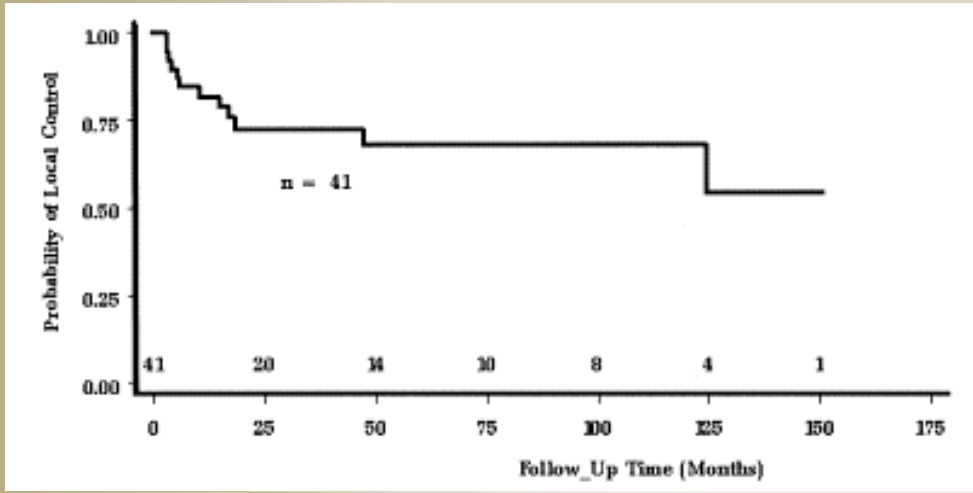
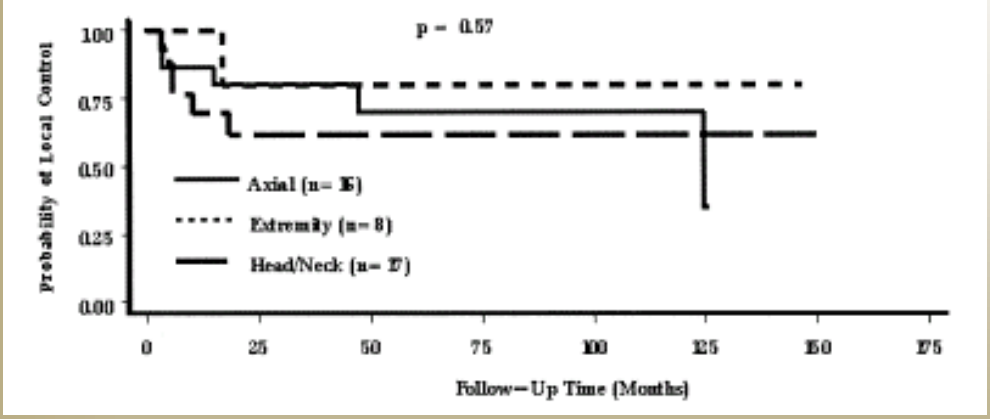
Delaney, Park et al., IJROBP 61(2), 2005



Local control:

68 % at 5-years



Local control:

Axial versus
Extremity versus
H&N location

P= n. s.

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Delaney, Park et al., IJROBP 61(2), 2005

Local control:

Total and subtotal resection: 78% versus Biopsy only: 40%

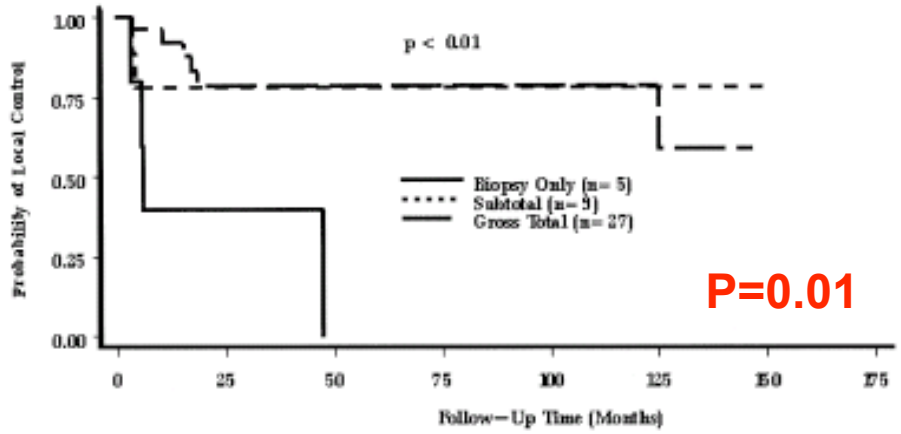

Fig. 2. Actuarial local tumor control according to extent of resection. Patients undergoing gross total and subtotal resection had improved local control compared with patients undergoing biopsy only ($p < 0.01$).

Dose-response ?

LC: 54 % <55 Gy ≥ 71% (P= n.s.)

NO subgroup analysis protons/photons versus photons

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Initial MGH / HCL report, 1995, IJROBP 31(3)

LOCALLY CHALLENGING OSTEO- AND CHONDROGENIC TUMORS OF THE AXIAL SKELETON: RESULTS OF COMBINED PROTON AND PHOTON RADIATION THERAPY USING THREE-DIMENSIONAL TREATMENT PLANNING

EUGEN B. HUG, M.D., MARKUS M. FITZEK, M.D., NORBERT J. LIEBSCH, M.D. AND JOHN E. MUNZENRIDER, M.D.

- 47 patients
- 1980-1992 tx with combined photons/protons
- 3 groups: Chordomas/Chondrosarc. (20 pts.), *Osteogenic Sarc. (15 pts.),* GCT, Osteo-and chondroblastomas (12 pts.)
- Dose: mean 73.9 Gy (Gr.I), *69.8 Gy (Gr.II),* 61.8 Gy (Gr. III) (55.3 – 82 Gy (RBE))
- F/U: mean: 3.2 years, min. 1/2 year, max. 11.3 yrs.)

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E. Hug et al. IJROBP 31(3), 1995

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Histology	No.	Anatomic site: Base of skull	C-spine	T-spine	L-spine	Sacrum	Total target dose*: Range (CGE)	Mean (CGE)
Group 1	(20)							
Chordoma	14	†	†	1	5	8	67.1–82.0	74.6
Chondrosarcoma	6	†	†	4	—	2	66.1–77.9	72.2
Group 2	(15)							
Osteogenic Sarcoma	15	7	3	—	2	3	61.1–80.0	69.8
Group 3	(12)							
Giant cell tumor	8	2	3	—	—	3	54.0–70.0	61.8
Osteoblastoma	2	1	1	—	—	—	63.9, 70.2	
Chondroblastoma	2	2	—	—	—	—	66.6, 70.2	

Histology	No.	Local Failure: Total	RT-mode*: Pre/-Postop	Postop	Bx only†	Extent of resection: Total	Subtotal	Bx only	Distant metastasis	Died of disease
Group 1	(20)									
Chordoma	14	5	4/10	1/2	0/2	1/4	4/8	0/2	2	1
Chondrosarcoma	6	0	—	0/4	0/2	0/4	0/2	—	0	0
Group 2	(15)									
Osteogenic Sarcoma	15	4	0/4	2/8	2/3	0/3	2/9	2/3	4	4
Group 3	(12)									
Giant cell tumor	8	1	1/1	0/5	0/2	0/3	1/2	0/3	1	0
Osteoblastoma	2	1		1/2	—	0/1	1/1	—	0	1
Chondroblastoma	2	0	—	0/2	—	—	0/2	—	0	0

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E. Hug et al. IJROBP 31(3), 1995

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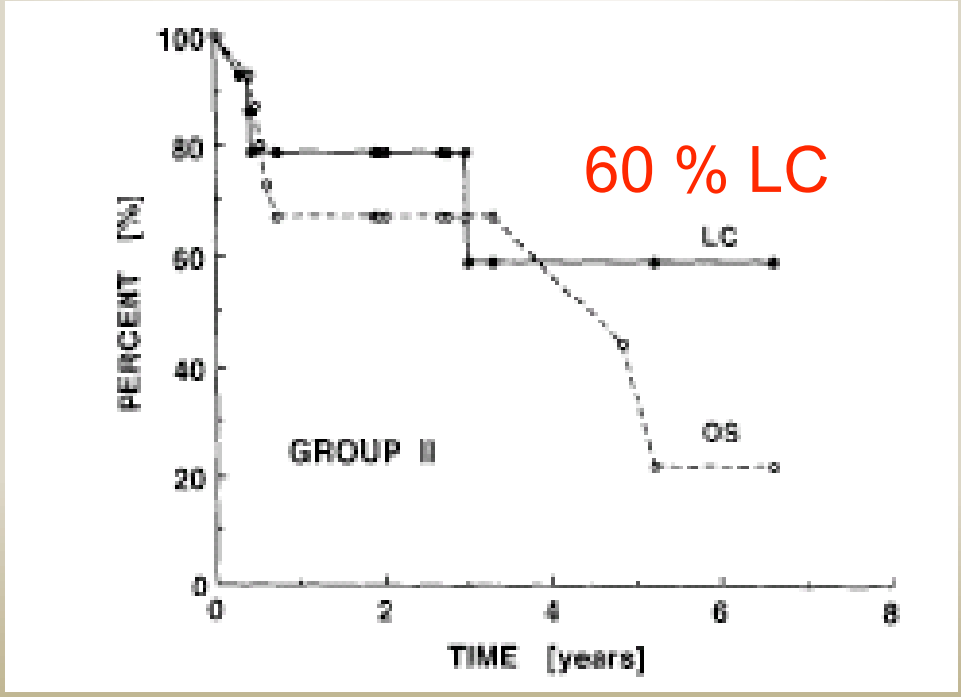
15 patients with osteogenic sarcoma of the axial skeleton

LC and OS after combined photon/proton RT



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Carbon Ion Therapy for Osteosarcoma

Local Control at 5 years: 65 %

before *carbon ion* RT

after *carbon ion* RT

Phase I/II Studie, Chiba, Japan

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Histologies

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- ***Osteogenic Tumors***
  - **Osteogenic Sarcoma**
  - (Ewing Sarcoma)
- ***Chondrogenic Tumors***
  - ***Chordomas***
  - ***Chondrosarcomas***
- ***Soft Tissue Sarcomas***
  - STS
  - Rhabdomyosarcoma

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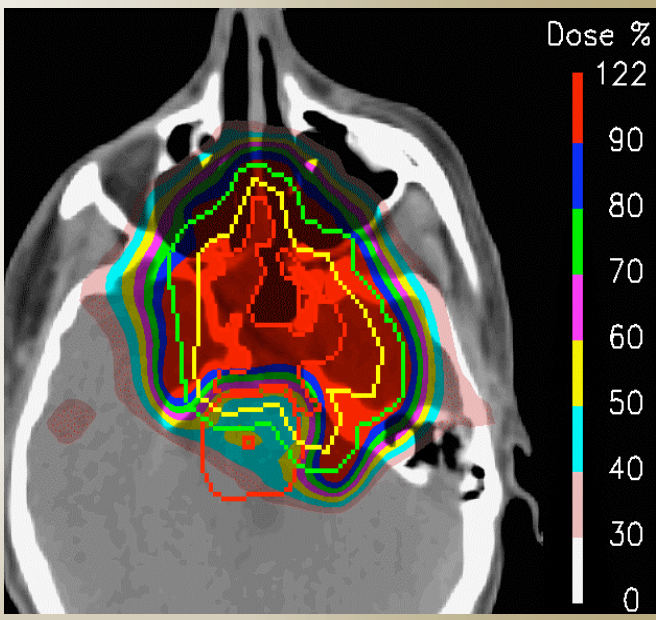
Proton-Radiotherapy for Chordomas and Chondrosarcomas:

- Practiced since 1973
- Published data: MGH, LBL; Loma Linda, PSI, Orsay
- Skull base and paraspinal location
- approx. 2500 patients treated with protons thus far



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Chordomas & chondrosarcoma: Population through 9/98

- 622 patients treated through 9/98
  - Chordomas (60%)
  - Mean age 39 (1.8 - 80 years)
  - Males 323 (52%)
  - Females 299 (48%)
  - Dose 66 - 83 CGE (CGE = p+ Gy X 1.1)
  - Median follow-up 41 months

Courtesy: John Munzenrider, ***MGH****/HCL*

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World wide largest experience: Mass. General Hospital (since 1974)

Chordomas: Local Control- Skull Base (Histology) 11/99

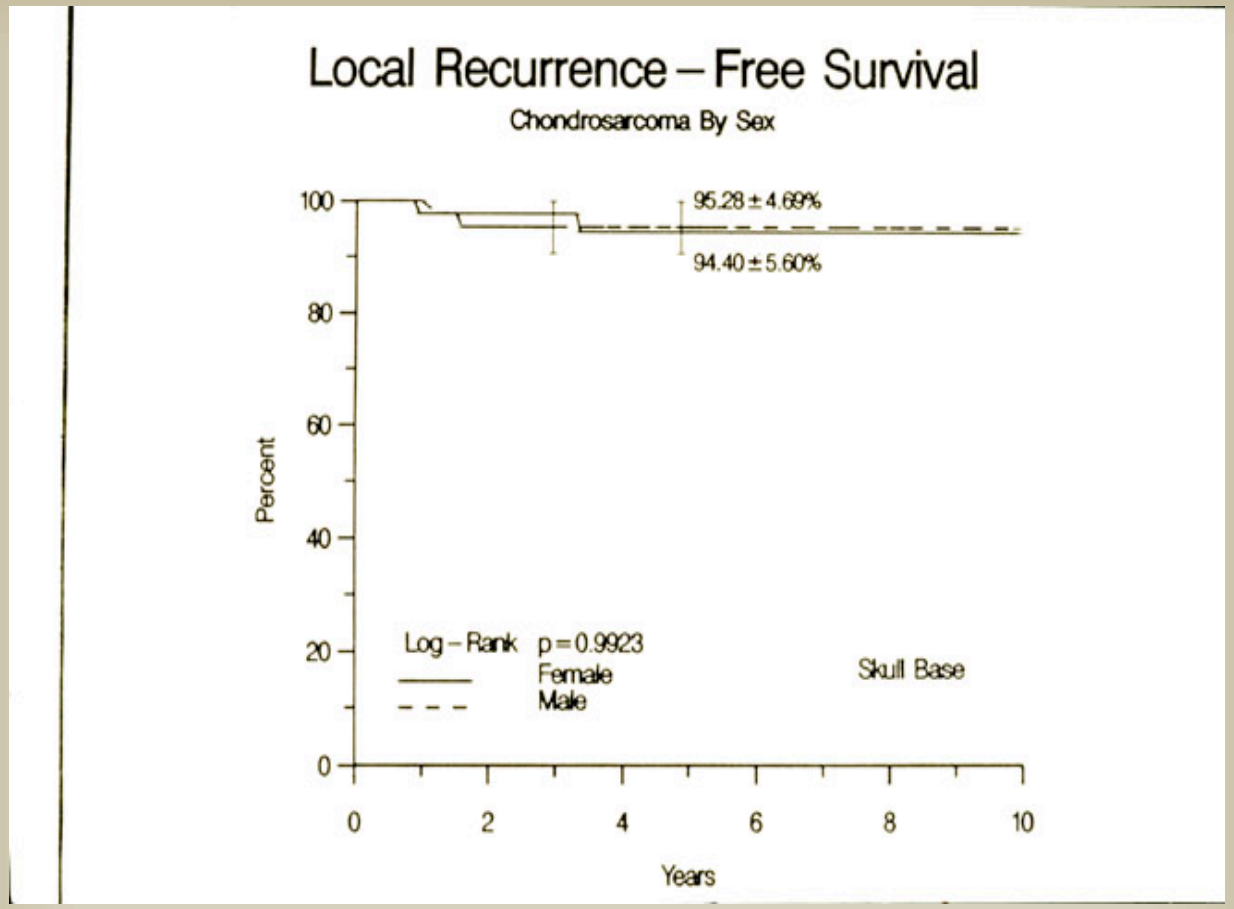
Local recurrence-free survival (skull base)

- Histology

	Chondrosarcoma	Chordoma	p
5 years	98 %	73 %	<.0001
10 years	95 %	54 %	<.0001

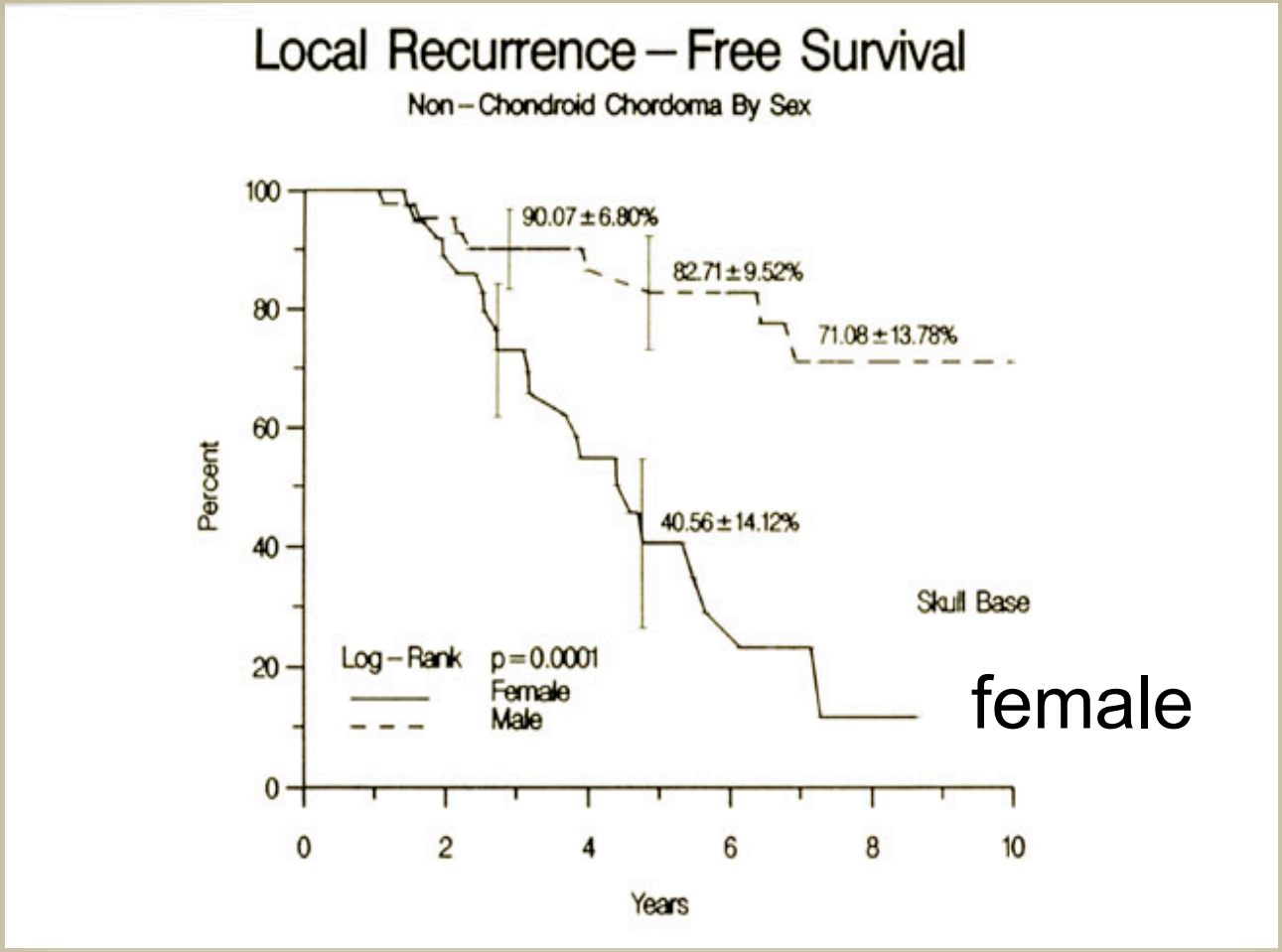
Courtesy: John Munzenrider, MGH/HCL

Long term tumor control: MGH data



Courtesy: John Munzenrider, MGH/HCL

Chordomas: Prognostic Factors



female

Courtesy: John Munzenrider, MGH/HCL

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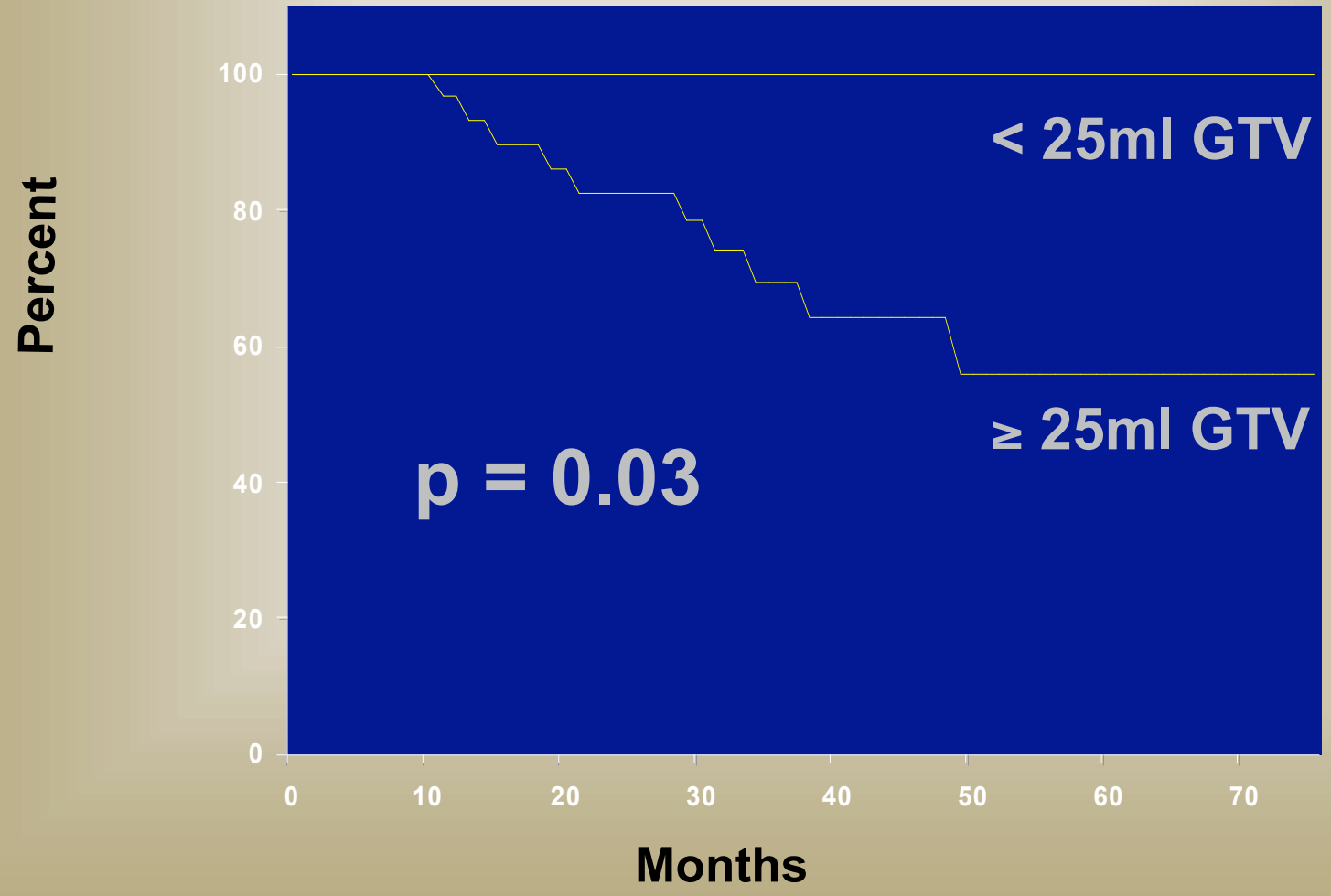
Proton RadiationTherapy (PRT)
for Chondrosarcomas and Chordomas of the Skull Base.

Hug, Laredo, Slater, Devries et al. J Neurosurg. 91:432-439, 1999

Tumor size at PRT and Local Control



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Proton RadiationTherapy (PRT)
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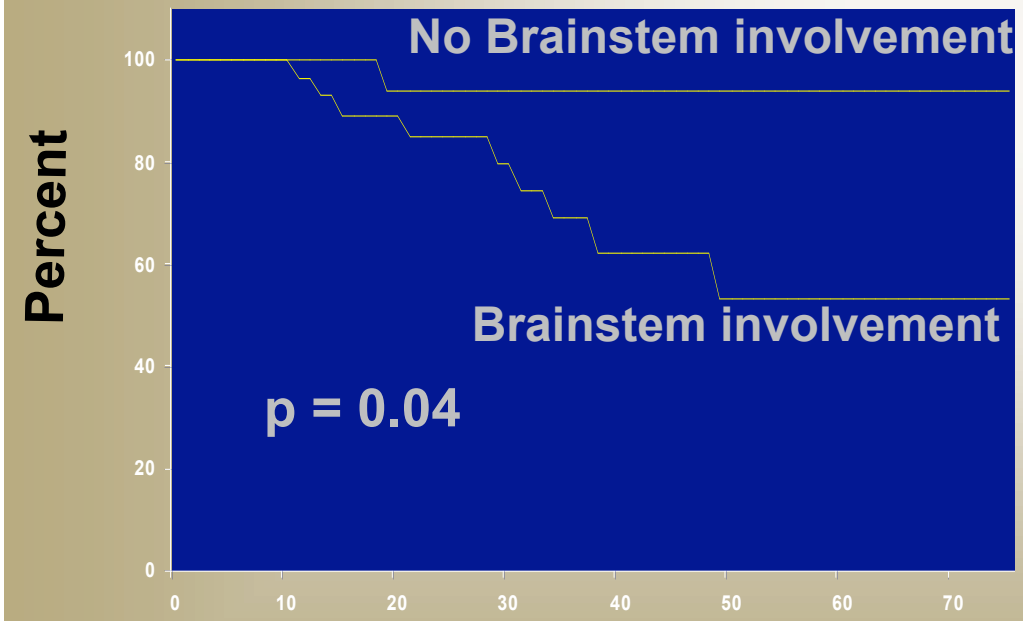
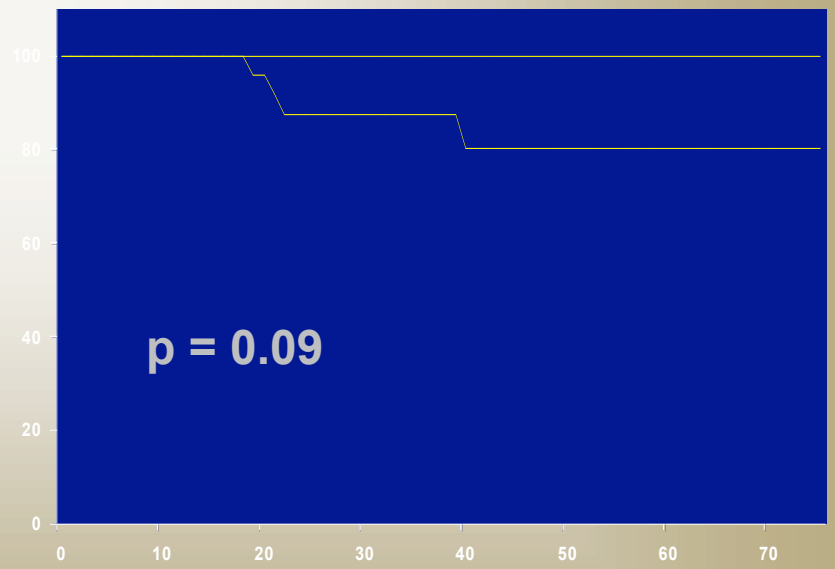
Hug, Laredo, Slater, Devries et al. J Neurosurg. 91:432-439, 1999

Local Control



Overall Survival



Months

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Proton-Radiotherapy for CHORDOMAS of the Skull Base and Axial Skeleton

Prognostic factors:

+++	Tumor Size
(++)	Skull Base versus Spine
+	Primary versus recurrent disease
(+)	Chondroid versus Non-Chondroid Pathology
++	Gender
(+)	Age
(+)	Pediatric versus Adult
+++	Ability versus Inability to deliver dose: Optimal/suboptimal Dose Distribution by involvement or abutment of critical structures
+++	Radiation Dose

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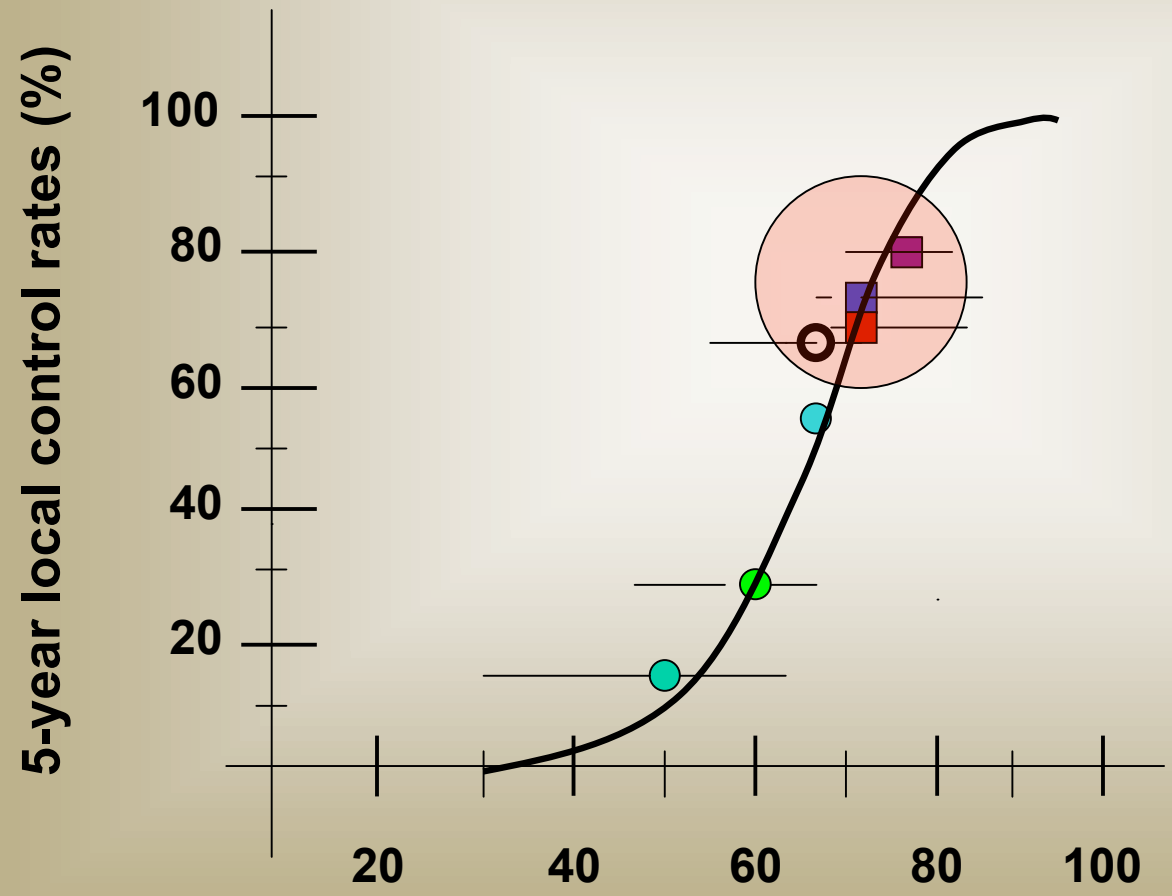
Chordomas of the Base of Skull



Photons

- Romero 1993
- Zorlu 2000
- Debus 2000

Protons

- Munzenrider 1999
- Ares 2007
- Hug 1999

C-Ions

- Schulz-Ertner

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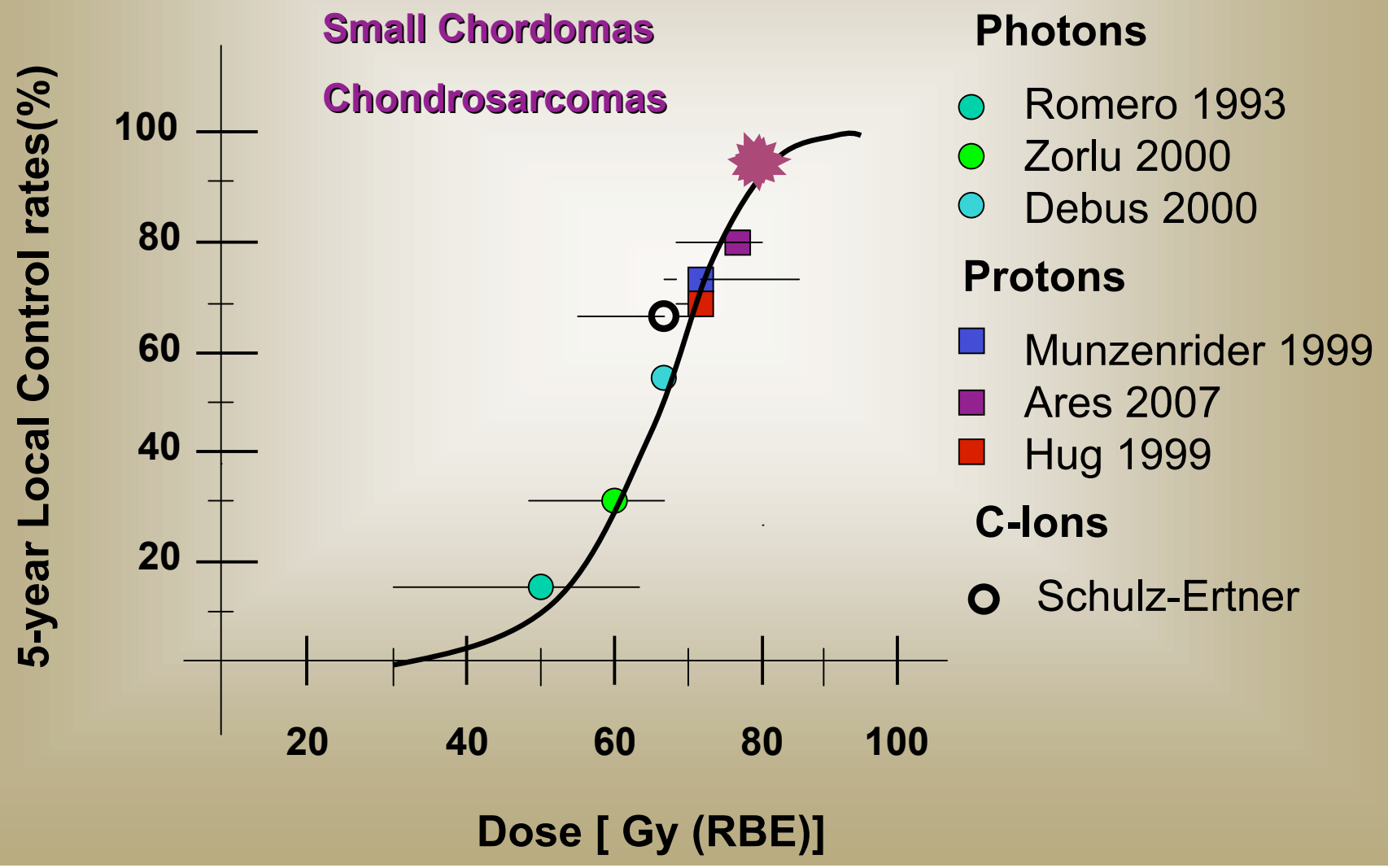
Chordomas and Chondrosarcomas of the Base of Skull



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Neoplasms of the Skull Base:
The present state of Tx for Chordomas and Chondrosarcomas

- The majority of ***Chondrosarcomas*** of the skull base are of low grade histology.
- Long-term outcome data suggest possible CURE for the majority of patients following subtotal surgical resection and high-dose radiation therapy (protons) to approx. 70 – 75 Gy.
- Gross total resection should not be pursued if increased surgical risks (the “last 5 % = 90% risk”)
- This represents a dramatic improvement of prognosis in a disease considered universally fatal 20 years ago

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RT for Skull Base Chordomas

GOAL:

Develop a risk-classification

low - intermediate - high

to correlate with recommendations for adjuvant Tx, i.e. treatment algorithm:,,

observation - aggressive Tx - palliative Tx

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Long-term Side Effects of Skull Base Irradiation

The risks of severe side effects following high dose,precision RT depend on several variables:

Tumor size, tumor compression of normal brain, critical structure involvement, dose to normal tissues, number of prior surgeries, general medical risk factors (diabetes, HTN, smoking,), KPS

Low-risk group: < 5%

High-risk group: > 10 % - ?? *

* RT as last modality after multiple failures

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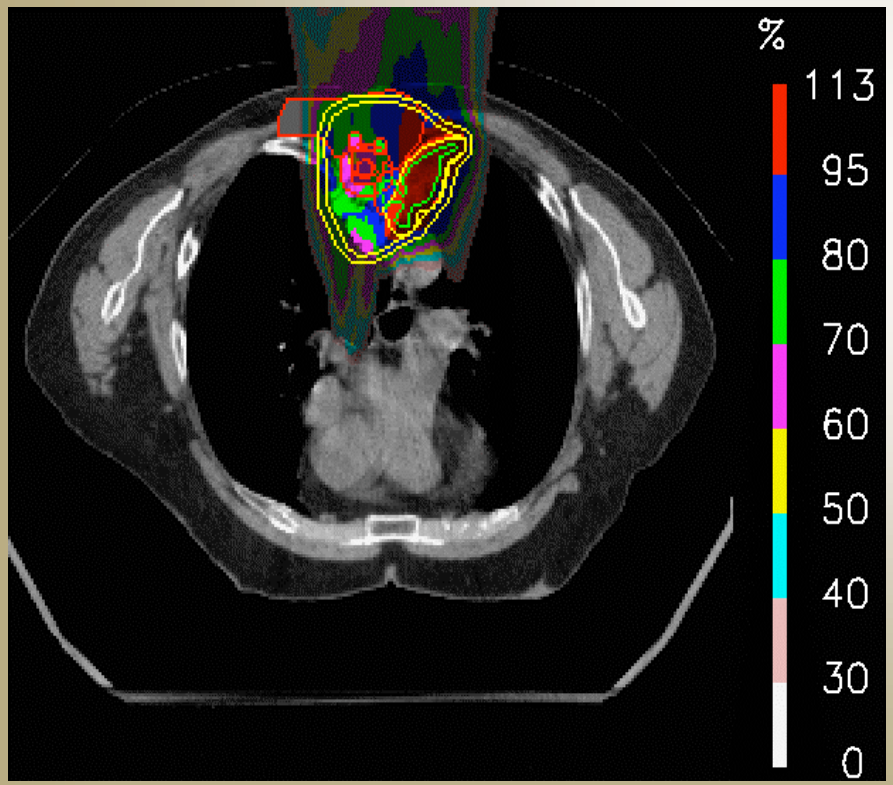
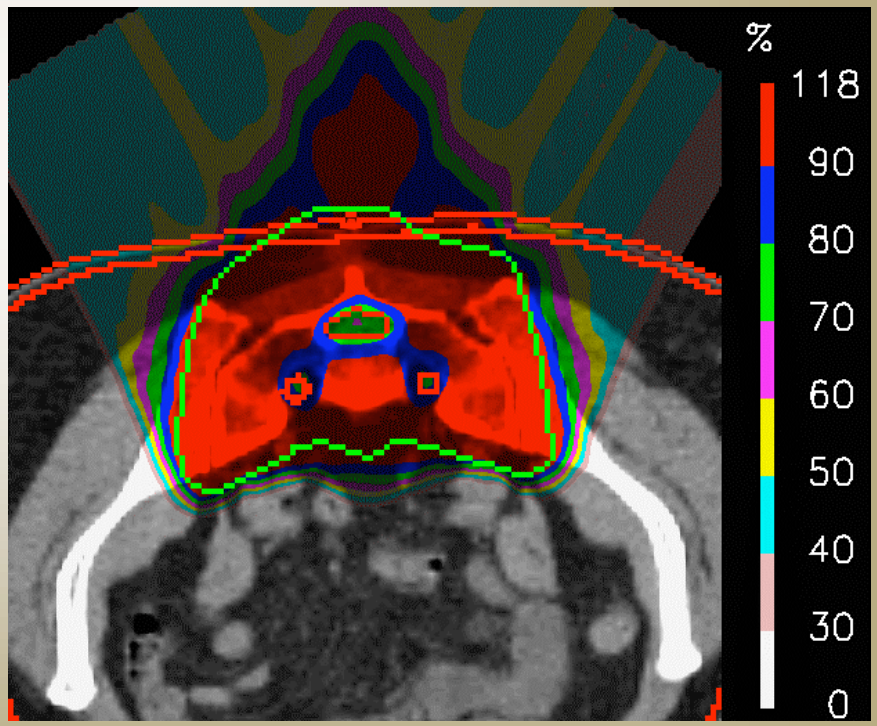
Extracranial *Chordomas of the Axial Skeleton* treated with spot scanning Proton Therapy at PSI:

Hans Peter Rutz et al.





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Extracranial *chordomas of the Axial Skeleton* treated with spot scanning Proton Therapy at PSI:

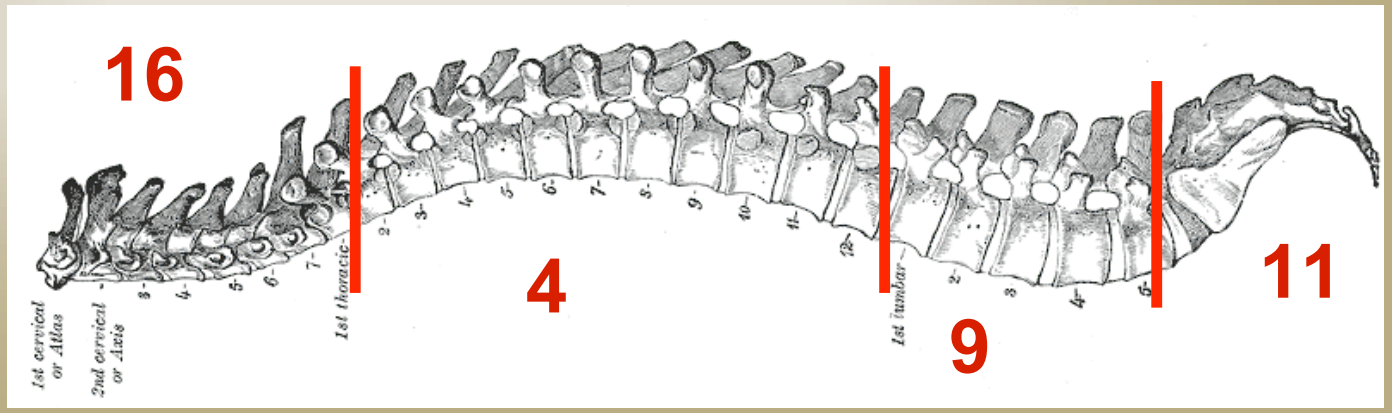
(Rutz et al.)

- Update of the initial publication (*Rutz HP et al. IJROBP 67(2):512; 2007*). Updated manuscript in progress.

- N = 40

- Tx: 1999 – 2005

- Location:



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Chordomas of the Axial Skeleton at PSI:

- Surgical Stabilization - Reconstruction (plates, screws, cage, rods etc.) in *21 / 40* patients.

- *19 / 40* patients without inserted instrumentation

- IMPT part of treatment plan since 2004

- Median total dose: 72 Gy (RBE) (range: 59.4 – 75.2 Gy (RBE))

- Follow-up period:
  - Minimum: 2 years (24 months)
  - Median: 43 months
  - Maximum: 91 months

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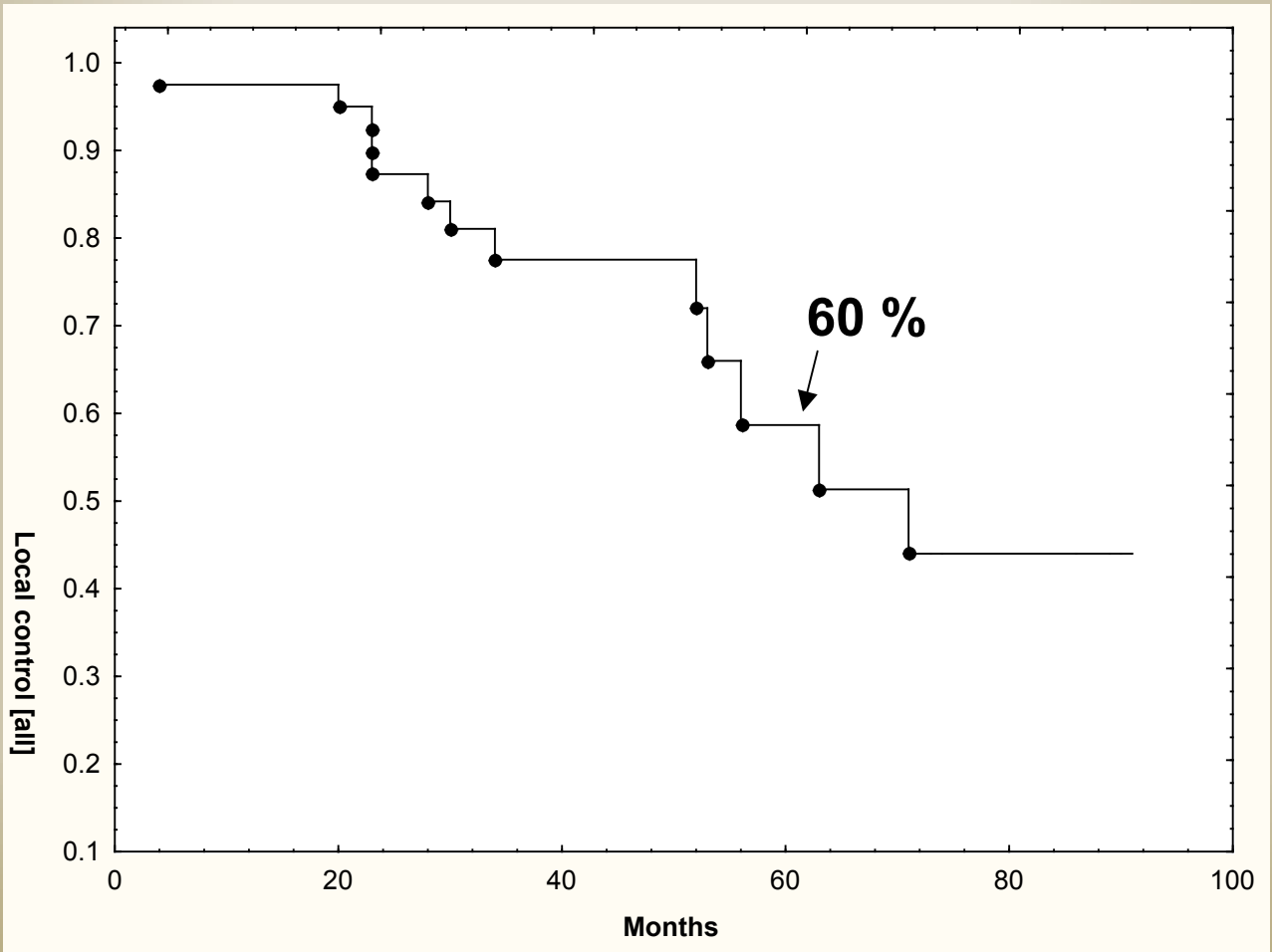
Chordomas of the Axial Skeleton at PSI: *5-year* outcomes data

Local control

13 / 40 patients with local failure



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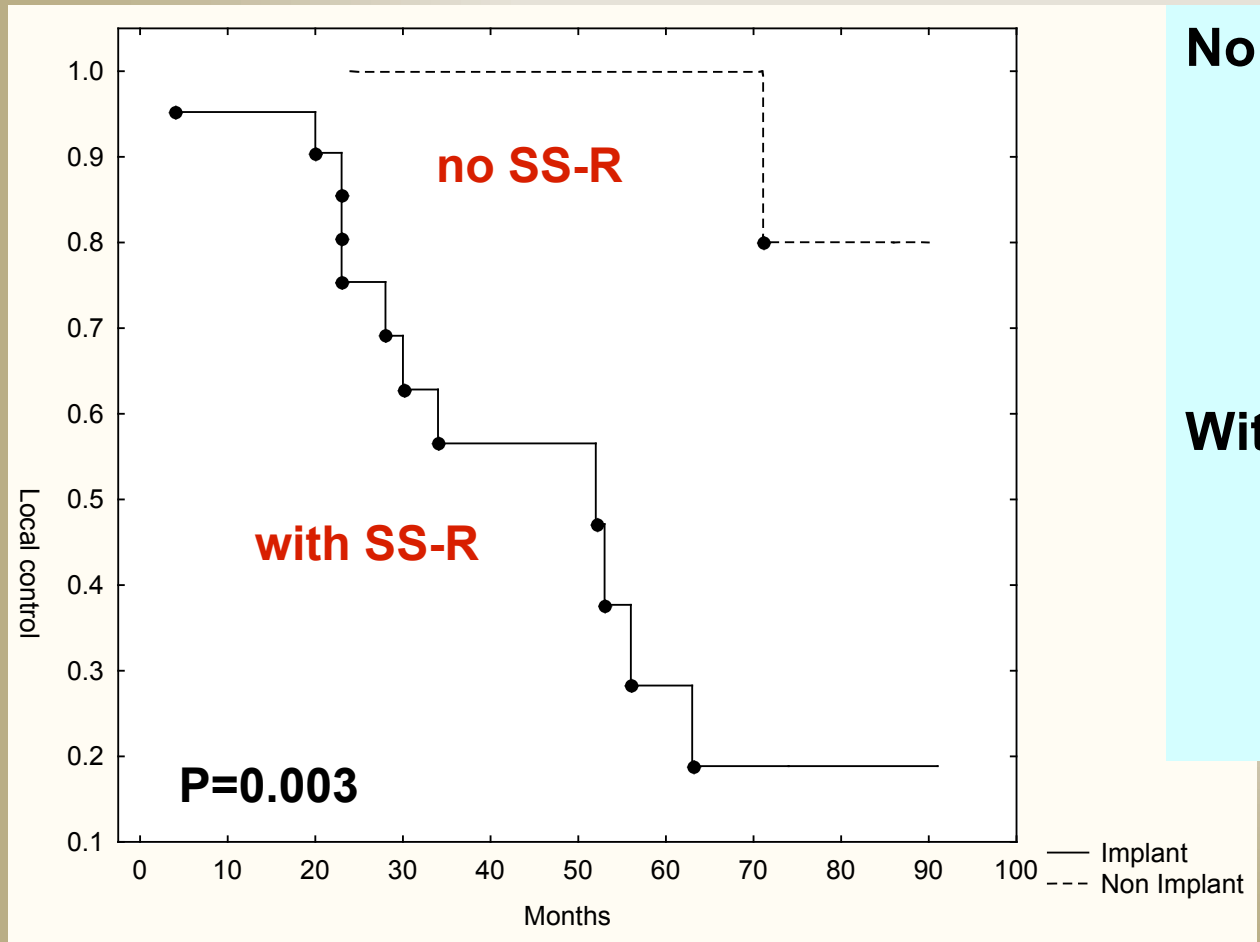
Chordomas of the Axial Skeleton at PSI: *5-year* outcomes data

Impact of Surgical Stabilization – Reconstruction (SS-R) on Local control



No SS-R:

- **only 1 LF in 19 pts.**

With SS-R:

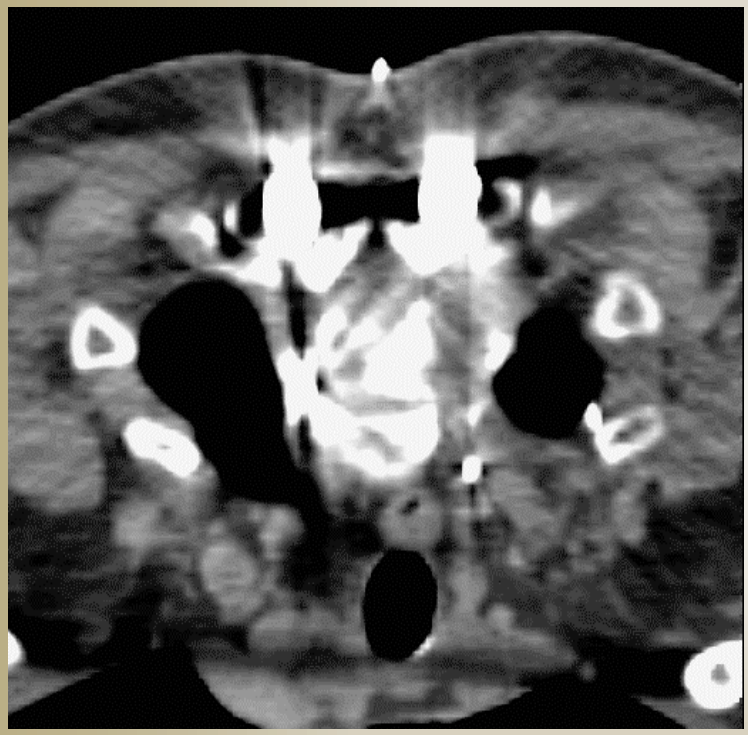
- **12 LF in 21 pts.**

or

- **12 / 13 Local Failures**

Extracranial chordoma

CT artifacts for surgical implants for stabilization / fusion on spinal axis tumors



- **Clinical factors:**
  - – Negative selection of patients with more advanced tumor – i.e. larger and more complex tumor presentation requiring more extensive surgery?
- **Treatment planning issues:**
  - – (Difficulties defining Targets?)
  - – Difficulties in dose calculation?
  - – Difficulties in range calculations?

Similar experience for passive scattering technique?

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Proton RT for *Sacral Chordomas*: MGH results

Park et al., MGH, IJROBP 65(5), 2006

- 27 patients, treated 1982 – 2002
- photons and/or protons
- 16 primary chordomas, 11 recurrent
- Combined S + RT = 21 patients
  - Mean dose 71 Gy(E) for primary
  - Mean dose 77 Gy (E) for recurrent chordoma
- RT alone: 6 patients
  - 60, 62, Gy photons and 73-77 Gy photons/protons

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Park et al., MGH, IJROBP 65(5), 2006

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Local Control following S + RT (21 pts.): Primary >>> Recurrent

Description	Time	Local control %	Disease free survival %	Overall survival %
14 *primary* chordomas treated by surgery & radiation	5 years	90.9 ± 8.7	90.9 ± 8.7	92.9 ± 6.9
	10 years	90.9 ± 8.7	90.9 ± 8.7	92.9 ± 6.9
7 *recurrent* chordomas treated by surgery & radiation	5 years	57.1 ± 18.7	42.9 ± 18.7	66.7 ± 19.3
	10 years	19.1 ± 16.8	14.3 ± 13.2	44.4 ± 22.2

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Park et al., MGH, IJROBP 65(5), 2006

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Local Control following RT alone (6 pts.):

Photons only:

- **60 Gy LFailure**
- **62 Gy LFailure**

Mixed photons / protons:

- ***77, 74, 77 Gy (E) Local control***
- **73 Gy (E) LFailure**

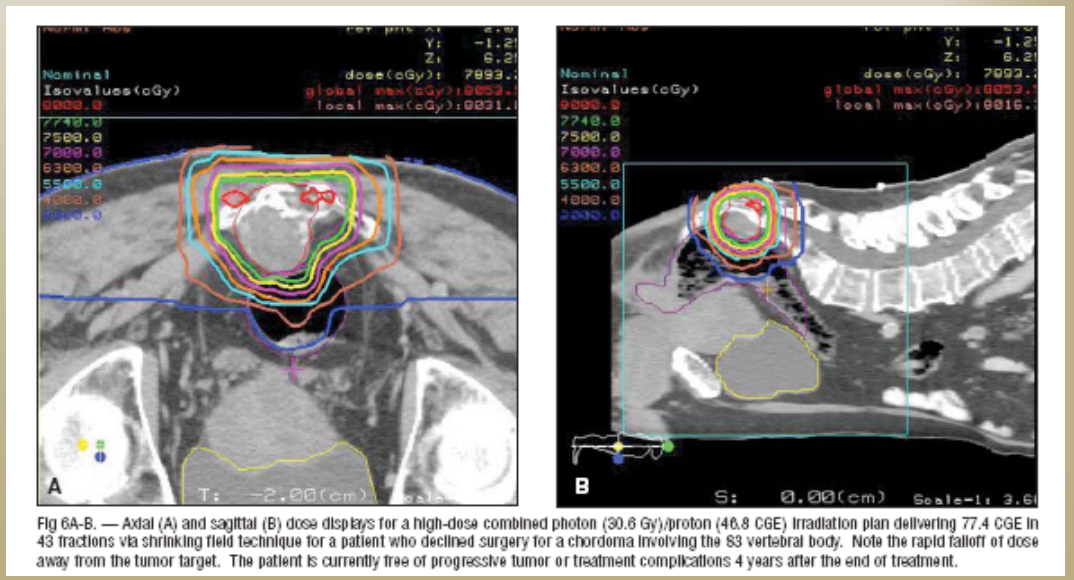

Fig 6A-B. — Axial (A) and sagittal (B) dose displays for a high-dose combined photon (30.6 Gy)/proton (46.8 CGE) irradiation plan delivering 77.4 CGE in 43 fractions via shrinking field technique for a patient who declined surgery for a chordoma involving the S3 vertebral body. Note the rapid falloff of dose away from the tumor target. The patient is currently free of progressive tumor or treatment complications 4 years after the end of treatment.

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Histologies

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- ***Osteogenic Tumors***
  - Osteogenic Sarcoma
  - Ewing Sarcoma
- ***Chondrogenic Tumors***
  - Chordomas
  - Chondrosarcomas
- ***Soft Tissue Sarcomas***
  - STS
  - Rhabdomyosarcoma

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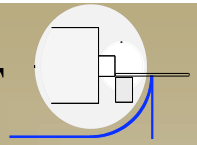

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Proton – Photon planning comparison

for Soft Tissue Sarcomas

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Planning Comparison for STS::
Photon IMRT versus *Proton IMPT*

Weber, Delaney et al., PSI + MGH, IJROBP 2004

Patient no.	Histology	Localization	Stage (UICC/AJCC)	Grade	CTV volume (cc)
1	Angiosarcoma	L1	IIB	3	41.4
2	Angiosarcoma	L1	IA	2	214.6
3	Leiomyosarcoma	T11–12	IA	1	520.1
4	Epitheloid sarcoma	T5–7	III	3	181.3
5	Chondrosarcoma	T5–7	Recurrent	1	360.5

Step 1: Planning assumptions: 77.4 Gy (RBE) to CTV with identical OAR constraints. Calculate target covergae and DVH‘s for normal tissues

Step 2: Attempt dose escalation with protons leaving OAR constraints unchanged

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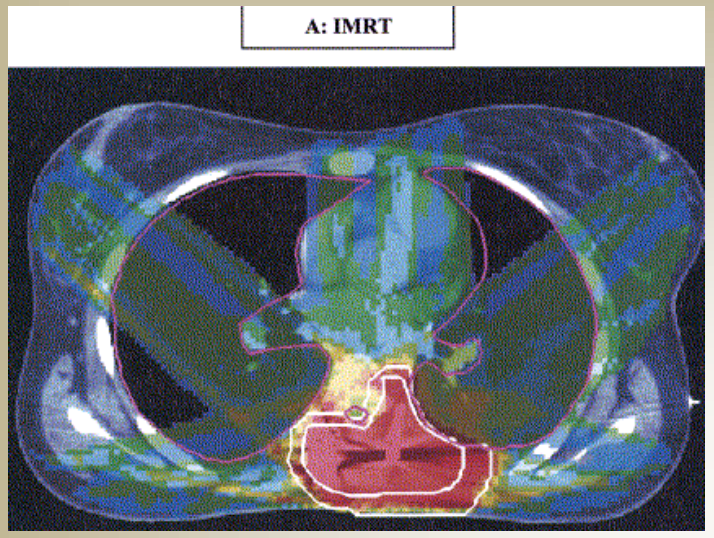
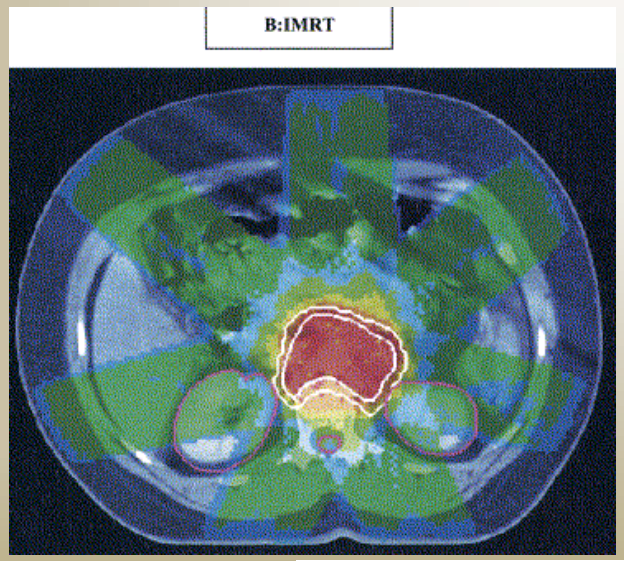
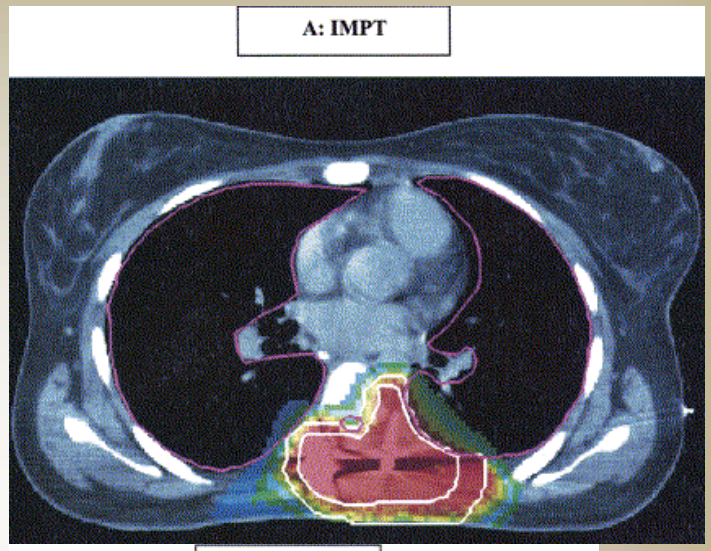
Weber, Delaney et al., PSI + MGH, IJROBP 2004 cont.

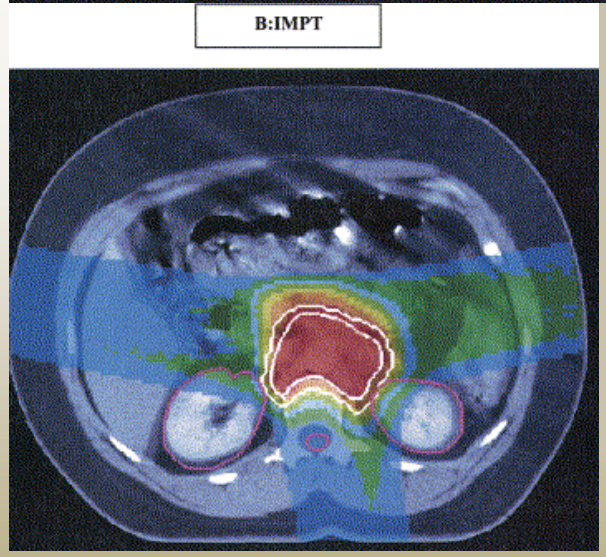
IMRT

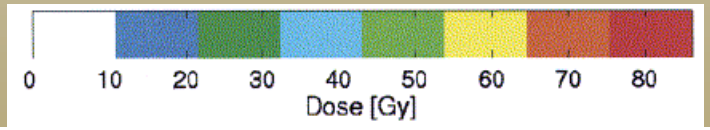




IMPT







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Weber, Delaney et al., PSI + MGH, IJROBP 2004 cont.

- **Integral Normal Tissue dose consistently reduced by IMPT (factor 1.3 – 25)**

OAR	IMRT: IMPT			
	D_{Max}	D_{Mean}	$D_{50\%}$	$D_{10\%}$
Spinal cord	1.0	1.4	1.7	1.1
Heart	6.0	24.7	30.8	35.3
Lung	1.1	6.5	32.7	11.3
Kidney	1.0	2.1	6.4	1.3
Stomach	2.6	6.9	40.0	7.4
Liver	1.0	1.3	1.1	1.0
Small bowel	*	*	*	*

- **Inhomogeneity coefficients and Conformity Indices were not significantly different**

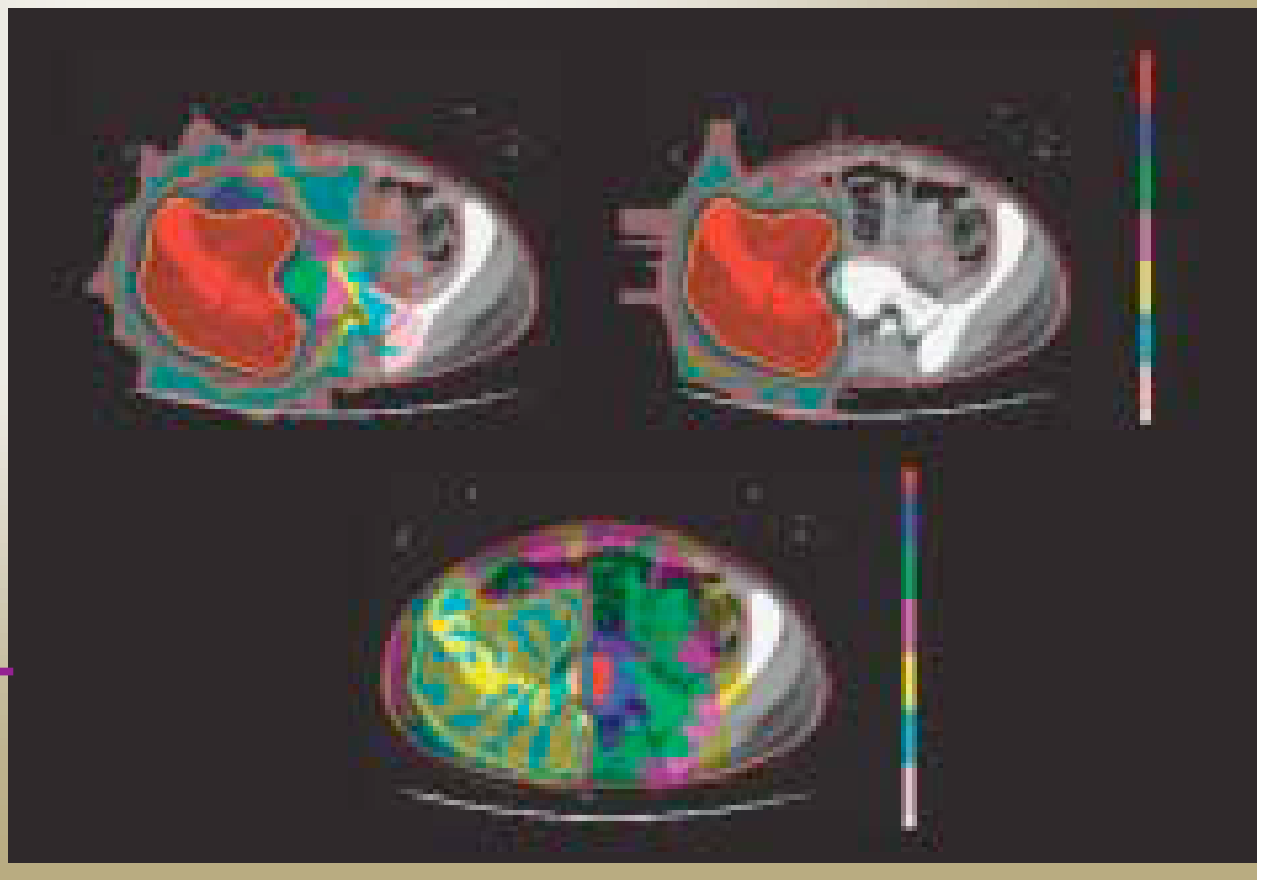
- The optimization IMPT algorithm was used to increase the total dose to the target by 10% and 20%, within the maximal OAR dose constraints.
  Dose escalation could be achieved in all patients, at the 20% (92.9 CGE) dose escalation level, regardless of tumor size, location, and geometry.

The Integral Dose Differential

Comparative dose distributions for 9-field photon intensity-modulated photon (IMXT) and 3-field intensity-modulated protonradiation (IMPT) treatment plans for a patient with pelvic Ewing's sarcoma.

(Courtesy of A.R. Smith and A.J. Lomax, in Delaney, Cancer Control, 2005)

IMXT **IMPT**



IMXT - IMPT

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Proton Therapy for *Adult Patients* with STS: the PSI experience

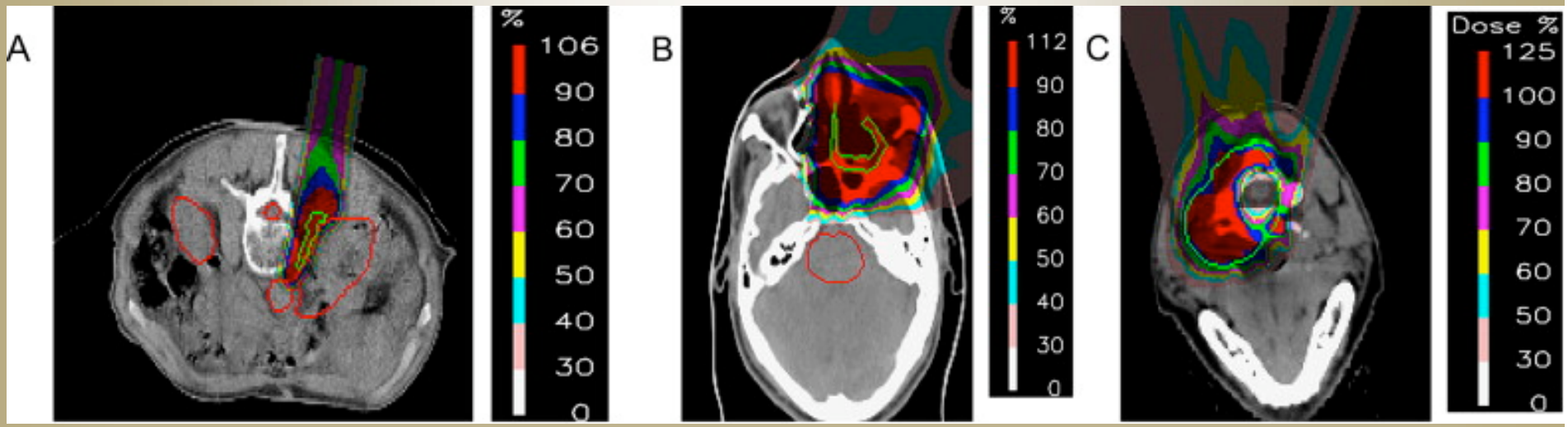
(Weber et al., IJROBP 2007)

- 13 patients with STS
- 1998-2005 tx with protons (6) or mixed protons/photons (7)
- Gross tumor: 9 / 13. R1 resection: 4 / 13
- Location: H&N, Skull Base, Paraspinal. Pelvis, Trunk, Reroperitoneal (2 pts), Shoulder (2pts.)
- Primary: 9 (69%), recurrent: 4 pts.
- Dose: median 69.4 Gy (RBE) (50.4 – 76 Gy (RBE))
- F/U: minimum 1 year, 12 pts. > 2 years, median for surviving patients: 48 months.

Weber et al., IJROBP 2007 cont.

Tumor histology: liposarcoma (*n* = 3), peripheral nerve sheet tumor (PNST, *n* = 3), leiomyosarcoma (*n* = 2), desmoid tumors (*n* = 2), angiosarcoma (*n* = 1), spindle cell sarcoma (*n* = 1), and malignant hemoangioperiocytoma (*n* = 1)

Treatment plan for (A) retroperitoneal, (B) head and neck, and (C) paravertebral sarcoma.
Sparing of the kidney (A), spinal cord (A, C), and brainstem (B).



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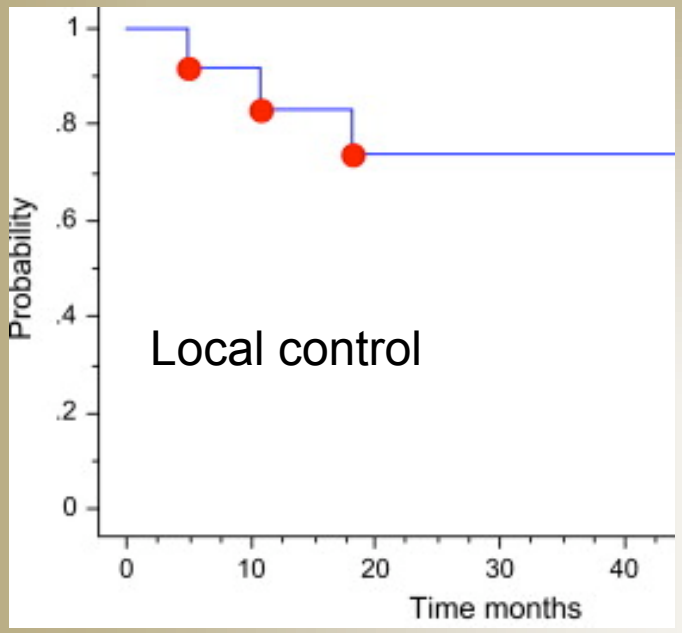
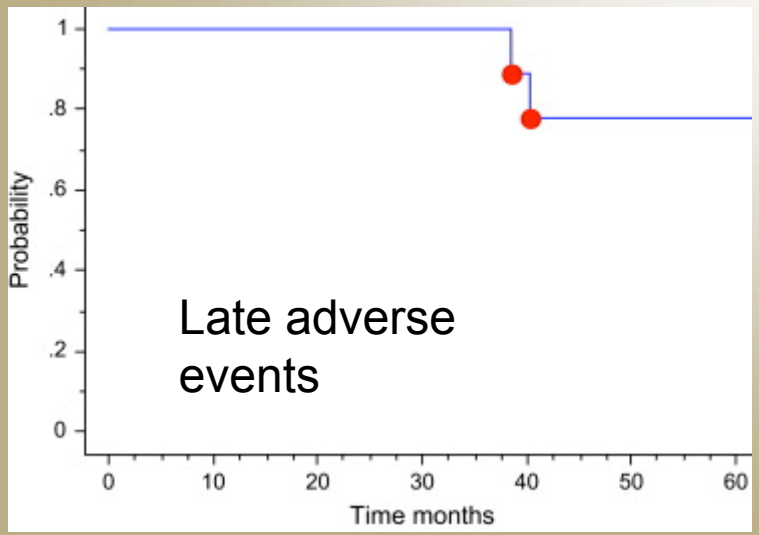
Weber et al., IJROBP 2007 cont.



<u>Local control:</u> 10 / 13 pts.

3-year actuarial LC: 74%



<u>Late adverse events</u>: 2 pts.

1 cataract

1 Grade 3 temporal lobe necrosis

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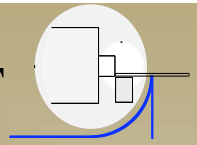

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Proton –Radiotherapy

for STS

in Children

CPT

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Proton Radiotherapy for *pediatric* STS treated at PSI

(Timmermann et al., PSI, IJROBP, 2007)

- 16 children with STS (including 12 with RMS or RMS-like histology)
- 14/16 children with chemotherapy
- Age: median 3.7 years (1.4-14.1 years). 9 children requiring anesthesia
- Tumor volume: 52 cc – 1225 cc
- Location: H&N, Skull Base, Paraspinal, Pelvis
- Proton RT Dose: median 50 Gy (RBE) (46 – 61.2 Gy (RBE) – doses according to CWS2002, MMT-95, COG-D9803 in 14 pts.
- F/U: median 18.6 months (4.3 -71 months)

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Timmermann et al., PSI, IJROBP 2007 cont.

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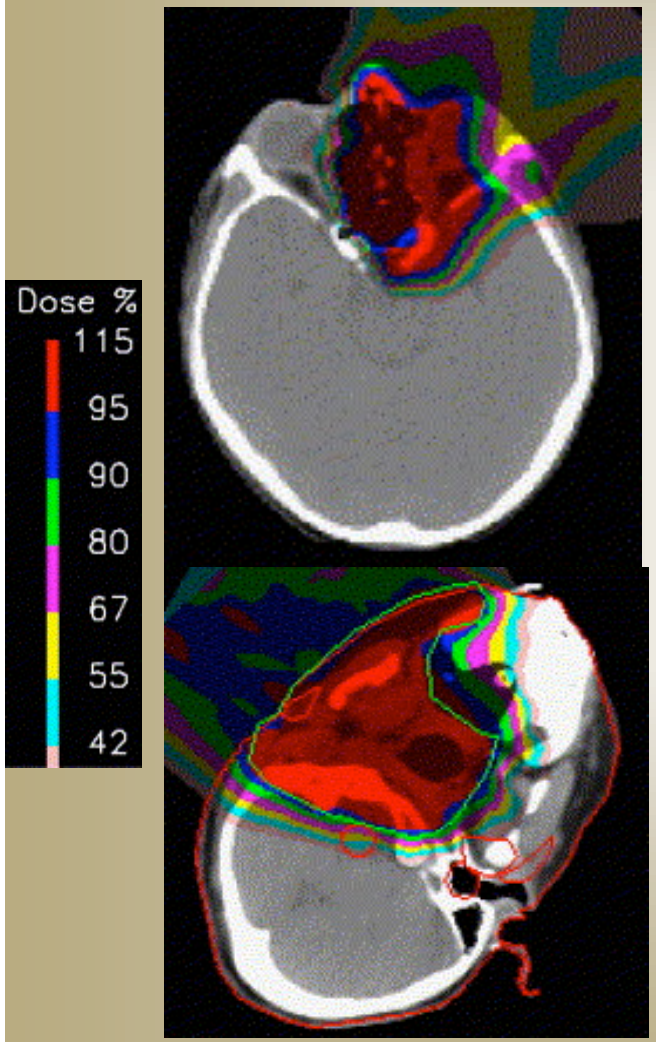
Outcome (very preliminary)



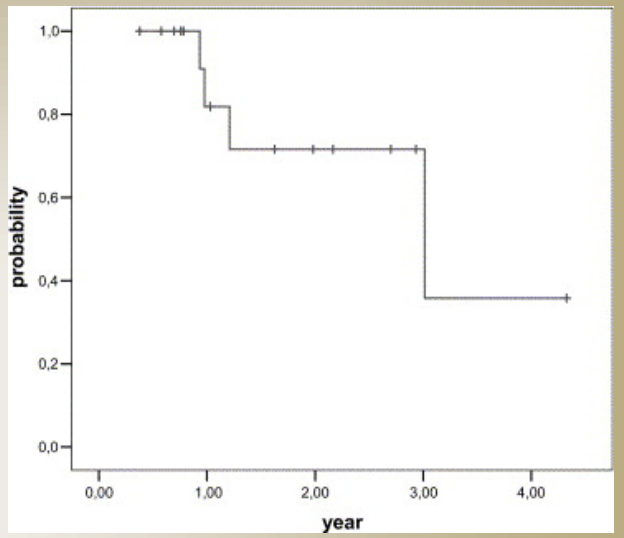
Local control:

12/16 = 75% at 2 years

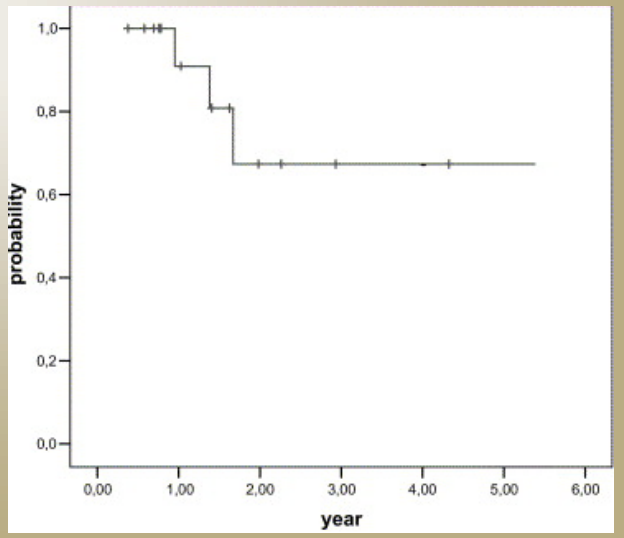
2/12 Failures in RMS- Group

2/4 in Non-RMS Group (after 50.4, 50 GY(RBE))

Local control



Overall Survival



Late toxicity: F/U too short

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Example Concept 2:

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Proton Radiation Therapy in the management of *pediatric base of skull tumors*

(Hug et al., MGH+LLUMC, IJROBP, 2002)

- 29 children with mesenchymal tumors
- 1992-1999 tx with protons or mixed protons/photons
- Age: median 12 years (1-19 years).
- Gross tumor: 28/29 patients (97%)
- Tumor histology grouped in „malignant“ versus „benign“
- Dose for malignant histologies according to adult experience
- F/U: mean 40 months (13 -92 months)

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Hug et al., MGH + LLUMC, IJROBP 2002 cont.

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	No. of Patients
TOTAL	29
Malignant Histology	20
Chordoma	10
Chondrosarcoma	3
Epithelioid Sarcoma	1
Malignant Fibrous Histiocytoma	1
Myxoid Sarcoma	1
Rhabdomyosarcoma	4

Median dose: 70 CGE (45 – 78.6)

Benign Histology	9
Giant Cell Tumor	6
Angiofibroma	2
Chondroblastoma	1

Median dose: 60.4 CGE (45 – 71.8)

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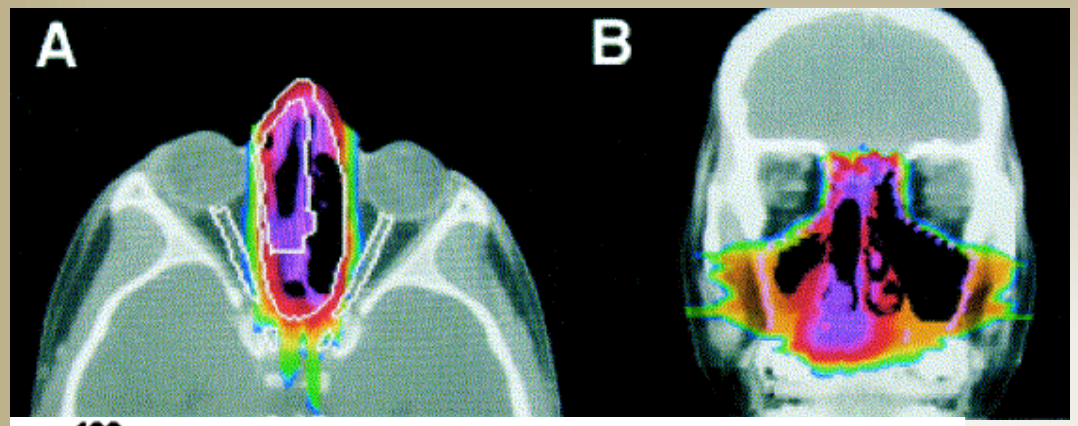
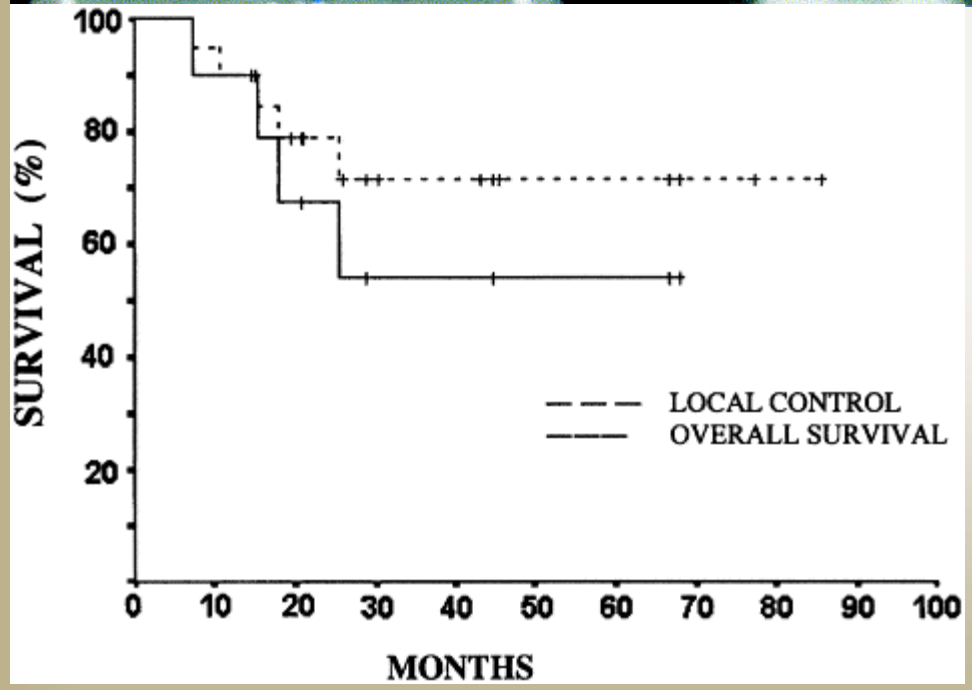
Example: 13 y.o. M with Malignant Fibrous Histiocytoma





CTV: 50.4 Gy (RBE)

GTV: 66.6 Gy (RBE)

20 pts. with Malignant Histology

5-yr LC: 72%

5-Yr OS: 56%

9 pts. Benign Histology

LC: 8/9, OS 100%

Severe late effects: 2 pts. (motor weakness, sensory deficit)

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Proton Radiotherapy for Sarcomas: Potential and Future

Pre-operative Proton-Radiotherapy:

- Presently infrequently performed for logistical reasons (referrals initiated after surgery)
- Dose-sparing of skin and SC-tissues identified as surgical access route for deep seated tumors.
- Further decrease of irradiated volume (compared to postop.RT)
- Mainly for deep seated tumors, including extremity sarcomas.
- Potential of decreasing wound healing delay or wound complications

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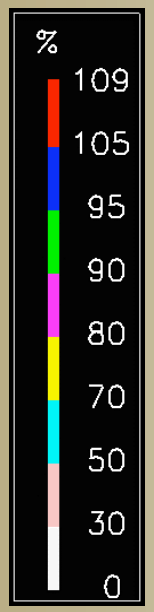
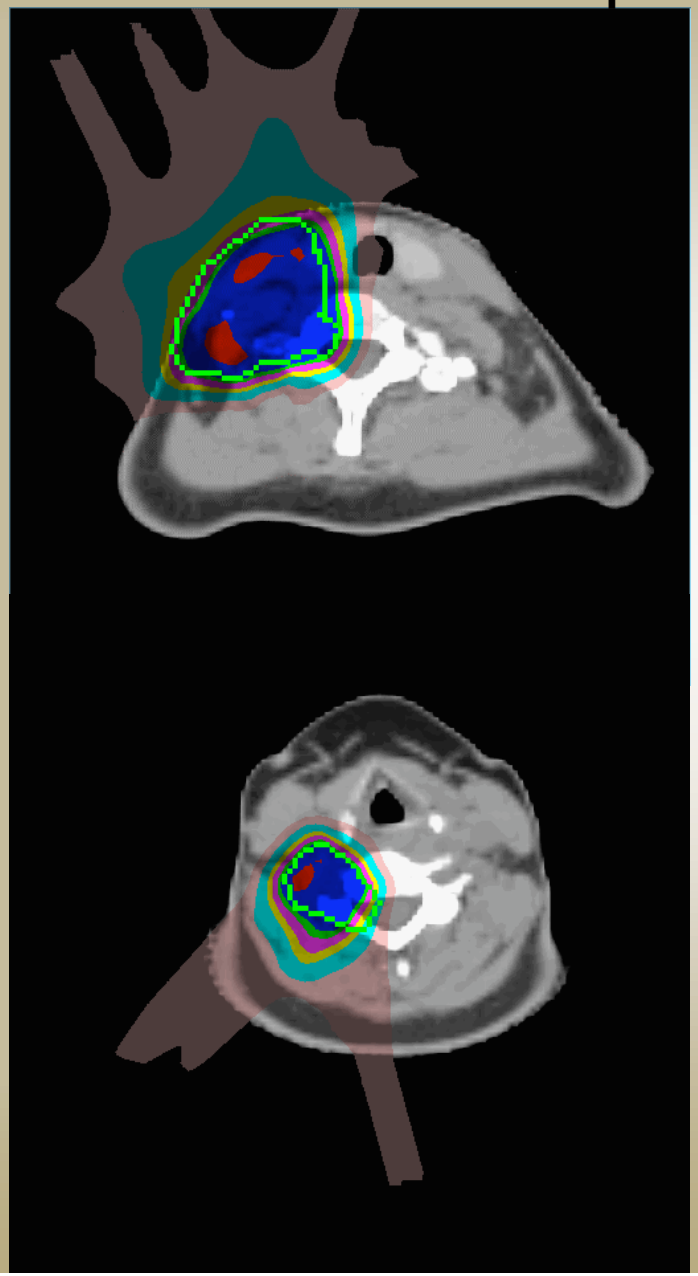
Patient: S.S., 44 y.o., Grade 2 neurofibrosarcoma
R1 resection versus possible small residual





Initial Volume (CTV) = preop. tumor extension plus margin plus scar

50 Gy (RBE) / 2 Gy

Boost volume (GTV) = postop. residual tumor plus 5 mm

18 Gy (RBE) / 2 Gy

Total dose: 68 Gy (RBE)

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Proton Radiotherapy for Sarcomas: Potential and Future

Proton-Radiotherapy for *EXTREMITY* Sarcomas:

- **Presently only rarely performed**
- **Decrease of Irradiated Volume, i.e. decrease of muscle mass at risk of fibrosis**
- **Potential to spare circumferential dose to bones, i.e. decreasing the risk of late fracture.**

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Proton Radiotherapy for Sarcomas: Potential and Future

Proton-Radiotherapy for *CENTRAL* Sarcomas:

- Well established indications for chondrogenic sarcomas - H&N, skull base, paraspinal, pelvis .
- Protons an excellent tool for areas, where doses > 70 Gy remain difficult to deliver
- There is a significant need to improve local control for unresectable /subtotally resected sarcomas in these locations.
- Excellent tool for pediatric population

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Proton Radiotherapy for Sarcomas: Potential and Future

Proton-Radiotherapy in case of *co-morbidity* unrelated to sarcoma and reducing normal tissue tolerance:

- **Example: Irritable bowel syndrom, Inflammatory bowel disease, Crohn‘s disease, Ulcerative Colitis and paraspinal, retroperitoneal, or pelvic sarcoma**
- **Reduction of Integral Volume, i.e. reduction of low-moderate dose important for adult patients**
- **„Safe“ OAR dose levels not established for affected organs**

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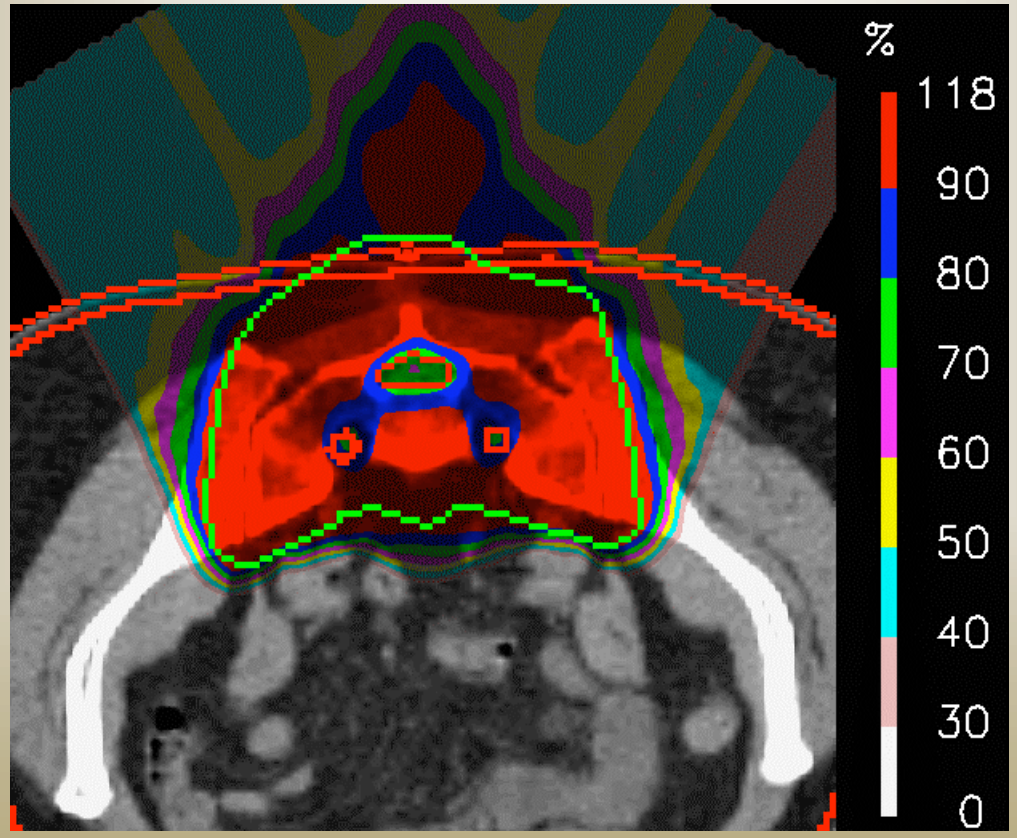
Proton-Radiotherapy:

Advantage of reduced normal tissue dose in adult patients with unrelated co-morbidity

Example: Sacral Sarcoma coincident with diagnosis of Crohn‘s disease



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Proton Radiotherapy for STS: possible trial designs

Scenario 1: „Proton- versus Photon - Radiotherapy for STS“. A Phase III Trial using moderately high dose levels

Scenario 2: „ High dose RT for high-risk STS using stereotactic precision-modality radiotherapy“. A Phase II trial open for QA-approved equipment

Scenario 3: „Dose-escalation study using proton/particle radiotherapy for unresectable STS“

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Proton Radiotherapy for STS: possible trial designs

Scenario 1: „Proton- versus EB-Photon Radiotherapy for ….Sarcoma“. A Phase III Trial using moderately high dose levels

Scenario 2: „ High dose RT for high risk Sarcoma using stereotactic precision-modality radiotherapy“. A Phase II trial open for QA-approved equipment

Scenario 3: „Dose-escalation study using proton/particle radiotherapy for unresectable ..S“

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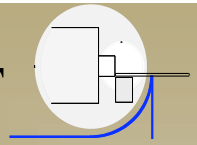

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THANK YOU