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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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Histologies

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

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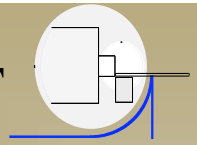

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Is there a place for Proton/Particle Radiotherapy in the treatment of Sarcomas ?

=

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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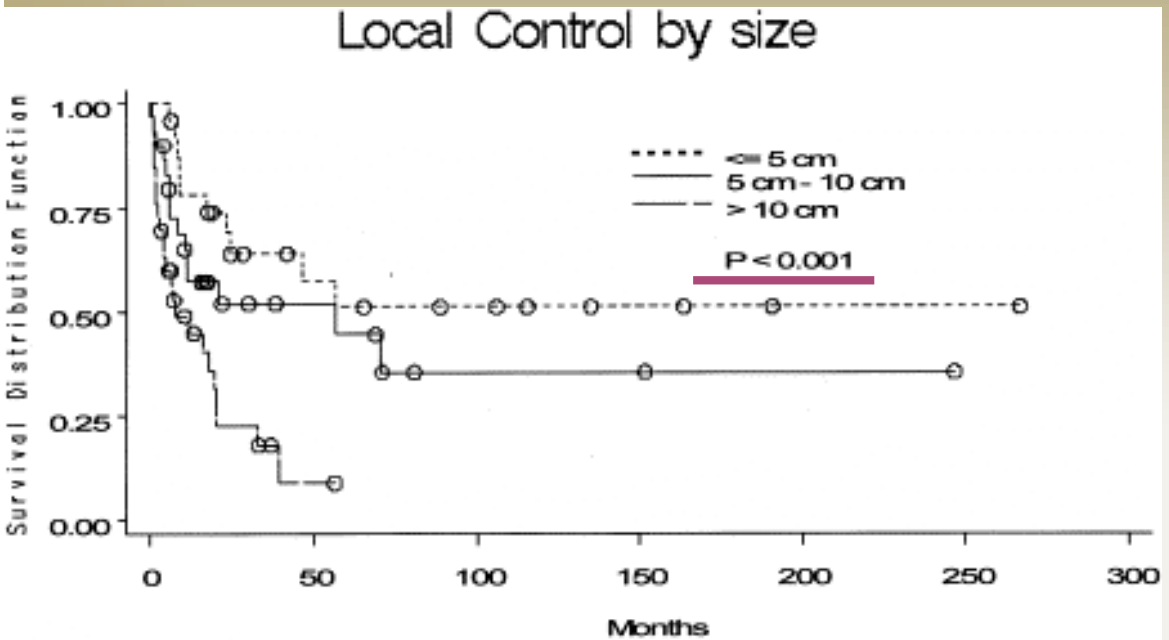
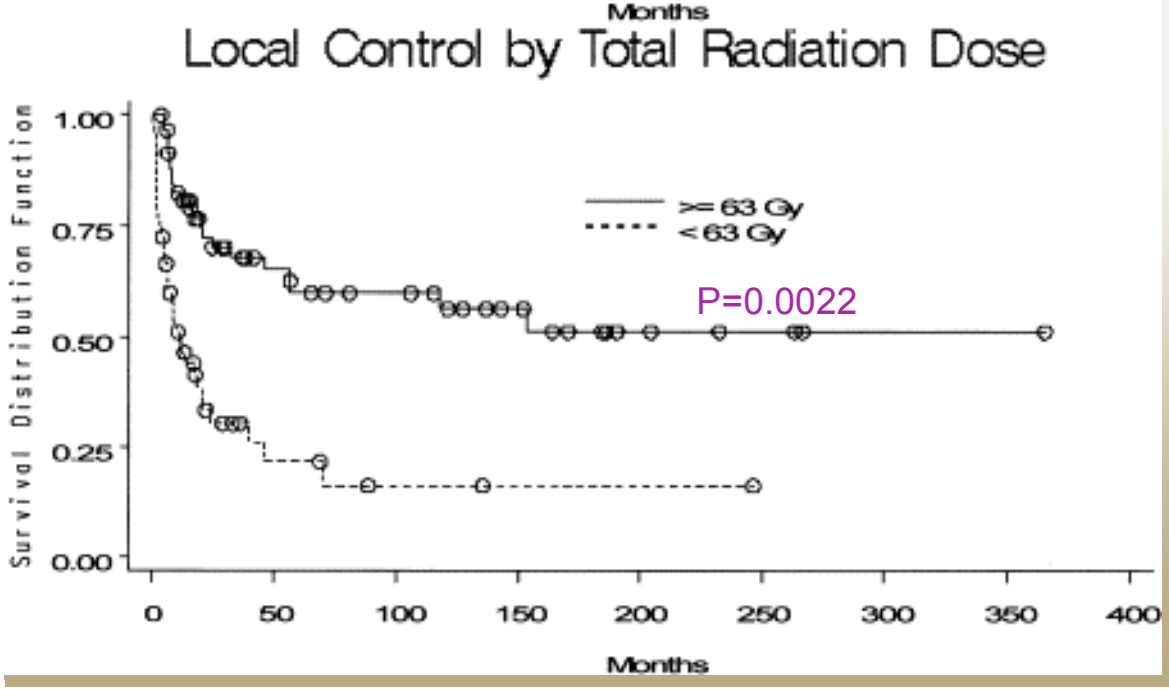
RT for *UNRESECTED Soft Tissue Sarcoma*

(Kepka, Delaney et al., MGH, IJROBP, 2005)

- 112 patients with STS
- RTx between 1970 - 2001
- Gross disease (unresected or unresectable)
- RT Dose: median 64 Gy (21 % > 70 Gy, max. 87.5 Gy) (included 4/112 pts. with Proton-RT
- F/U: median 139 months (max. 365 months)
- Location: 43% extremities, 26% retroperitoneal, 24 % H&N, 7% trunk
- Tumor size: median 8 cm (max. 30 cm)

Kepka, Delaney et al., MGH, IJROBP, 2005 cont.





Prognosticators for LC –multivariate analysis:

Size

RT-Dose

AJCC Stage

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Kepka, Delaney et al., MGH, IJROBP, 2005 cont.

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Grade 3-4 Complications: 18/112

	Type of complication	Radiation dose (details on techniques)
9/18: wound healing delay or skin necrosis	WHD requiring amputation	76 Gy (1.2 Gy per fraction, b.i.d)
	WHD coupled with massive tissues necrosis requiring amputation	75 Gy (1.8 Gy per fraction, b.i.d)
	WHD requiring amputation	64 Gy (2 Gy per fraction)
	WHD requiring major surgery	66 Gy (2 Gy per fraction)
	WHD requiring major surgery	75 Gy (60 Gy with 2 Gy per fraction)
	WHD requiring major surgery	76 Gy (2 Gy per fraction, b.i.d)
	WHD requiring major surgery	68 Gy (1.8 Gy per fraction)
	Skin necrosis and cellulites after minor injury requiring skin graft	70 Gy (2 Gy per fraction)
9/18 fibrosis, bone necrosis, ureteral and sigmoid stenosis, SM	Skin necrosis requiring skin graft	68 Gy (2 Gy per fraction)
	Severe neuropathy	66 Gy (2 Gy per fraction)
	Severe neuropathy	75 Gy (1.8 Gy per fraction, b.i.d)
	Severe fibrosis, limb strength leaving useless leg	68 Gy (2 Gy per fraction)
	Severe fibrosis, limb strength leaving useless leg	70 Gy (50 Gy at 2 Gy and 20 Gy IORT)
	Bone necrosis and bone fracture	65 Gy (2 Gy per fraction)
	Ureteral stenosis requiring surgery	68.5 Gy (2 Gy per fraction)
	Ureteral stenosis requiring surgery	56 Gy (2 Gy per fraction)
	Sigmoid stenosis requiring surgery	68.5 Gy (2 Gy per fraction)
	Radiation induced malignancy	66.5 Gy (1.8 Gy per fraction)

8% < 68 Gy dose ≥ 26 %

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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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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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Histologies

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- *Osteogenic Tumors*
- *Chondrogenic Tumors*
- *Soft Tissue Sarcomas*

- *Indications and Sites presently treated with Protons*
- *Published Data*

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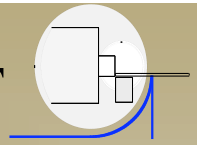

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- ***Indications and Sites presently treated with Protons***
  - **Skull Base**
  - **Paraspinal / Neck /Trunk / Pelvis**
  - **(Extremities)**
- ***Published Data***
  - **Retrospective review**
  - **Prospective data gathering**
  - **Phase I-II studies**
  - **(obviously) no Level I evidence (Phase III randomized trial)**

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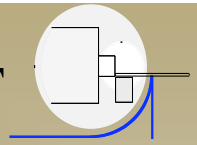

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There is a paucity of proton-literature specifically on Osteosarcoma and Soft Tissue Sarcomas

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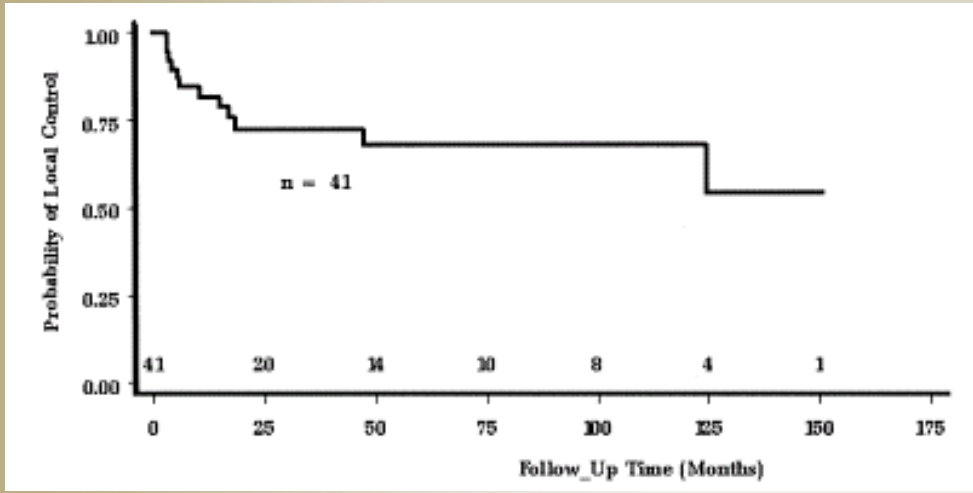
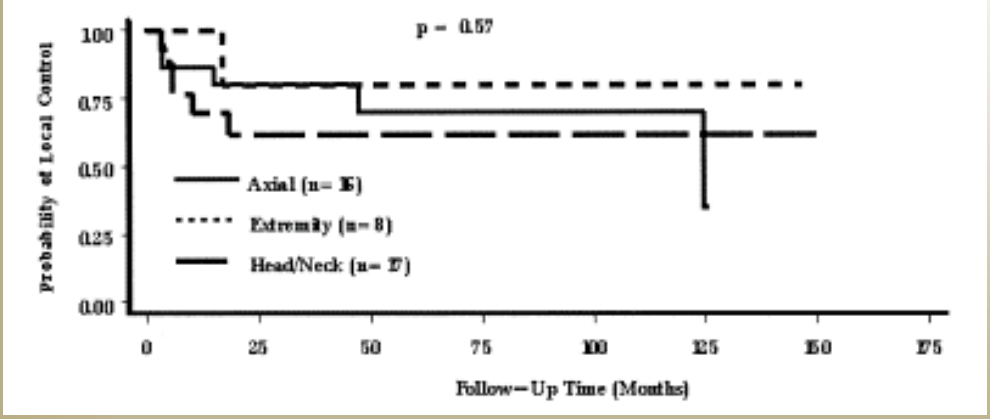
Delaney, Park et al., IJROBP 61(2), 2005



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%

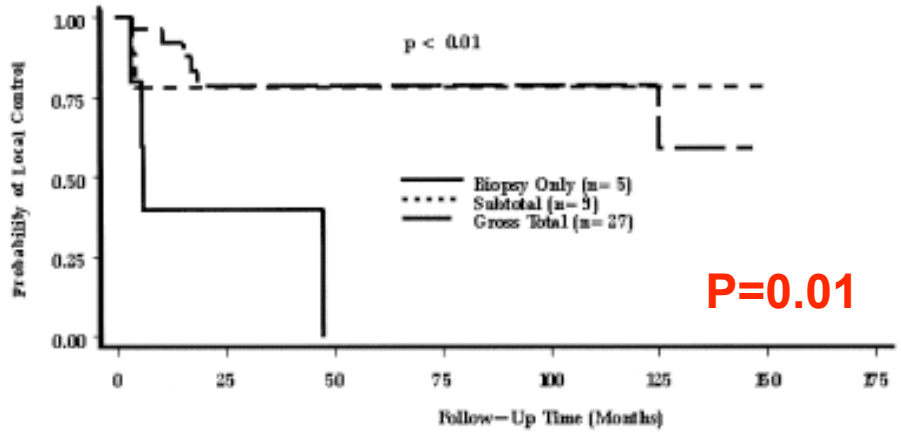

Fig. 2. Actuarial local tumor control according to extent of resection. Patients undergoing gross total and subtotal resection had improved local control compared with patients undergoing biopsy only ($p < 0.01$).

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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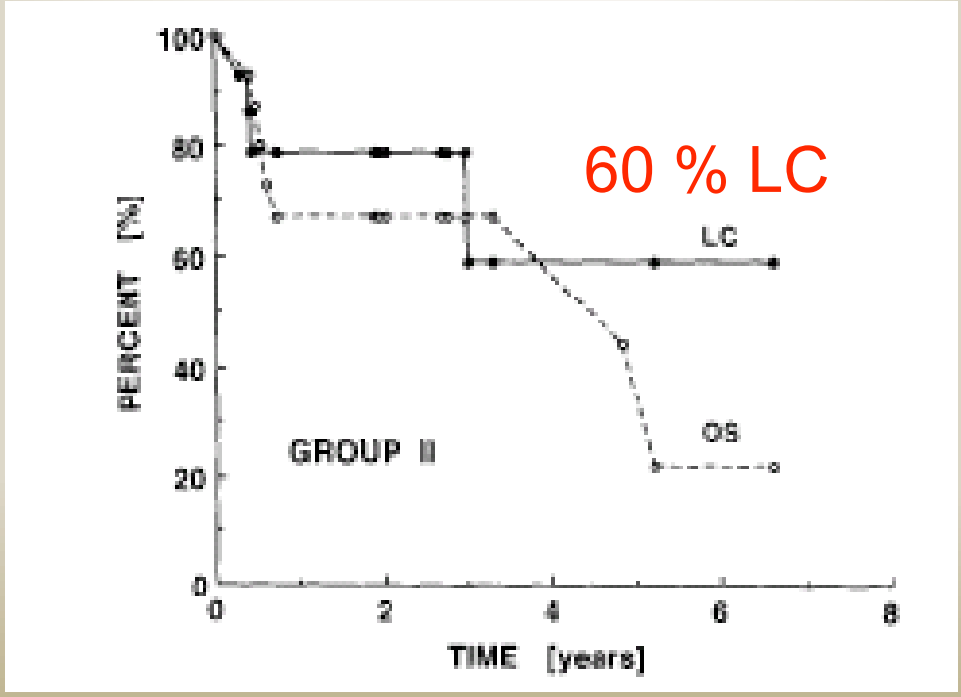
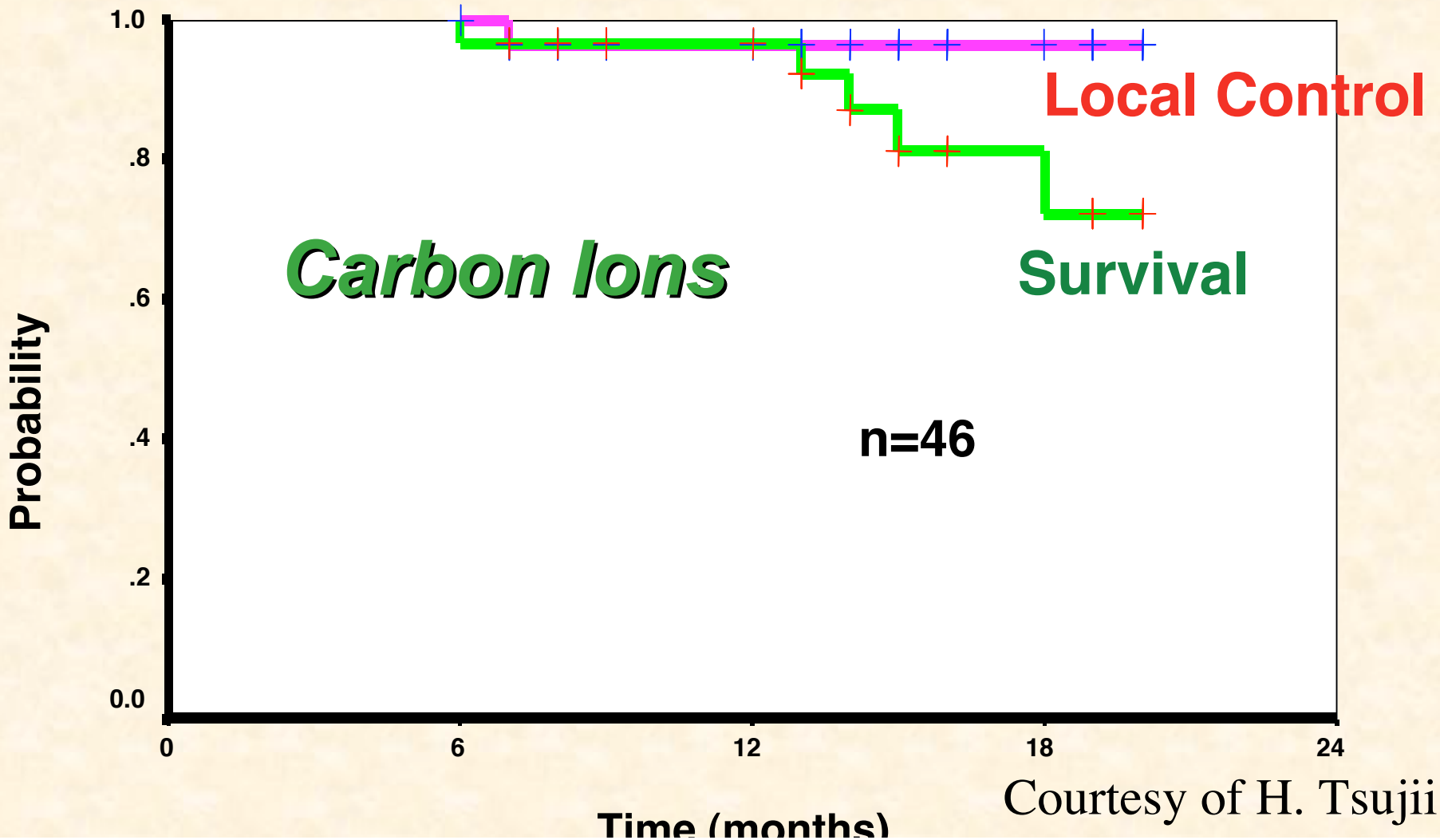
15 patients with osteogenic sarcoma of the axial skeleton

LC and OS after combined photon/proton RT



Bone and Soft Tissue Sarcoma (Phase II: 9901)

Fixed dose: 70.4 or 73.6 GyE/16fr/6wks



Courtesy of H. Tsujii

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Osteosarcoma of the Pelvic Bone

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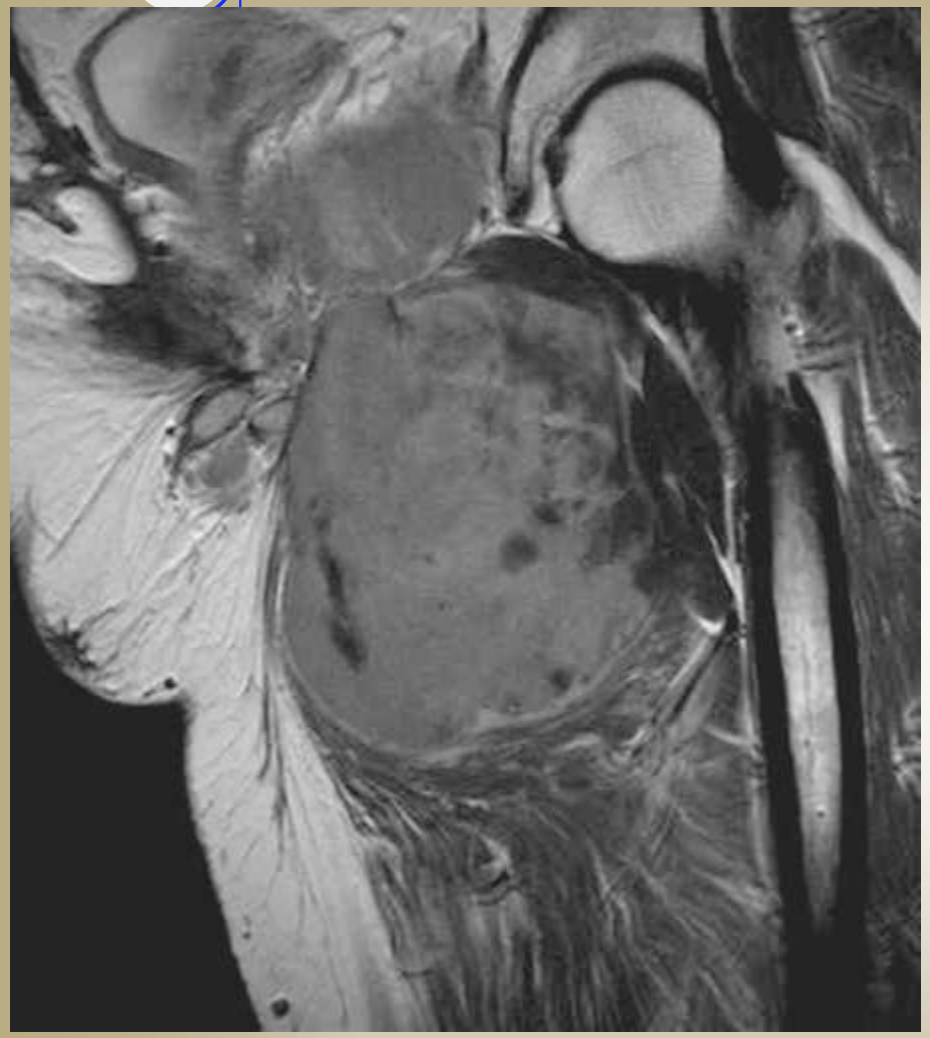

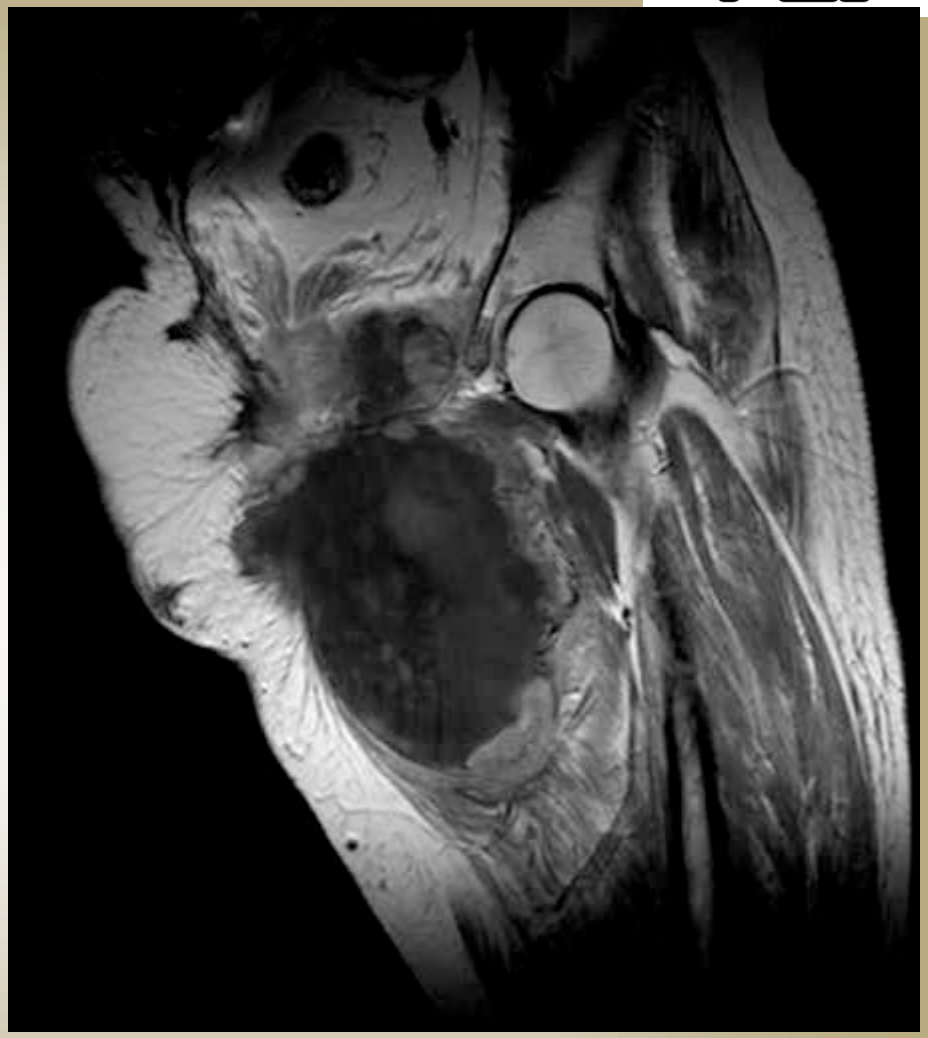

before *carbon ion* RT

after *carbon ion* RT

Phase I/II Studie, Chiba, Japan

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  - STS
  - Rhabdomyosarcoma

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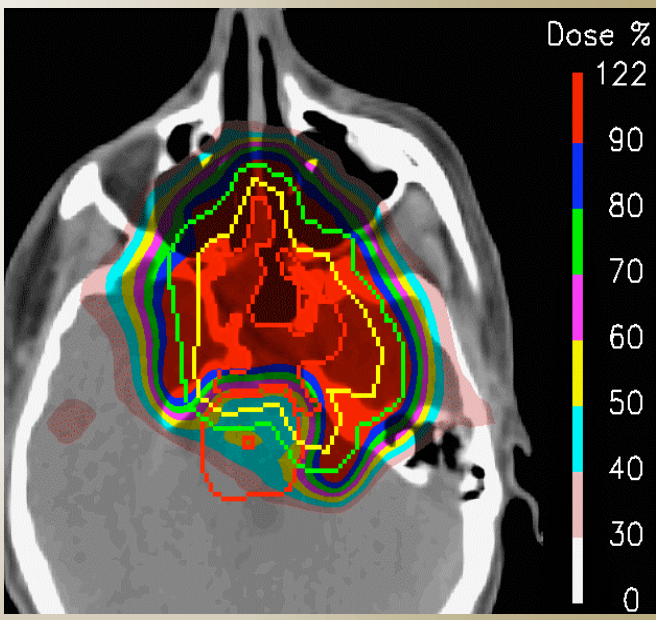
Proton-Radiotherapy for Chordomas and Chondrosarcomas:

- 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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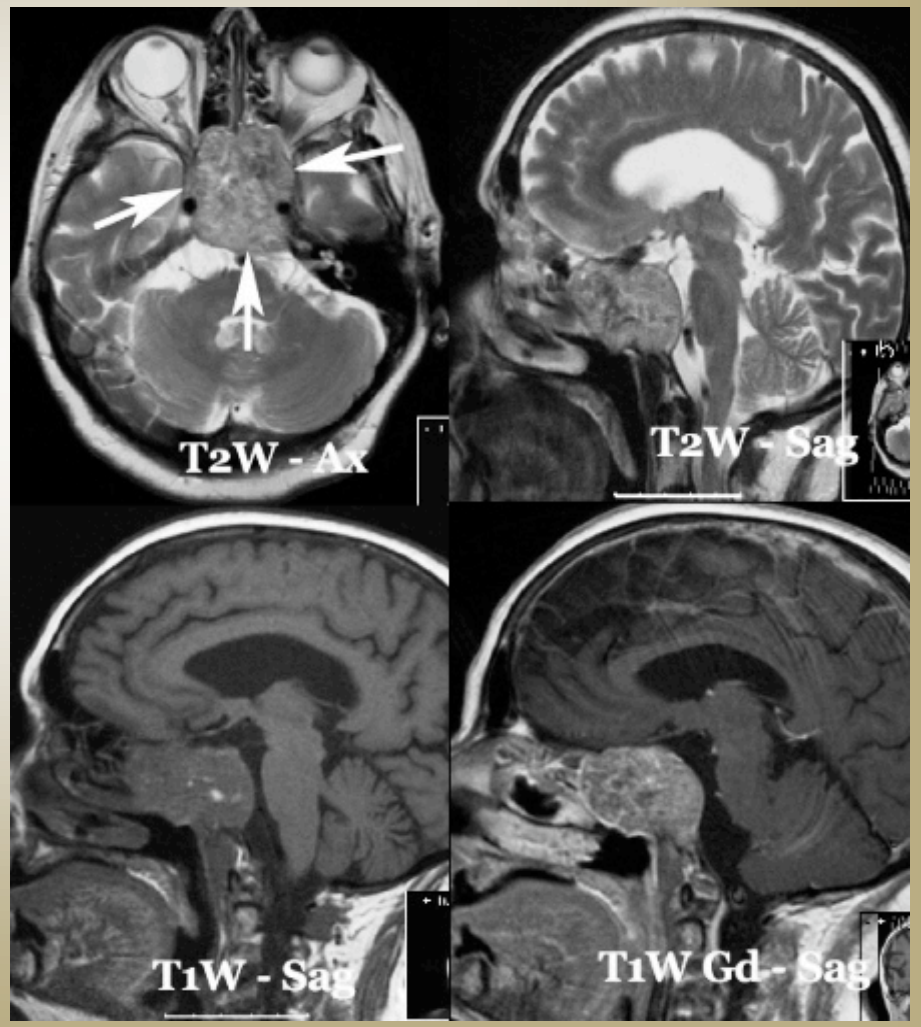
Proton Radiation Therapy for

Skull Base Chordomas and Chondrosarcomas:



Published Results:

- **Massachusetts General Hospital**
- **Loma Linda Univ. Med Center**
- **Paul Scherrer Institute**
- **Centre de Protontherapie d'Orsay**

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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

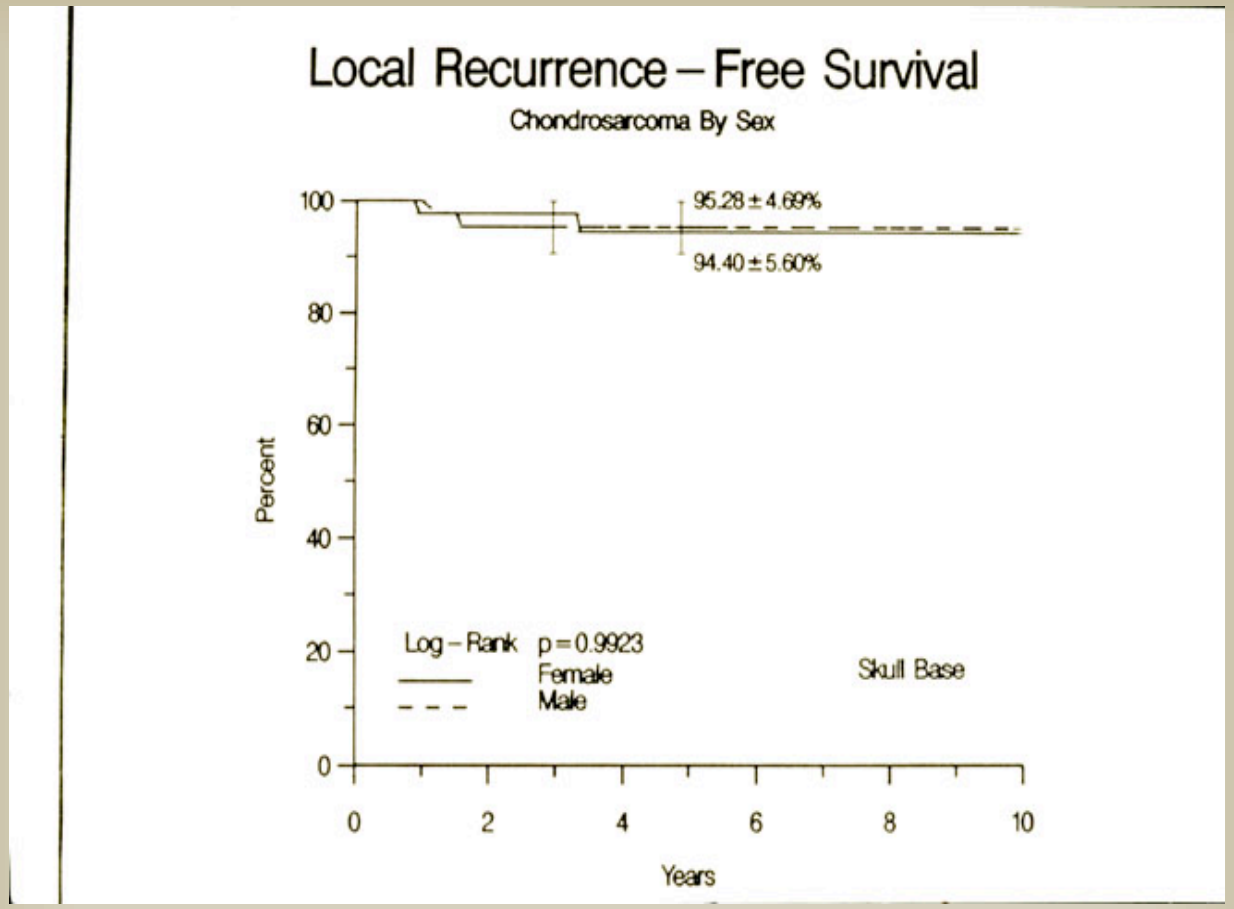
Local recurrence-free survival (skull base)

- Histology

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

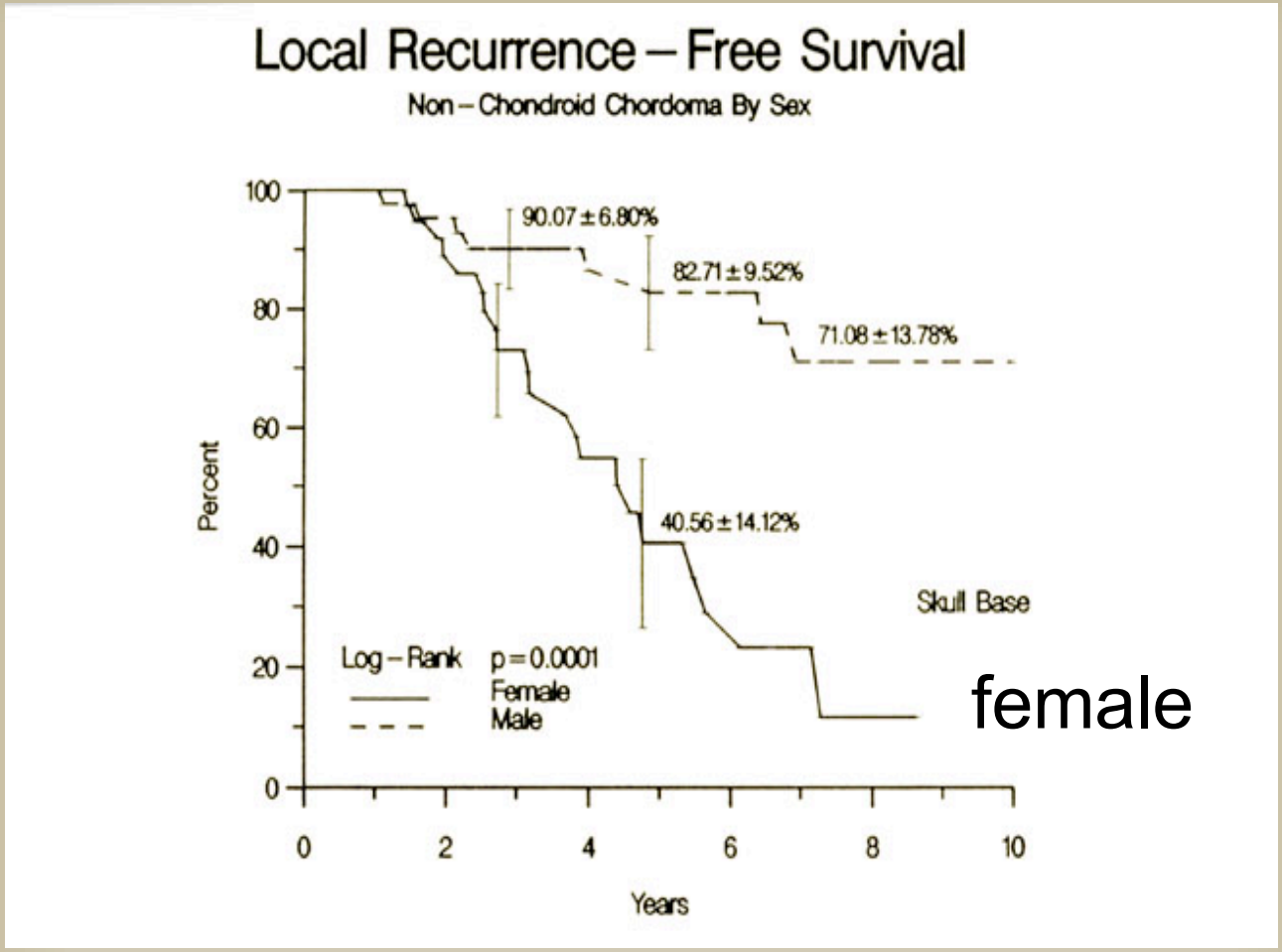
Courtesy: John Munzenrider, MGH/HCL

Long term tumor control: MGH data



Courtesy: John Munzenrider, MGH/HCL

Chordomas: Prognostic Factors



female

Courtesy: John Munzenrider, MGH/HCL

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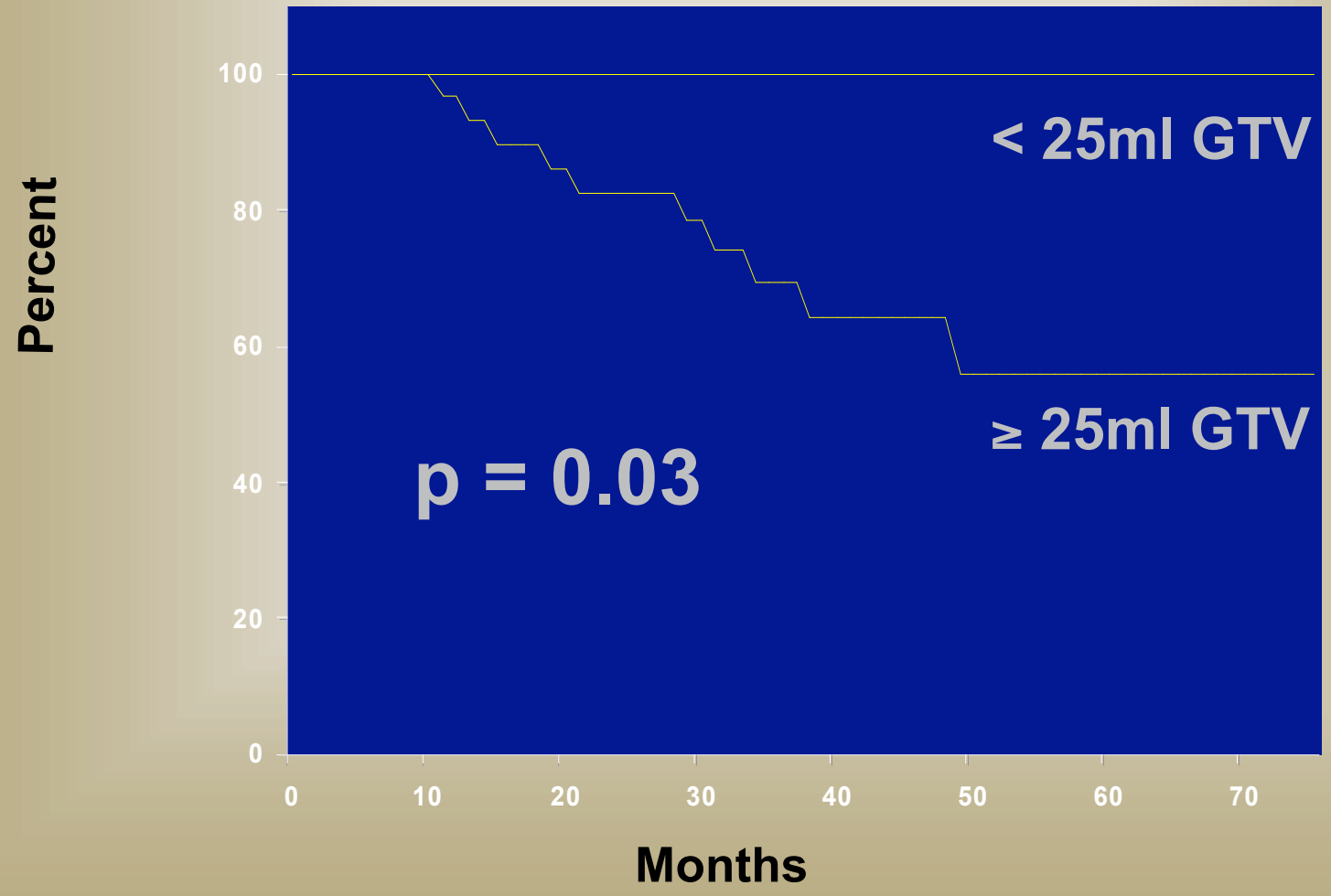
Proton RadiationTherapy (PRT)
for Chondrosarcomas and Chordomas of the Skull Base.

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

Tumor size at PRT and Local Control



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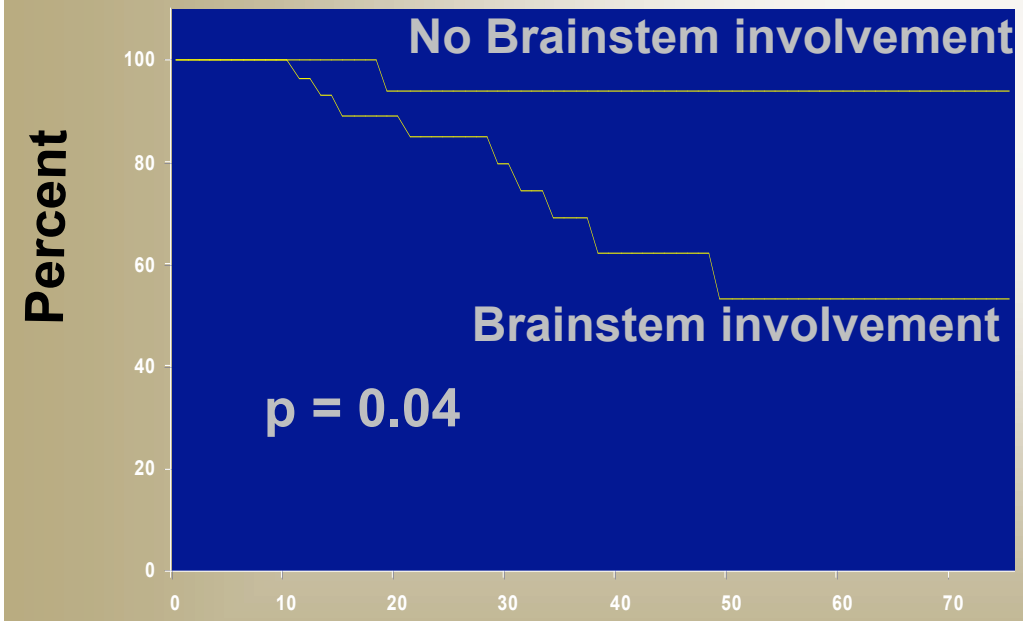
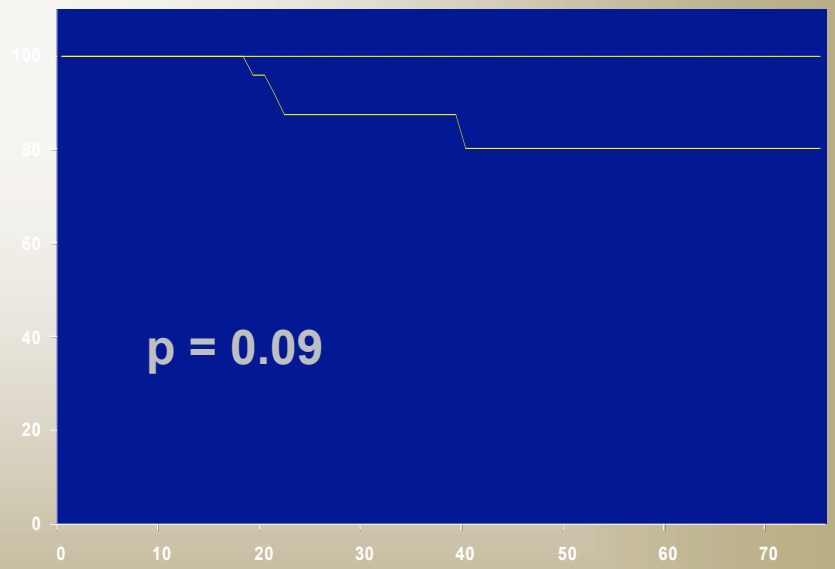
Local Control



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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Skull Base Chordomas and Chondrosarcomas at PSI: *5-year outcome** *of spot scanning based PT*

To be presented by Dr. Ares

- **Mean follow-up time: > 3 years**
- **Local Control for Chordomas: > 75%**
- **Local control for Chondrosarcomas: > 90 %**
- **High Grade Toxicity: < 7%**

* Ares, Lomax, Hug, Goitein – in preparation

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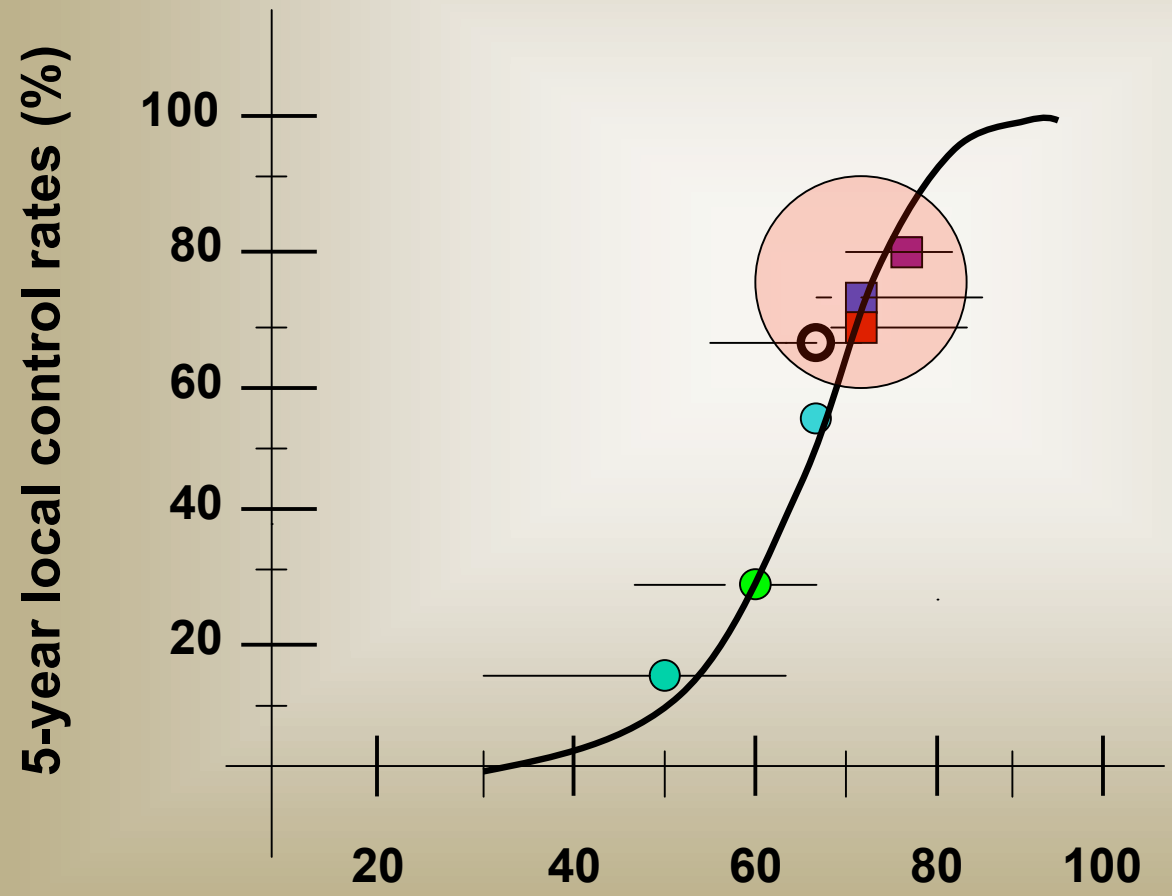
Chordomas of the Base of Skull



Photons

- Romero 1993
- Zorlu 2000
- Debus 2000

Protons

- Munzenrider 1999
- Ares 2007
- Hug 1999

C-Ions

- Schulz-Ertner

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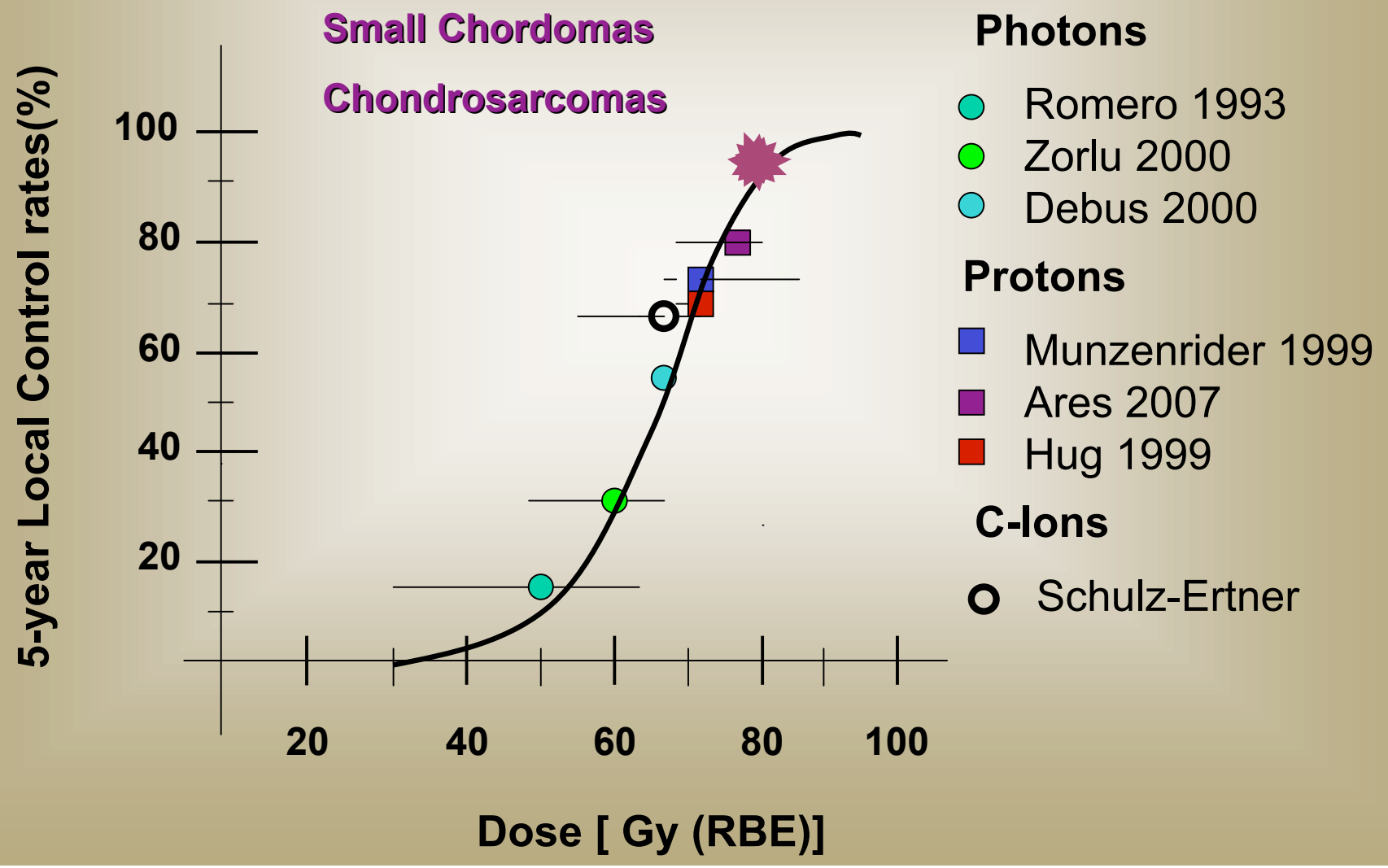
Chordomas and Chondrosarcomas of the Base of Skull



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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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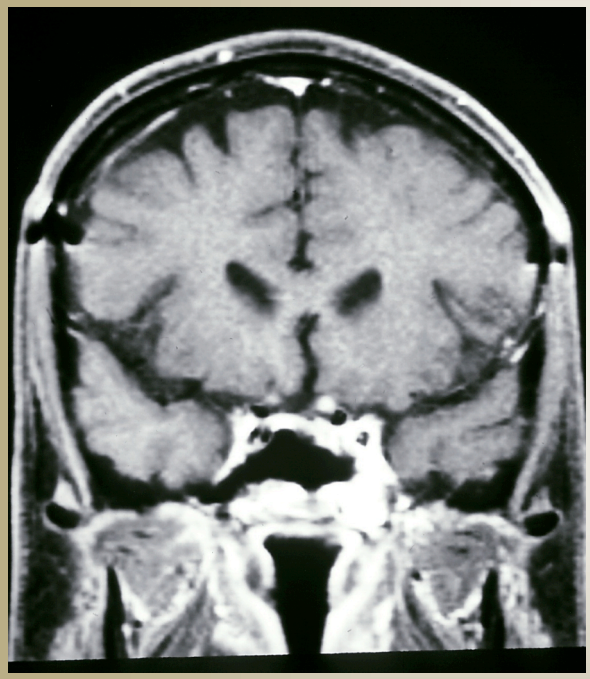
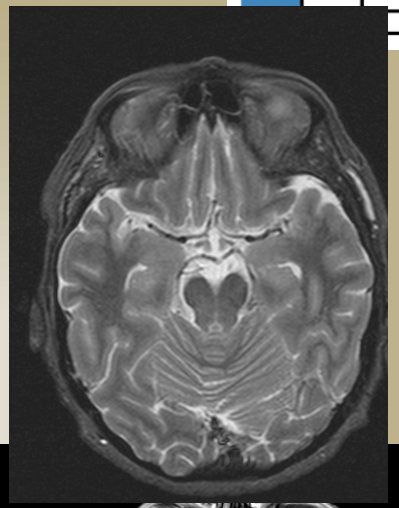
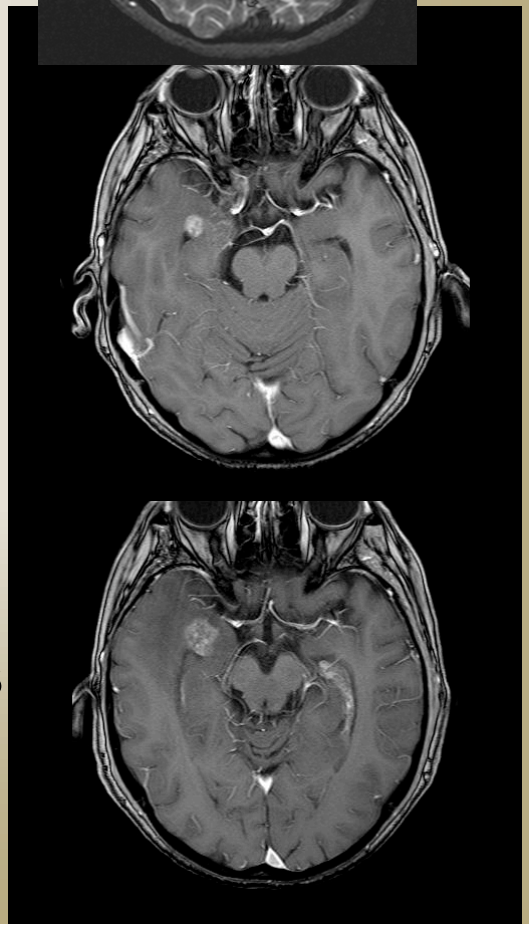
Optic neuropathy and temporal lobe toxicity





1.5 yrs.



2.0 yrs

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Dose limitations for OAR at PSI

OAR	Dmax
Brainstem surface	64 CGE
Brainstem center	53 CGE
Optic Chiasm	60 CGE
Optic Nerves	60 CGE

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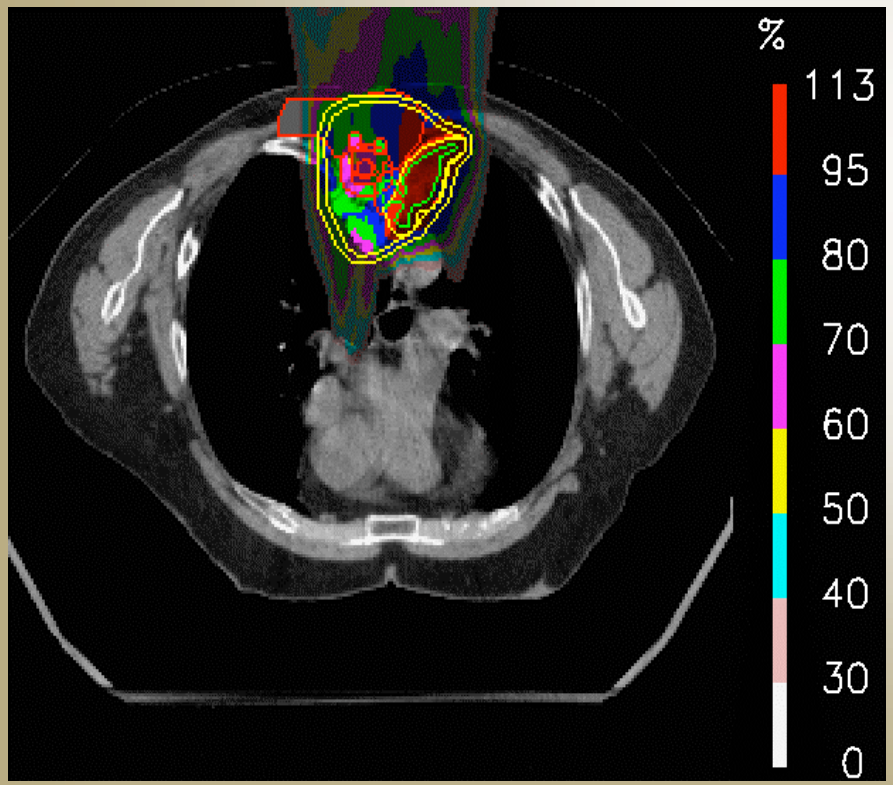
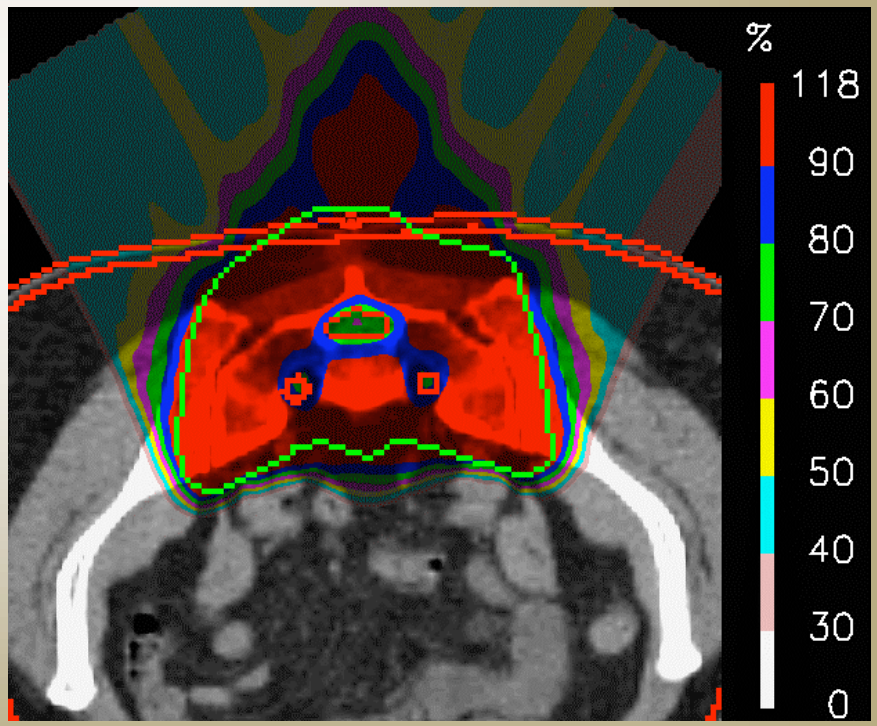
Extracranial *Chordomas of the Axial Skeleton* treated with spot scanning Proton Therapy at PSI:

Hans Peter Rutz et al.





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

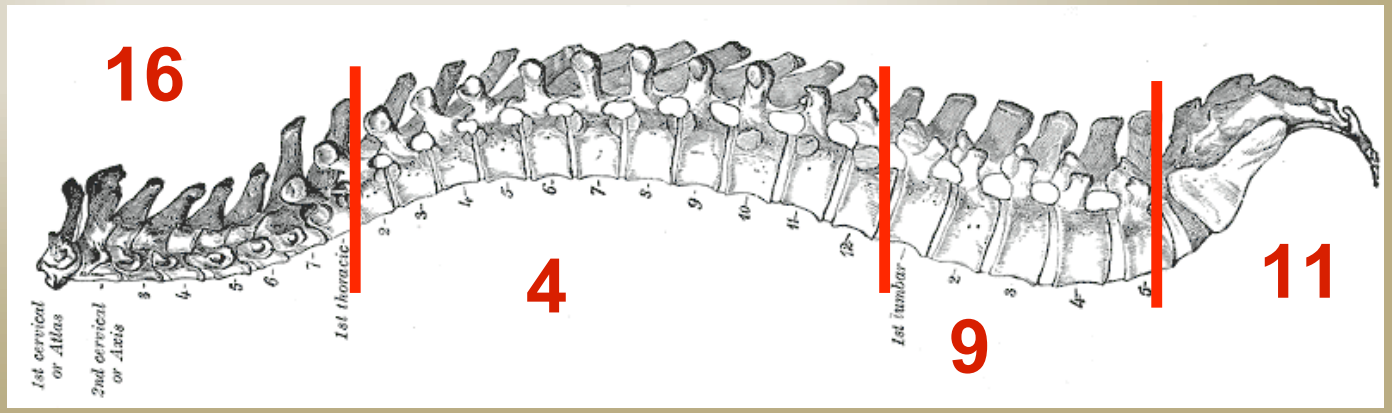
(Rutz et al.)

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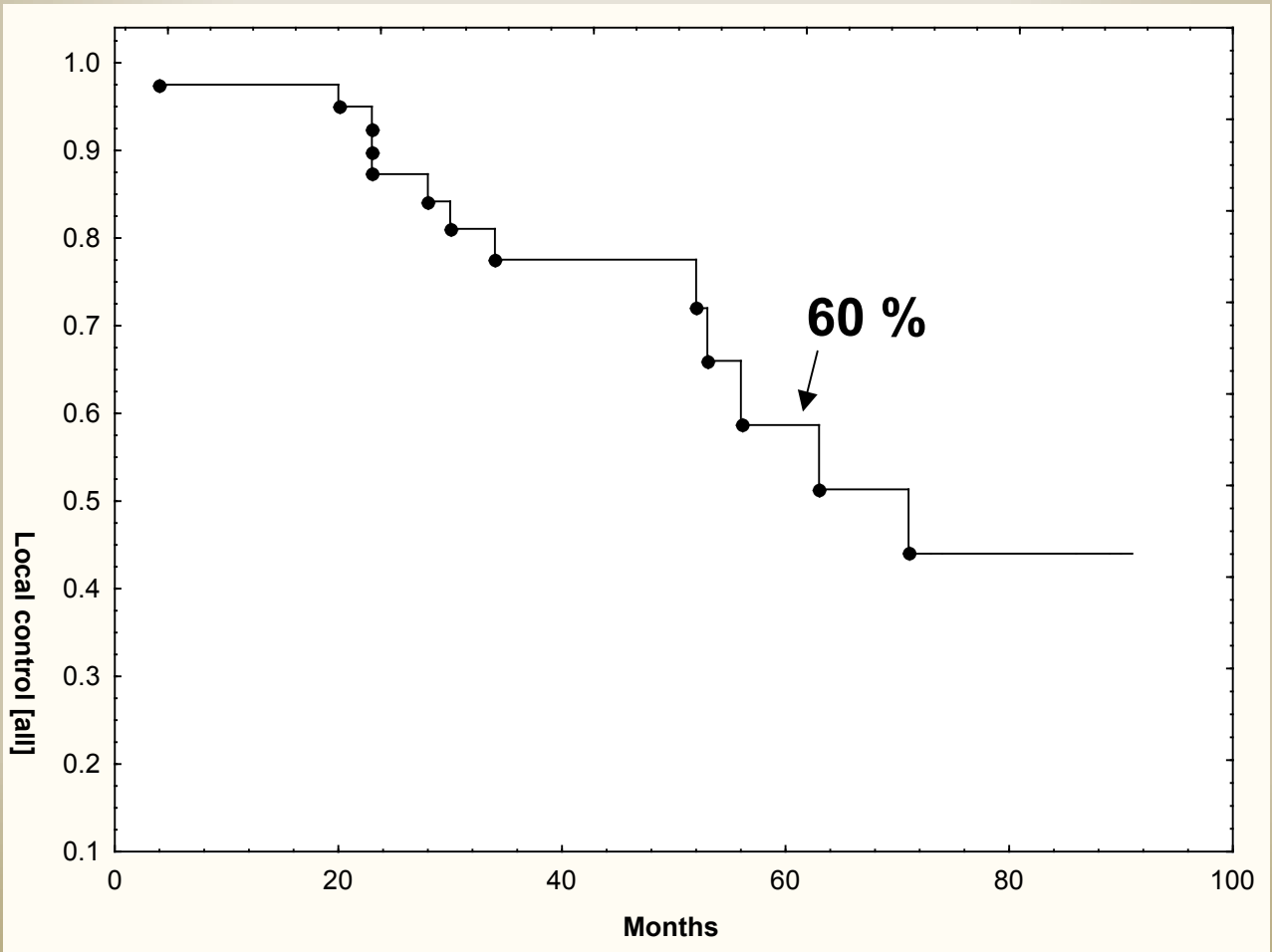
Chordomas of the Axial Skeleton at PSI: *5-year* outcomes data

Local control

13 / 40 patients with local failure



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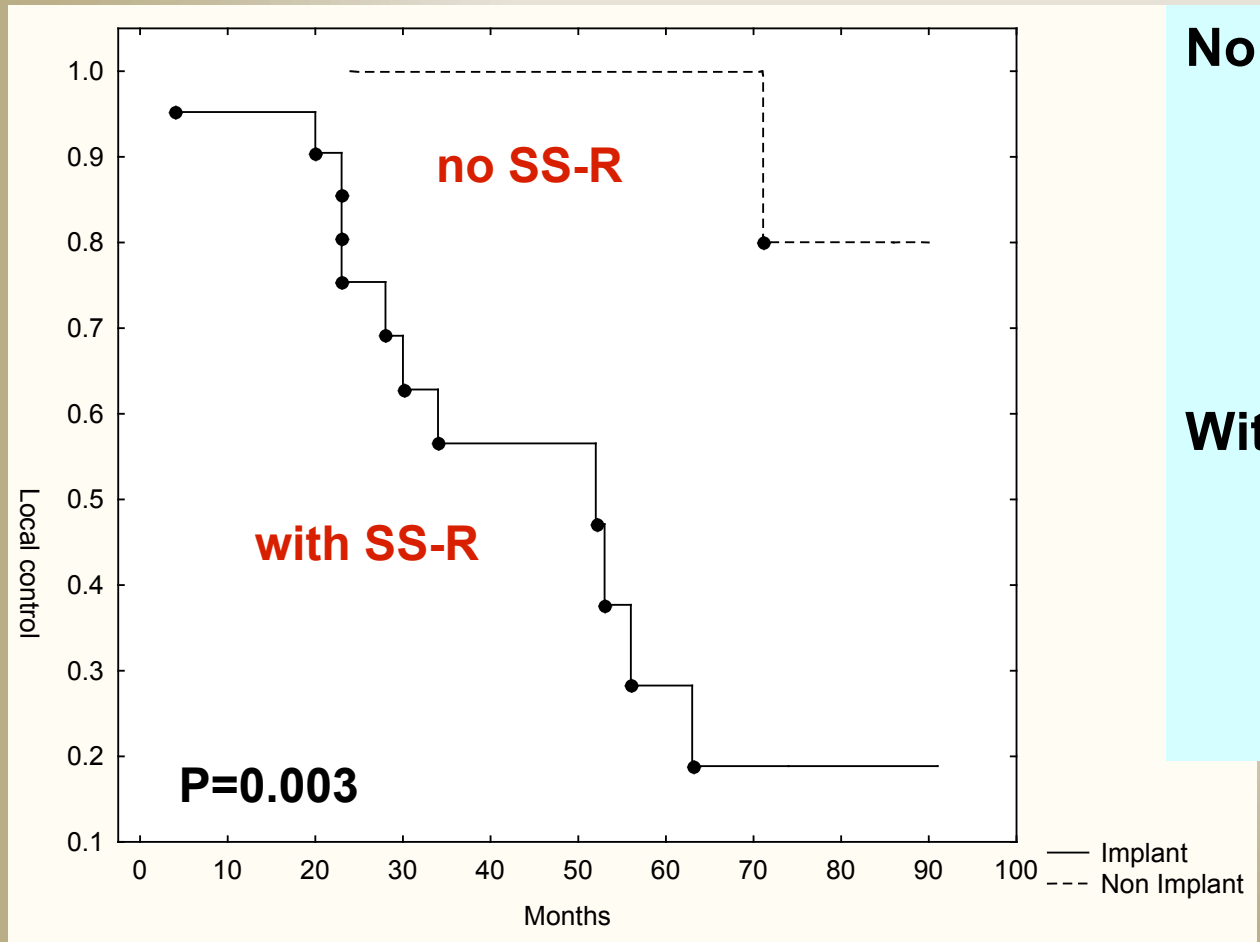
Chordomas of the Axial Skeleton at PSI: *5-year* outcomes data

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



No SS-R:

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

With SS-R:

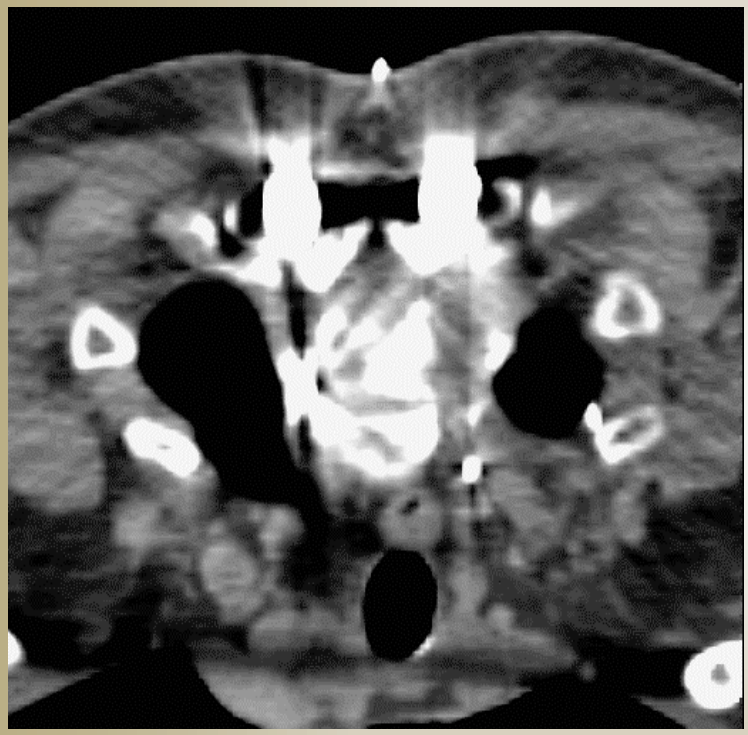
- **12 LF in 21 pts.**

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**

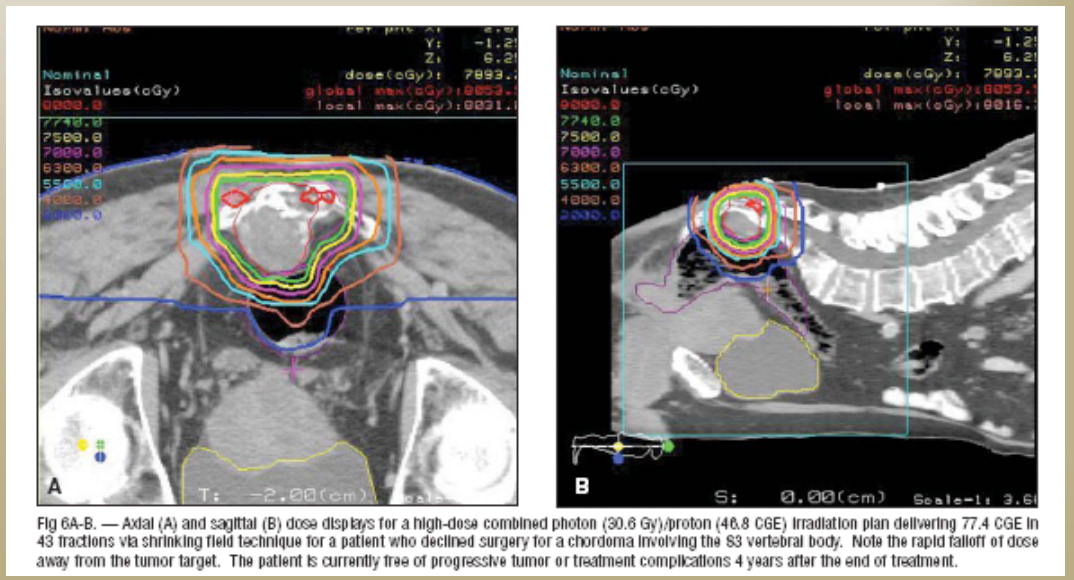

Fig 6A-B. — Axial (A) and sagittal (B) dose displays for a high-dose combined photon (30.6 Gy)/proton (46.8 CGE) irradiation plan delivering 77.4 CGE in 43 fractions via shrinking field technique for a patient who declined surgery for a chordoma involving the S3 vertebral body. Note the rapid falloff 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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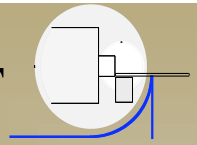

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Proton – Photon planning comparison

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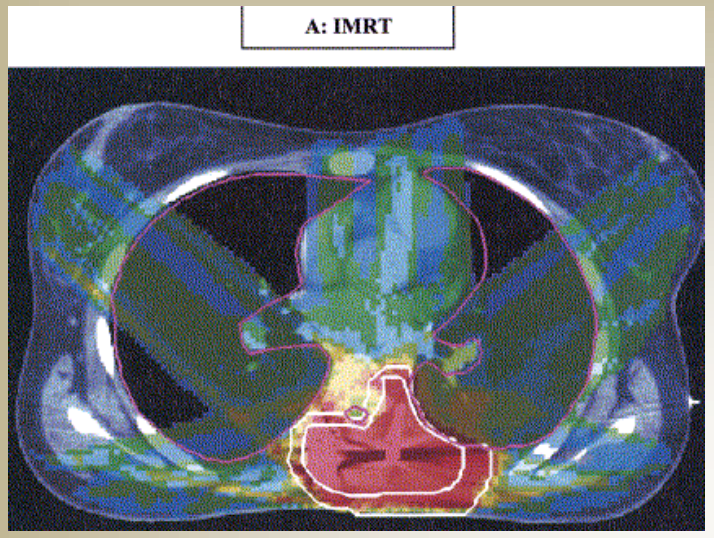
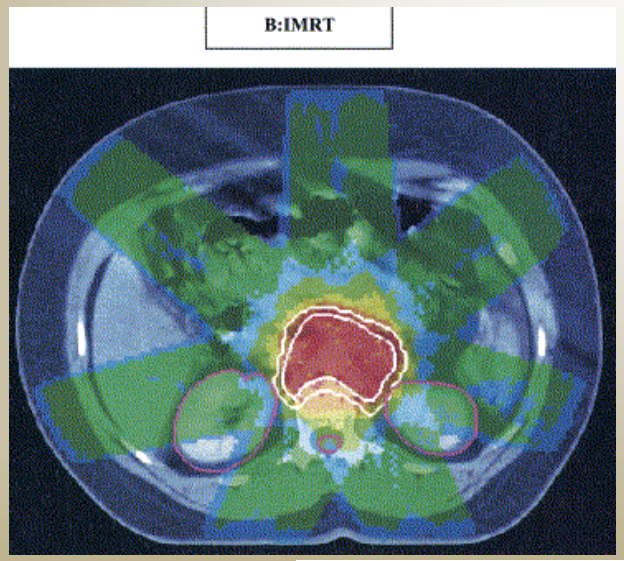
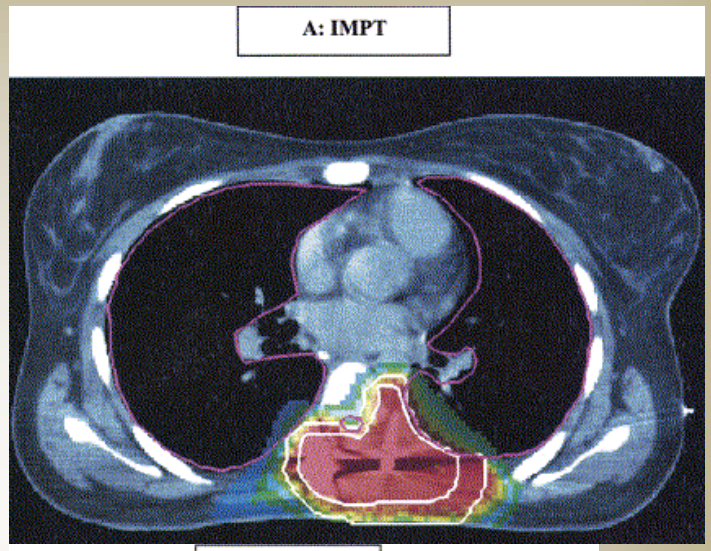
Weber, Delaney et al., PSI + MGH, IJROBP 2004 cont.

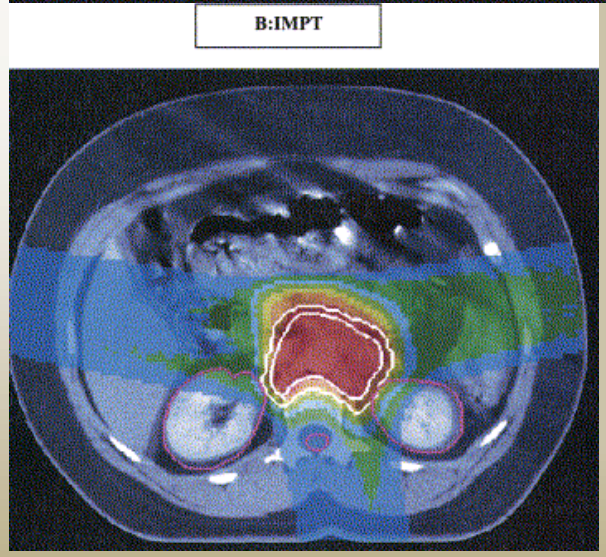
IMRT

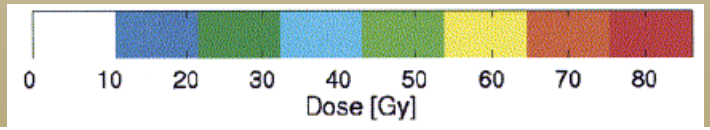




IMPT







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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**

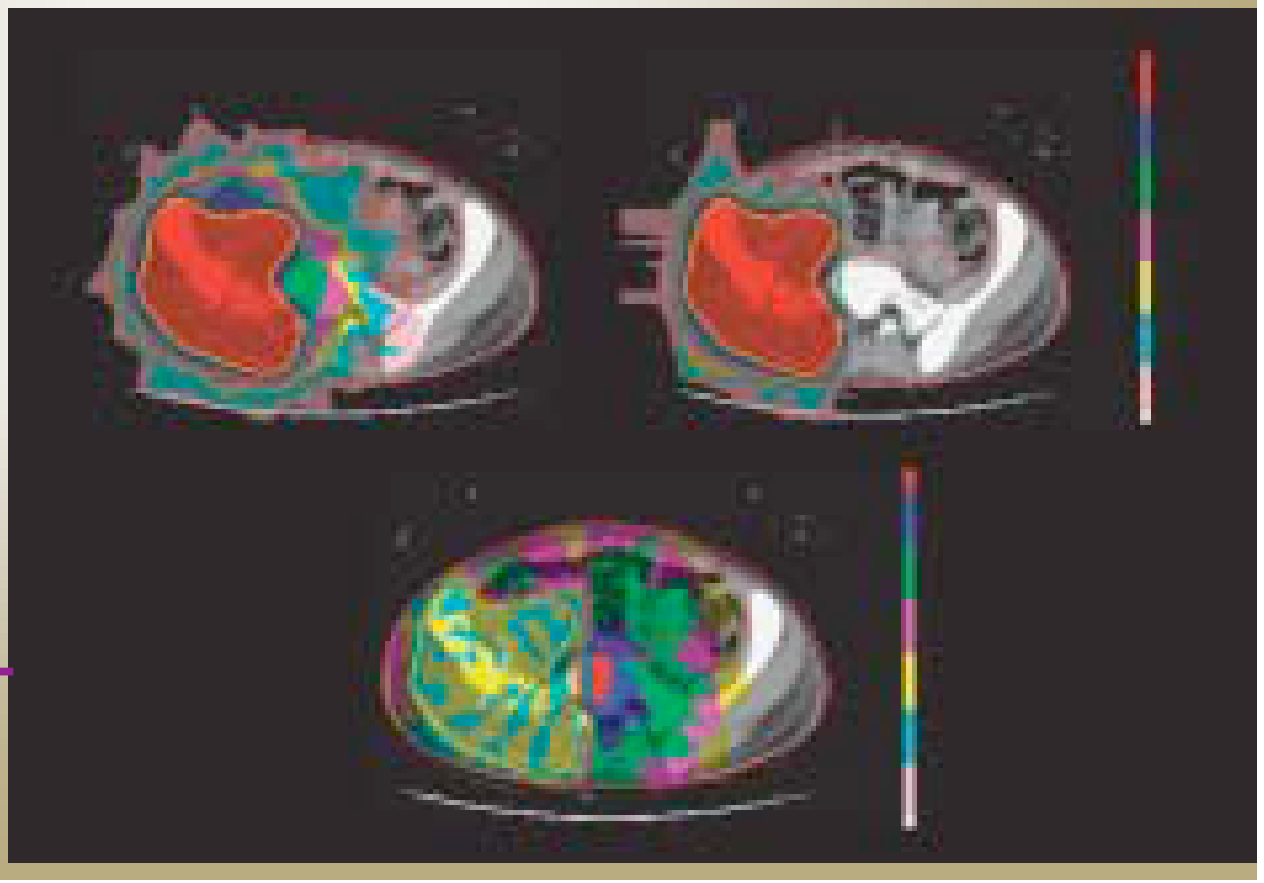
- The optimization IMPT algorithm was used to increase the total dose to the target by 10% and 20%, within the maximal OAR dose constraints.
  Dose escalation could be achieved in all patients, at the 20% (92.9 CGE) dose escalation level, regardless of tumor size, location, and geometry.

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

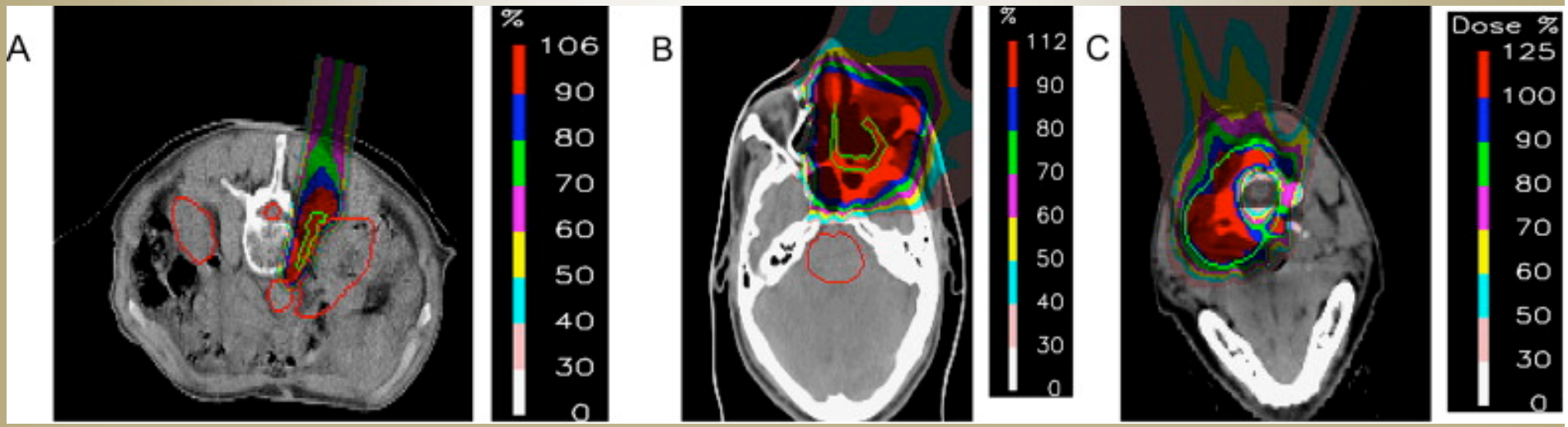
(Weber et al., IJROBP 2007)

- 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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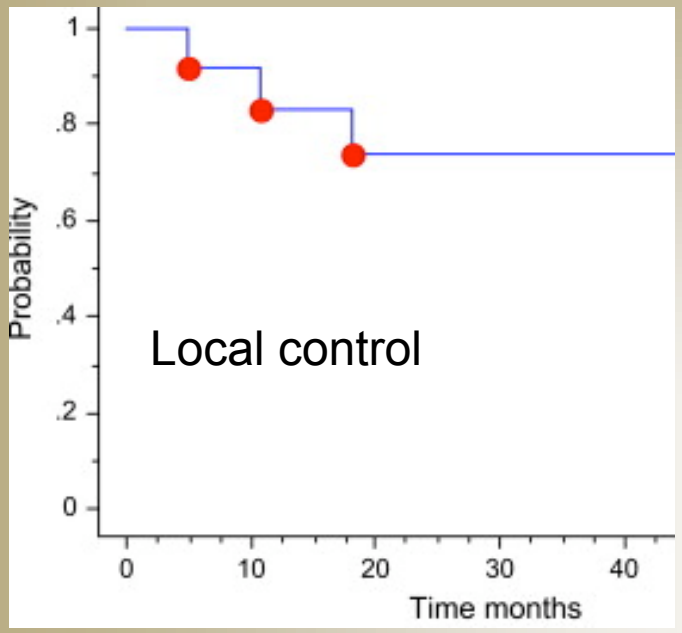
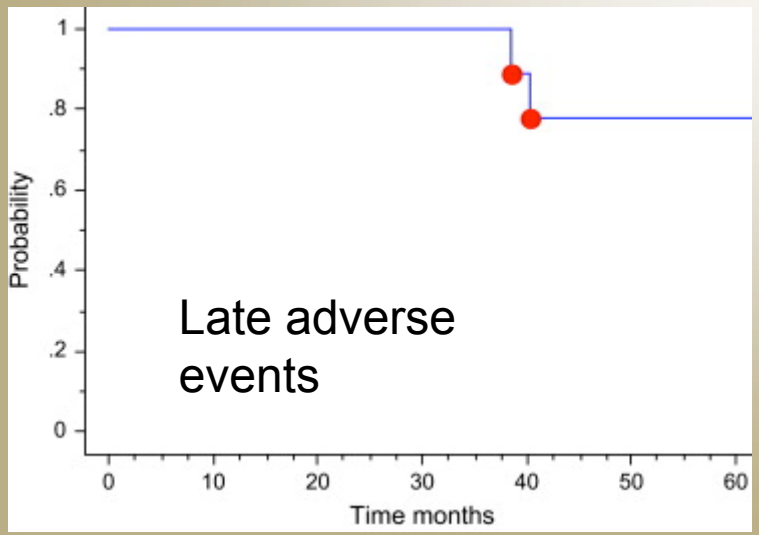
Weber et al., IJROBP 2007 cont.



<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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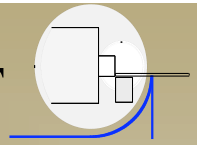

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PSI

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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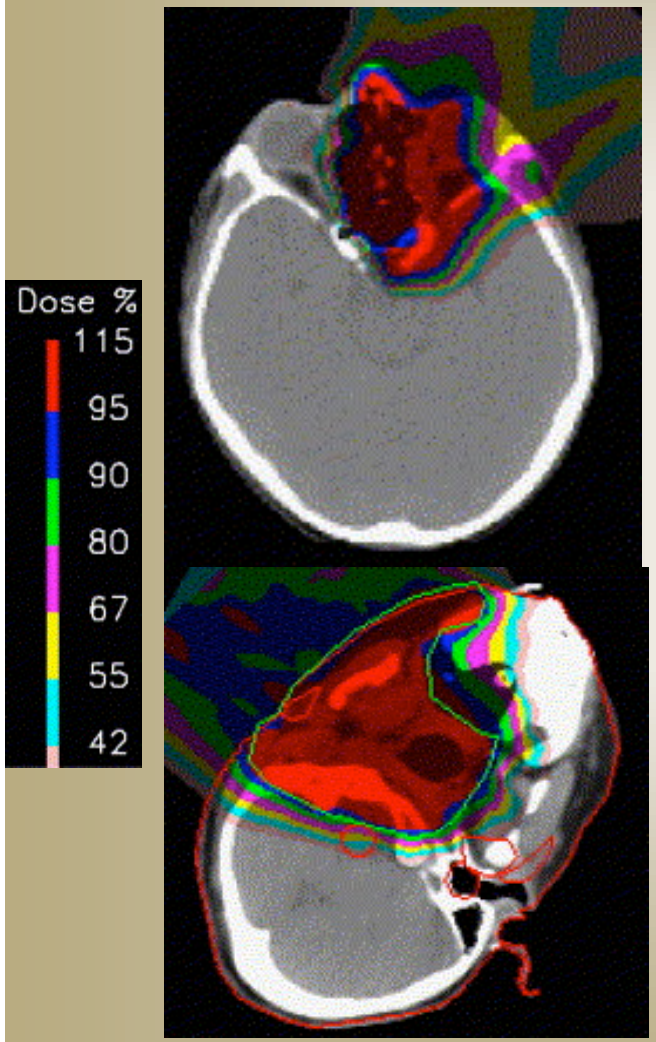
Outcome (very preliminary)



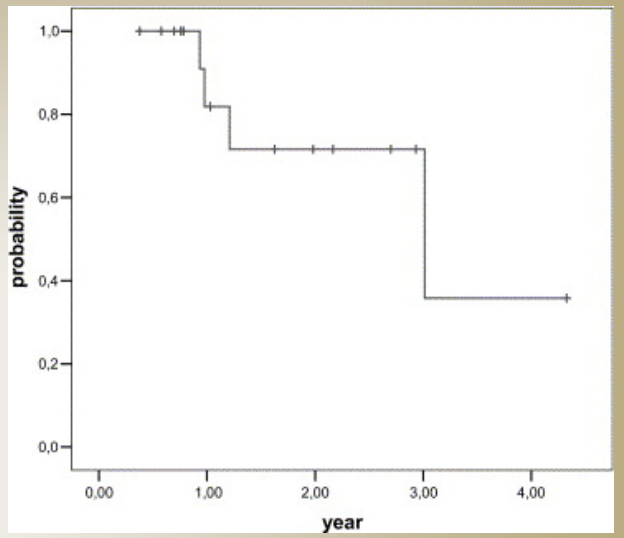
Local control:

12/16 = 75% at 2 years

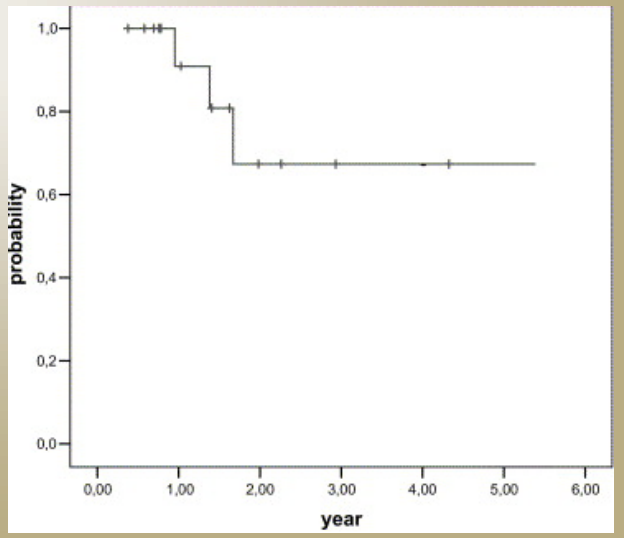
2/12 Failures in RMS- Group

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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2 principal Concepts for applying Proton RT in relation to Photon-RT Pediatric Clinical Trials

Concept 1

↓

Enrollement in photon trials or Tx according to photon trial study board recommendations

↓

dose and volume regimen identical to photon concepts

Advantage: Proton-RT emdedded in multi-institutional concepts. Matched-case comparability of outcomes data with photons

Disadvantage: no increase in tumor control probability from protons by applying Tx-prescriptions similar to photons

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2 principal Concepts for applying Proton RT in relation to Photon-RT Pediatric Clinical Trials

Concept 2

High risk STS (mainly Non-RMS STS with gross residual)

↓

Apply high doses based on peds. skull base chordoma data

↓

High dose proton-RT: 68 -76 Gy(RBE)

↓

Enrollement in photon trials only if high doses permissible

Low risk STS (mainly RMS STS)

↓

Enrollement in photon trial

Example: COG / IRS RMS dose and volume regimen

↓

Normal tissue sparing advantage, but no expectation for increased tumor control

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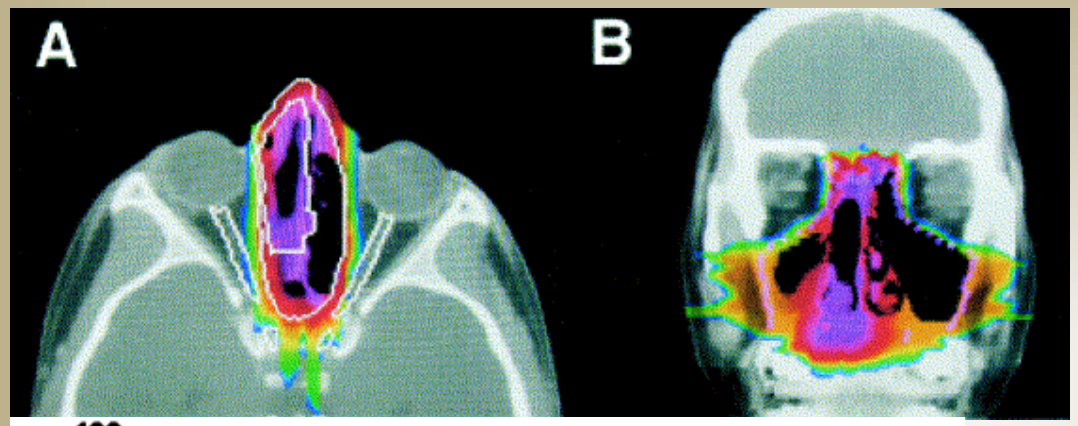
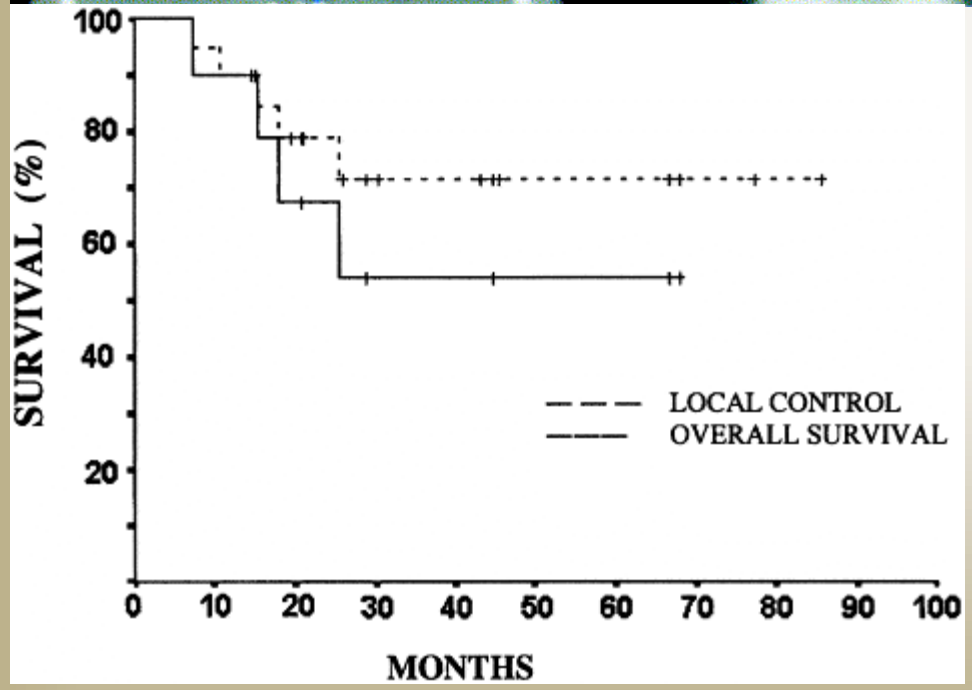
Example: 13 y.o. M with Malignant Fibrous Histiocytoma





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/Particle - Radiotherapy for Sarcomas:

There is a need for improving local controle by RT for high-risk, unresected/resectable sarcomas

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Potential and Future

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Increasing Local Control by dose escalation:

- Residual disease or unresectable disease
- Disease at high risk for failure

Decreasing Late Adverse Events by reduction of Integral dose:

- Improving functional outcome by reducing normal tissue dose
- Reducing risks of Secondary malignancy

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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 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 radiotherapy for unresectable ..S“

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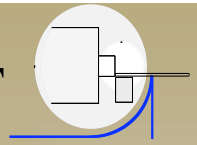

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PSI

THANK YOU