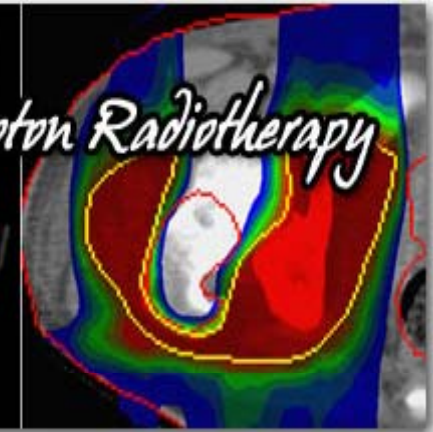


*A Symposium on the Promises and Perils of Proton Radiotherapy*

May 8 – 9, 2009

Baltimore, MD



# Proton Radiation Therapy of Tumors of the Cranial Base

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Harvard Medical School

Uncommon primary malignant bone tumors  
arising from cranial base

**Chordoma:** Arises from remnants of  
embryonal notochord

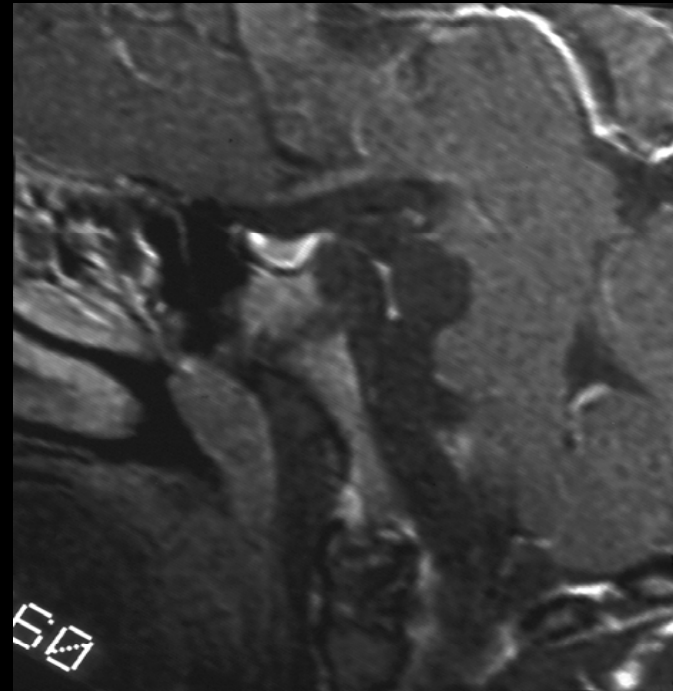
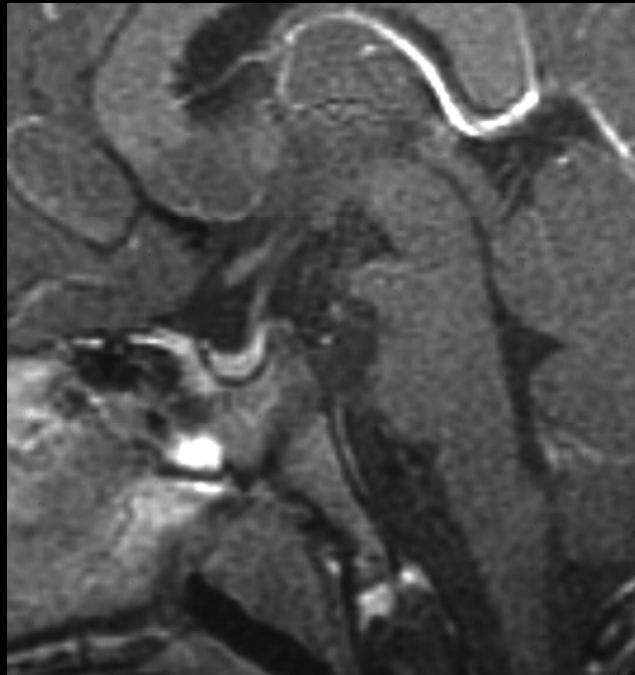
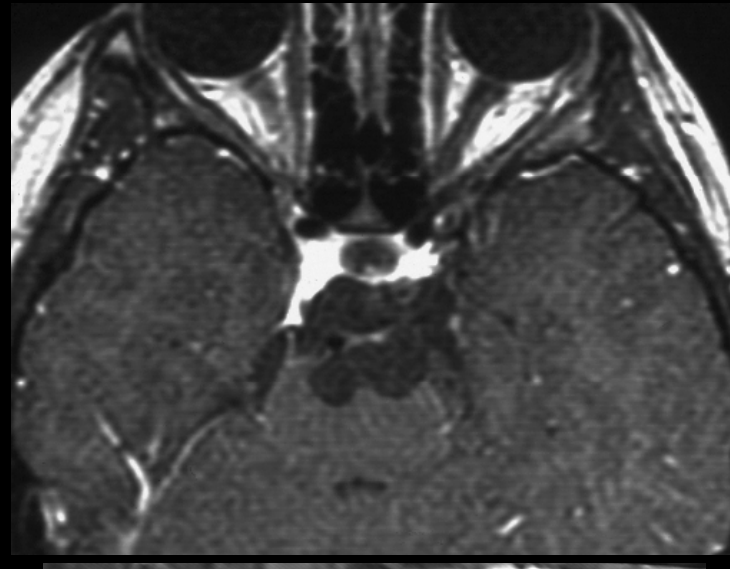
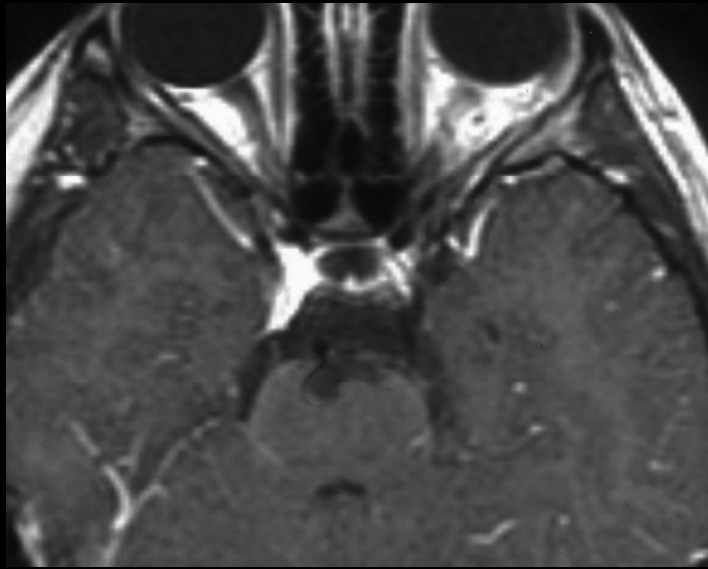
**Chondrosarcoma:** Arises from remnants of  
embryonal chondrocranium

# Anatomic Location



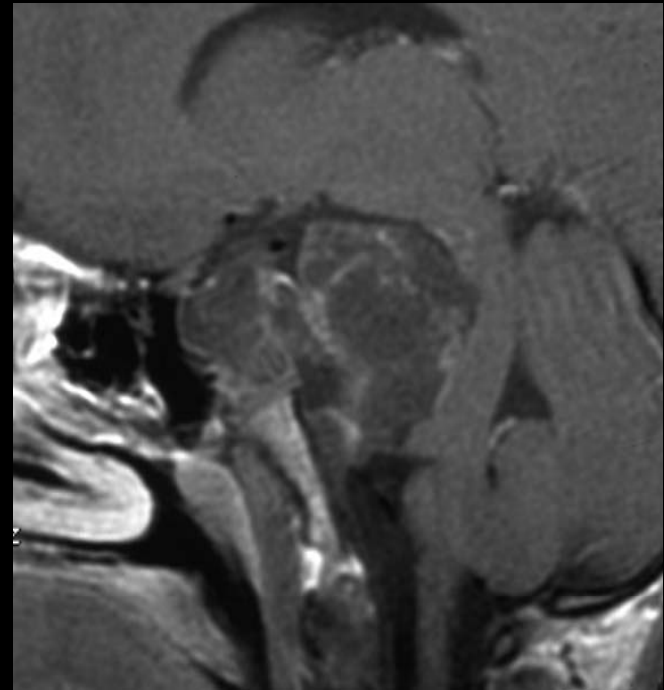
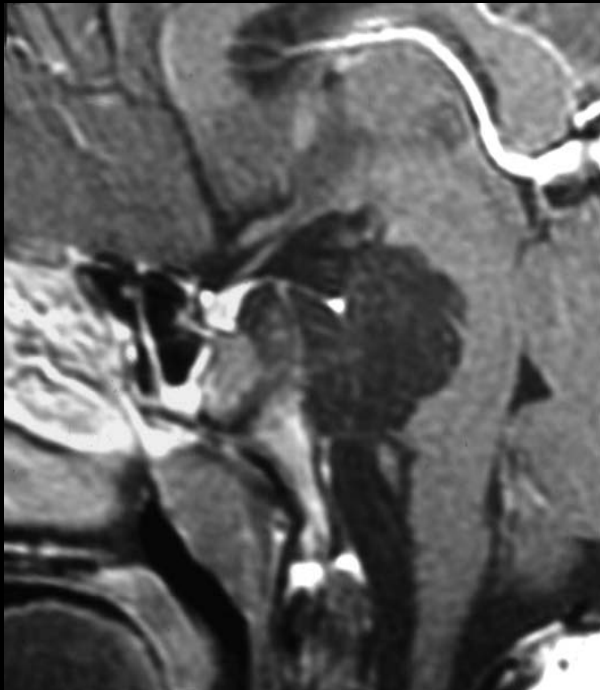
# Natural History

- Indolent tumor growth
- Low metastatic potential



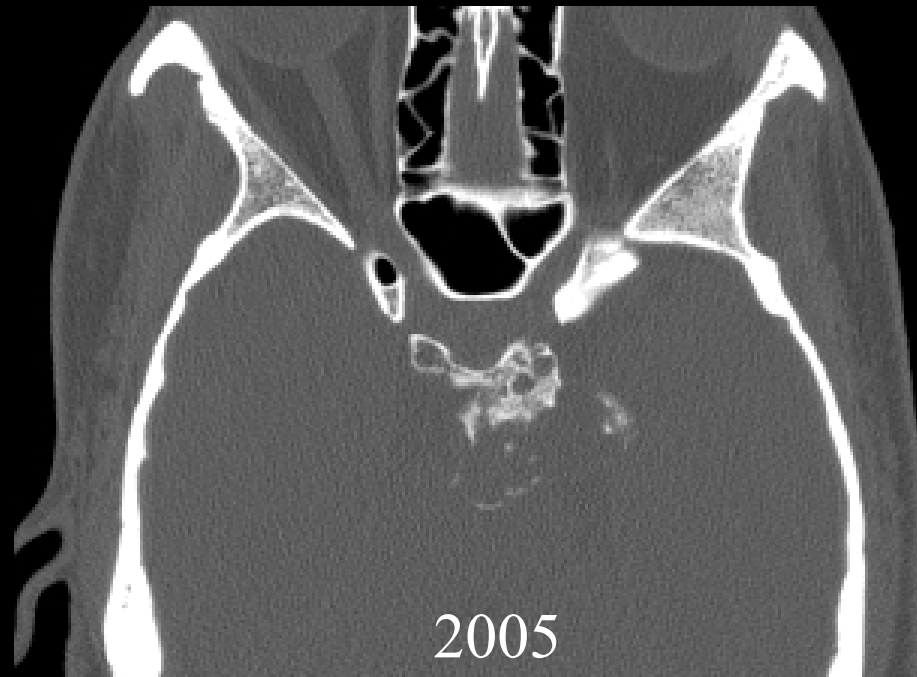
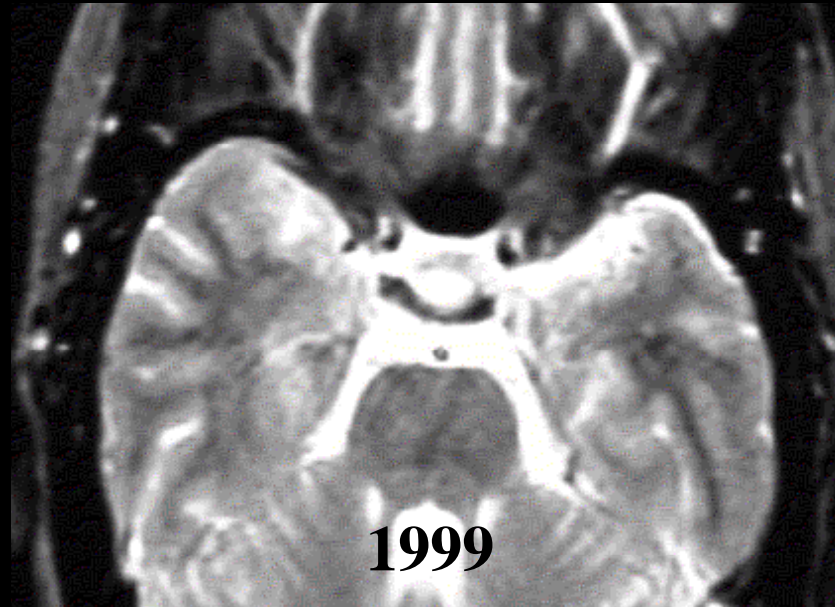
3/1997

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3/1999



# Clinical Symptoms & Signs: Chordoma

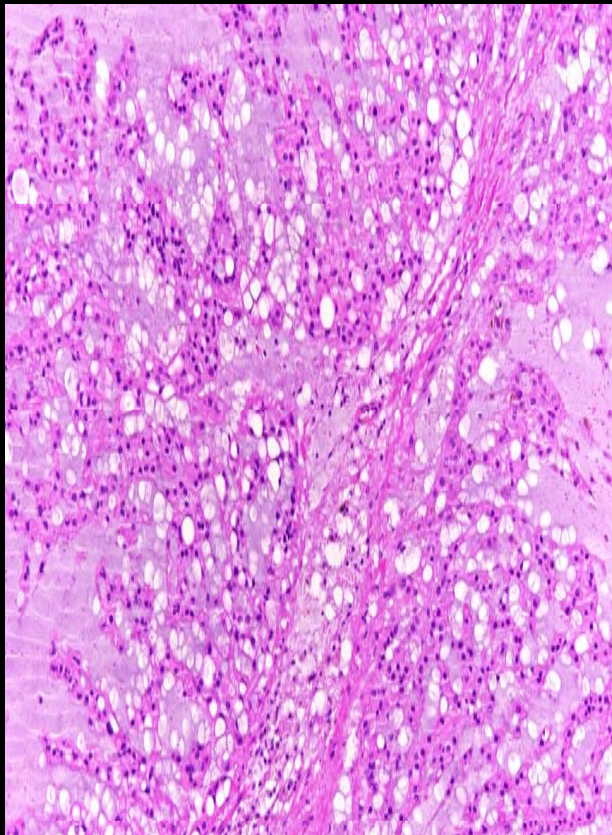
Headaches	52 %	CN	II	3 %
Neck pain	24 %		III	11 %
Airway obstruction	17 %		IV	1 %
Nausea/vomiting	8 %		V	1 %
Dysphagia	6 %		VI	42 %
Dysphonia	3 %		VII	3 %
Eust. tube dysfct.	6 %		VIII	3 %
Torticollis	10 %		IX	9 %
Ataxia	24 %		X	7 %
			XI	3 %
			XII	20 %



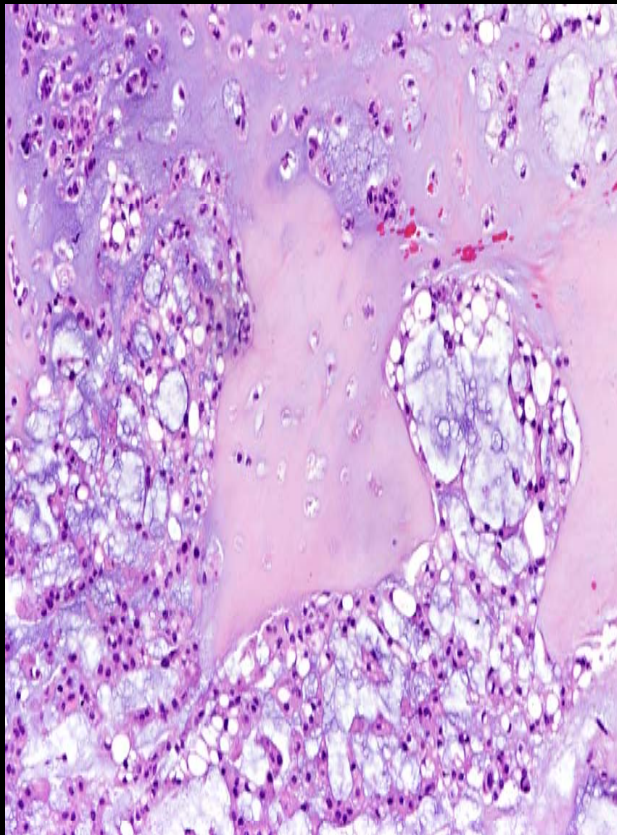
# Clinical Symptoms & Signs: Chondrosarcoma

• Headaches	40 %
• Nasal obstruction	5 %
• Eustachian tube dysfunction	5 %
• Pituitary dysfunction	3 %
• Ataxia	3 %
• CN Deficits	81 %
CN II	4 %
CN III	9 %
CN IV	2 %
CN V	10 %
CN VI	50 %
CNs VII, VIII	7 %
CNs IX, X, XI	9 %
CN XII	6 %

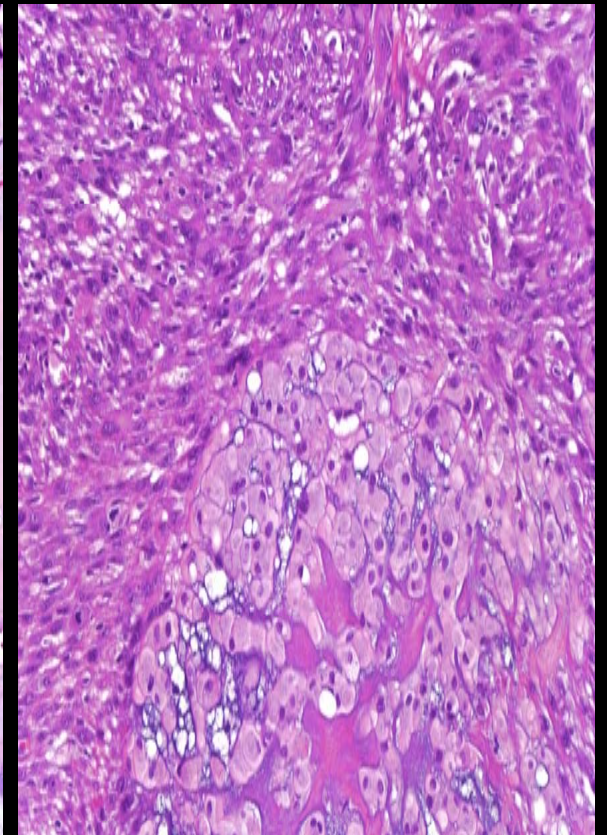
# Histology of Chordoma



conventional

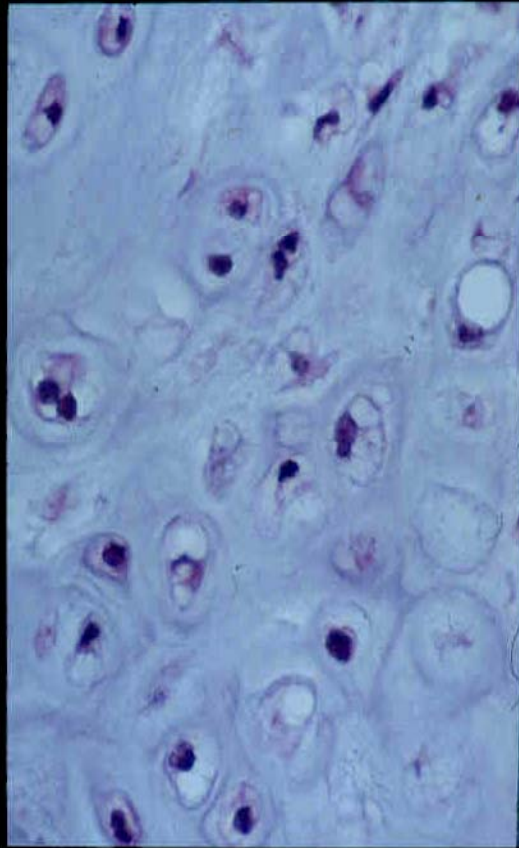


chondroid

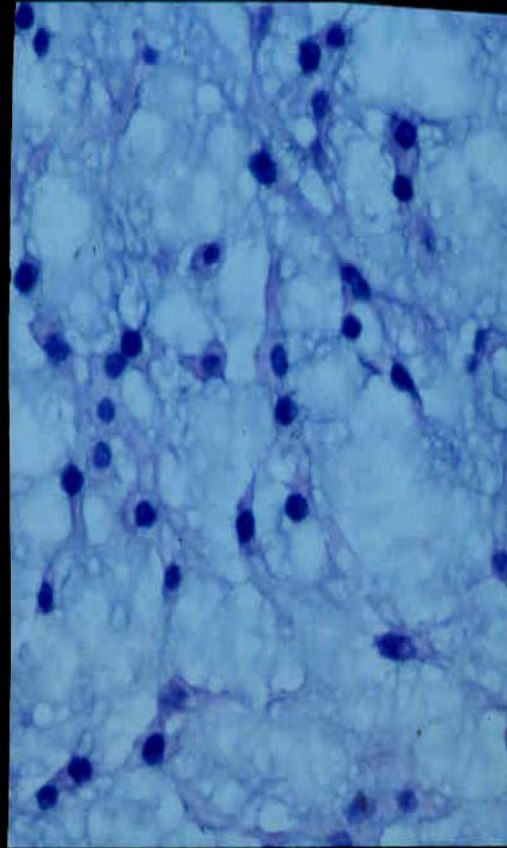


de-differentiated

# Histology of Chondrosarcoma



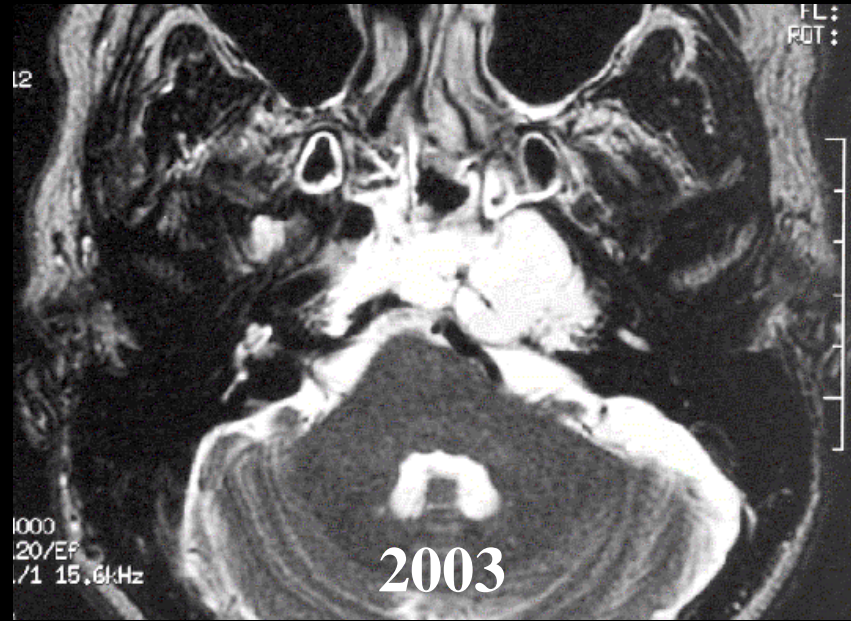
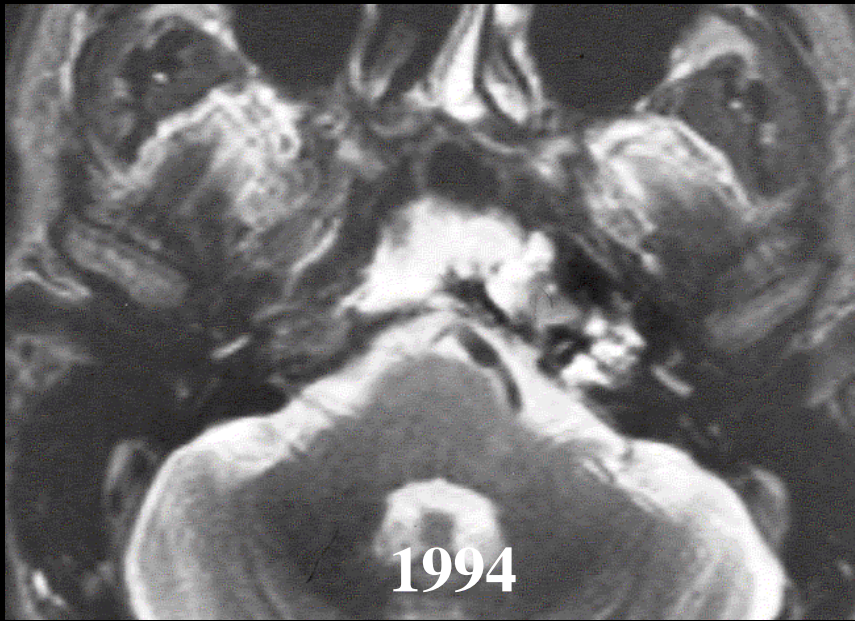
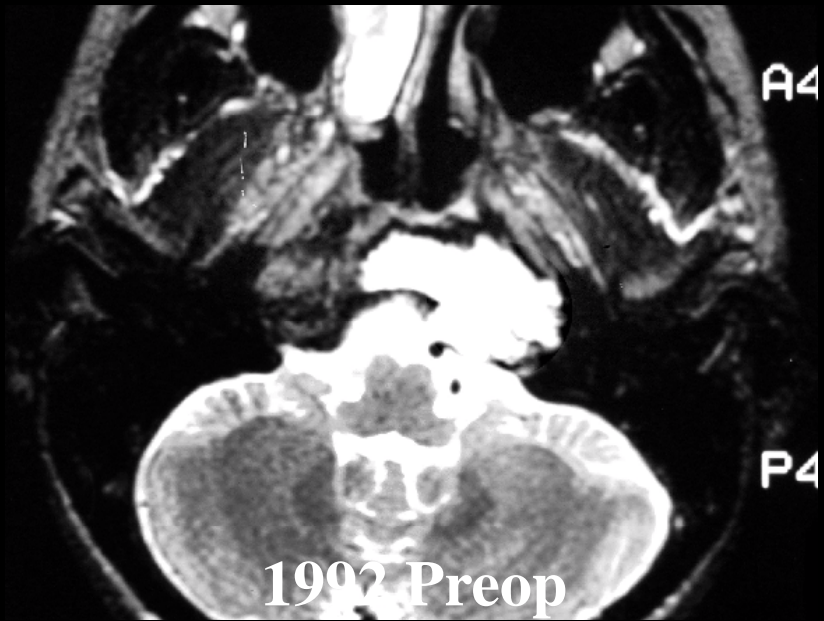
hyaline



myxoid

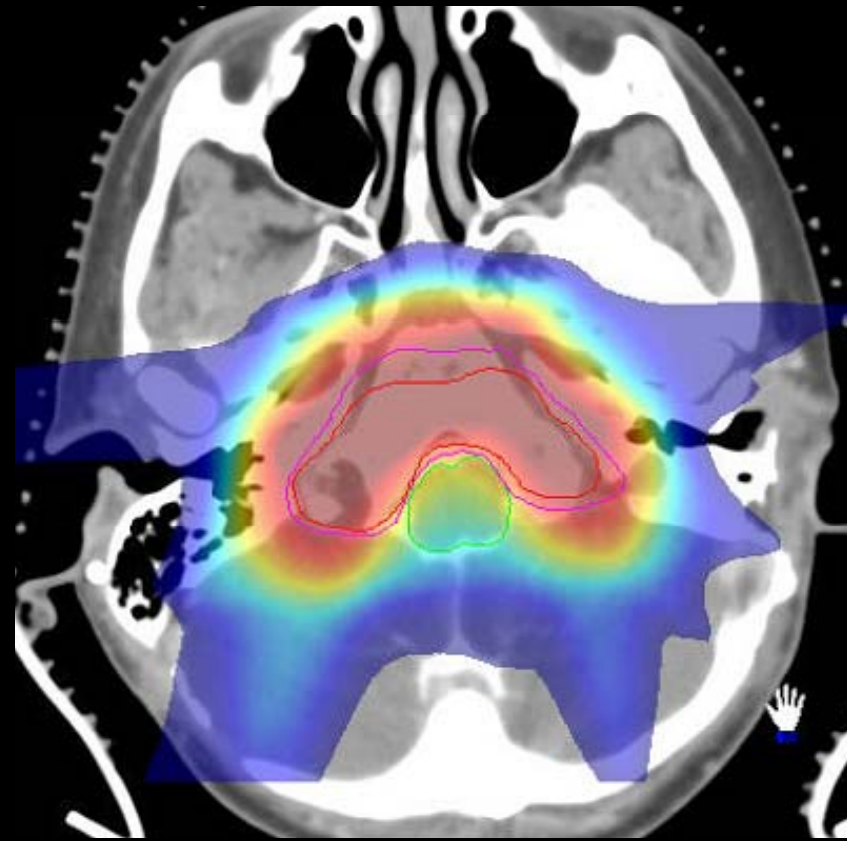
# Cranial Base Surgery

- Gross total tumor resection uncommon
- Propensity of cranial base tumors to recur locally



# Proton Radiation Therapy

High-dose fractionated precision conformal radiation therapy of targets in close proximity to critical, dose-limiting anatomical structures.



Effective dose Gy(RBE) = RBE x proton dose [pGy]

RBE = 1.1 (rel. radiobiological effectiveness)

pGy = proton-Gy

# Definition: Local Tumor Control (LC)

Freedom from tumor progression:

= Absence of radiographic features  
of tumor progression

Since 1975

600 pts. with **chordoma** of the cranial base

- 500 adults
- 100 children

400 pts. with **chondrosarcoma** of the cranial base

have received high-dose postoperative precision  
conformal fractionated photon-proton RT  
at the Massachusetts General Hospital



# Tumor Dose

**Chordoma:** Adults TD = 70 - 83 Gy(RBE)/37 - 44 fxs

Children TD = 79 Gy(RBE)/42 fxs

**Chondrosarcoma:** TD = 70 Gy(RBE)/35 fxs

## Normal Tissue Dose Constraints

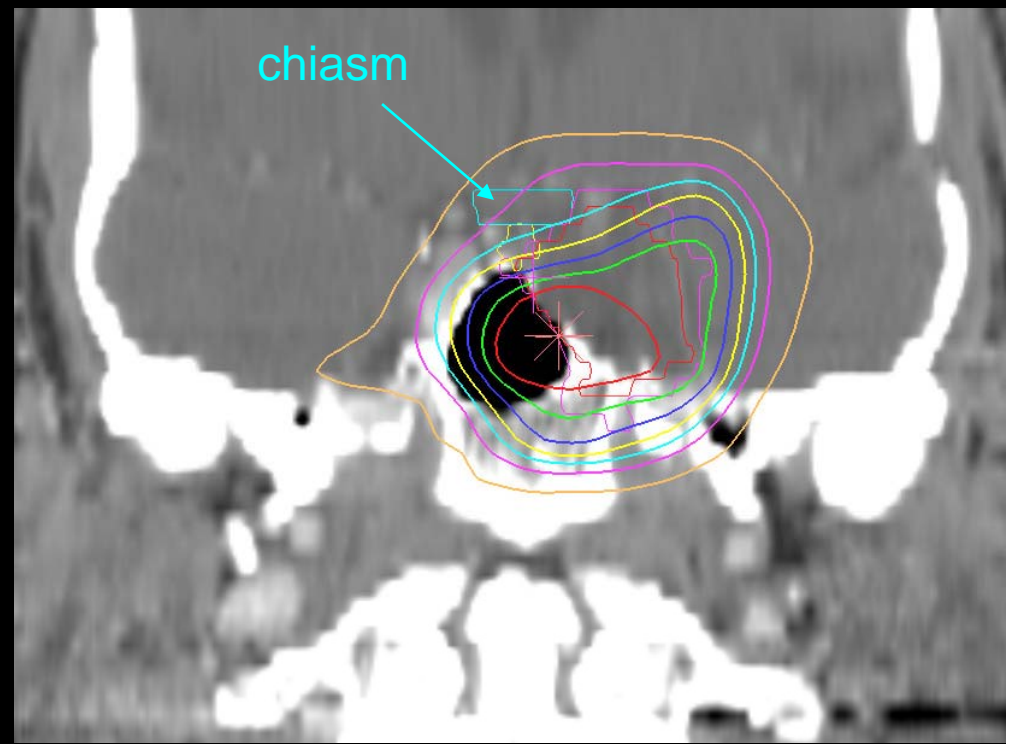
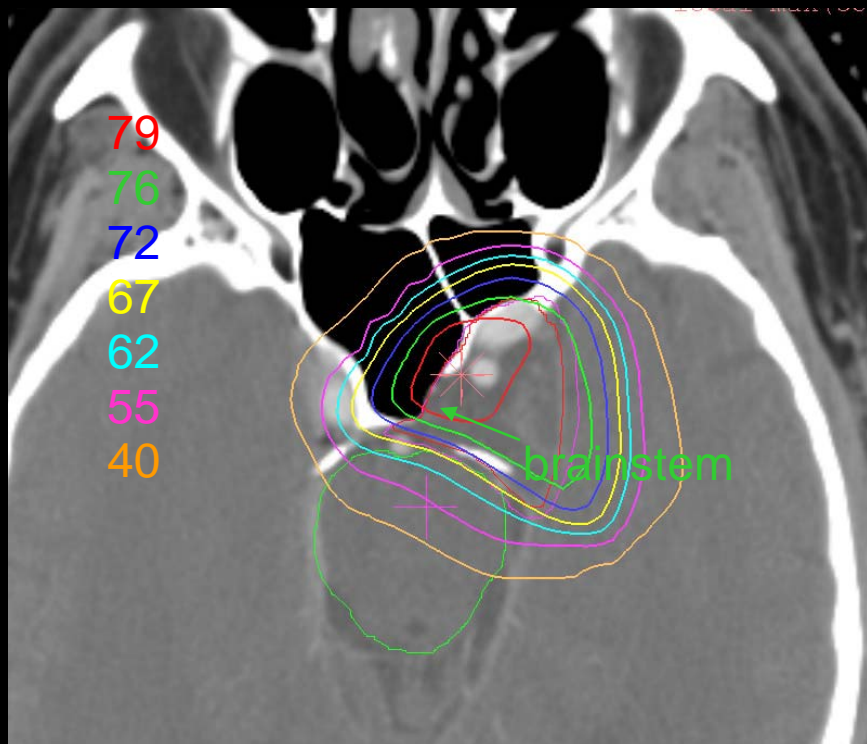
Optic Pathway:  $D \leq 62 - 66$  CGE

Brain Stem:Surface  $D \leq 67 - 70$  CGE

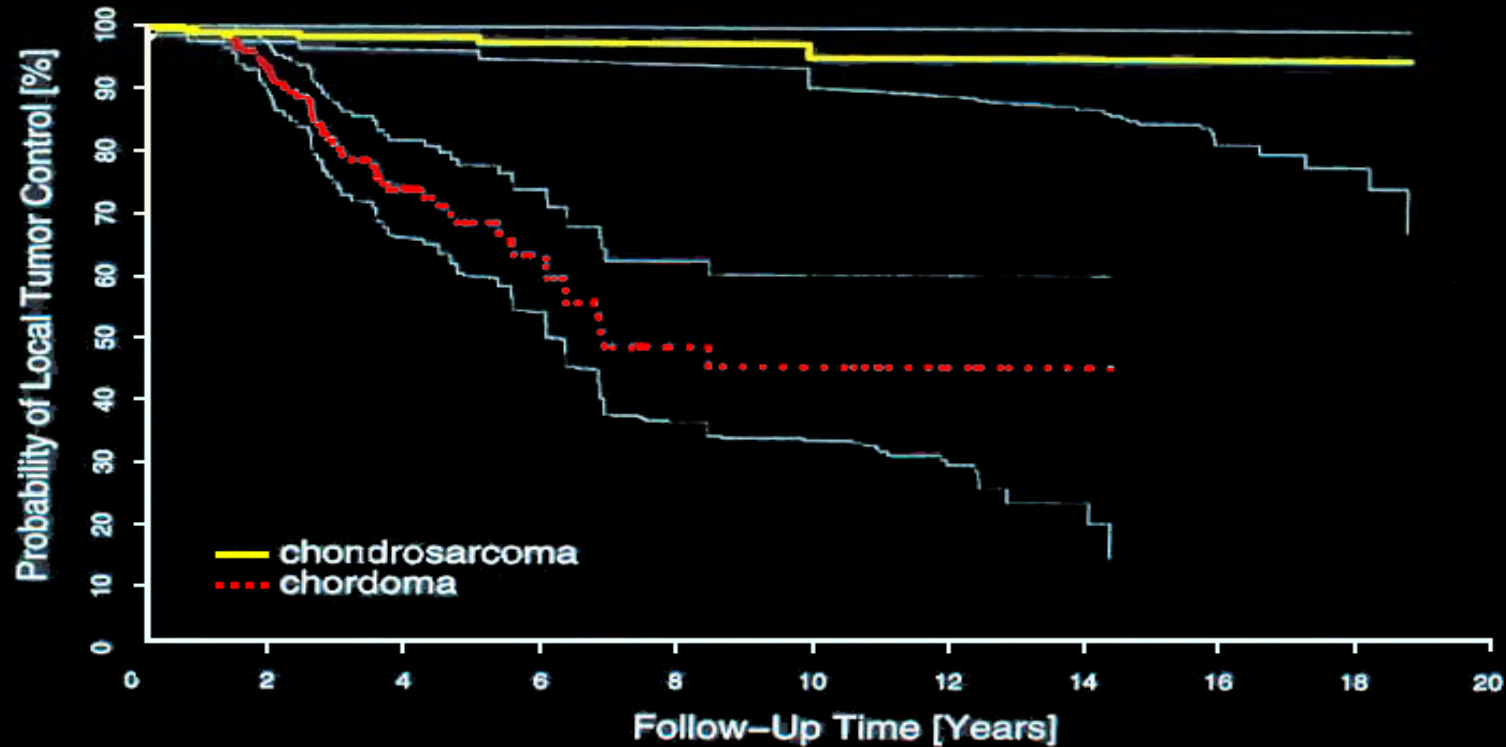
Center  $D \leq 55 - 58$  CGE

# Normal Tissue Dose Constraints

Optic Pathway:	$D < 62 \text{ Gy(RBE)}$
Brain stem: surface:	$D < 67 \text{ Gy(RBE)}$
center:	$D < 55 \text{ Gy(RBE)}$



# Local Tumor Control



## Chordoma (adults)

LC = 75 % at 5 yrs.

= 55 % at 10 yrs.

## Chondrosarcoma

LC = 98 % at 5 yrs.

= 95 % at 10, 15 yrs.

# Local Tumor Control: Chordoma

## Adults

LC = 75 % at 5 yrs.  
= 55 % at 10 yrs.

## Males

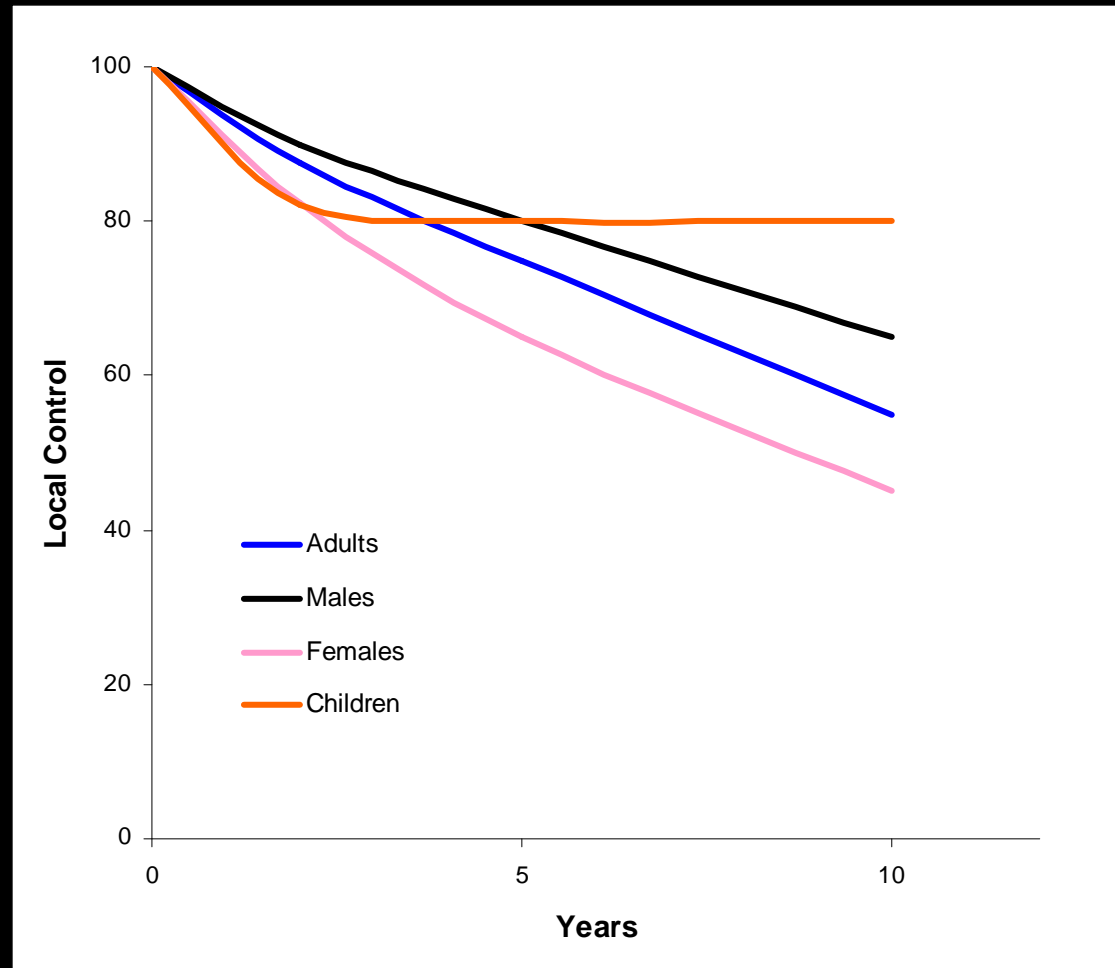
LC = 80 % at 5 yrs.  
= 65 % at 10 yrs.

## Females

LC = 65 % at 5 yrs.  
= 45 % at 10 yrs.

## Children

LC = 80 % at 5, 10 yrs.



# Local Tumor Control

100 children with chordoma of the  
cranial base

median F/U = 9.5 years

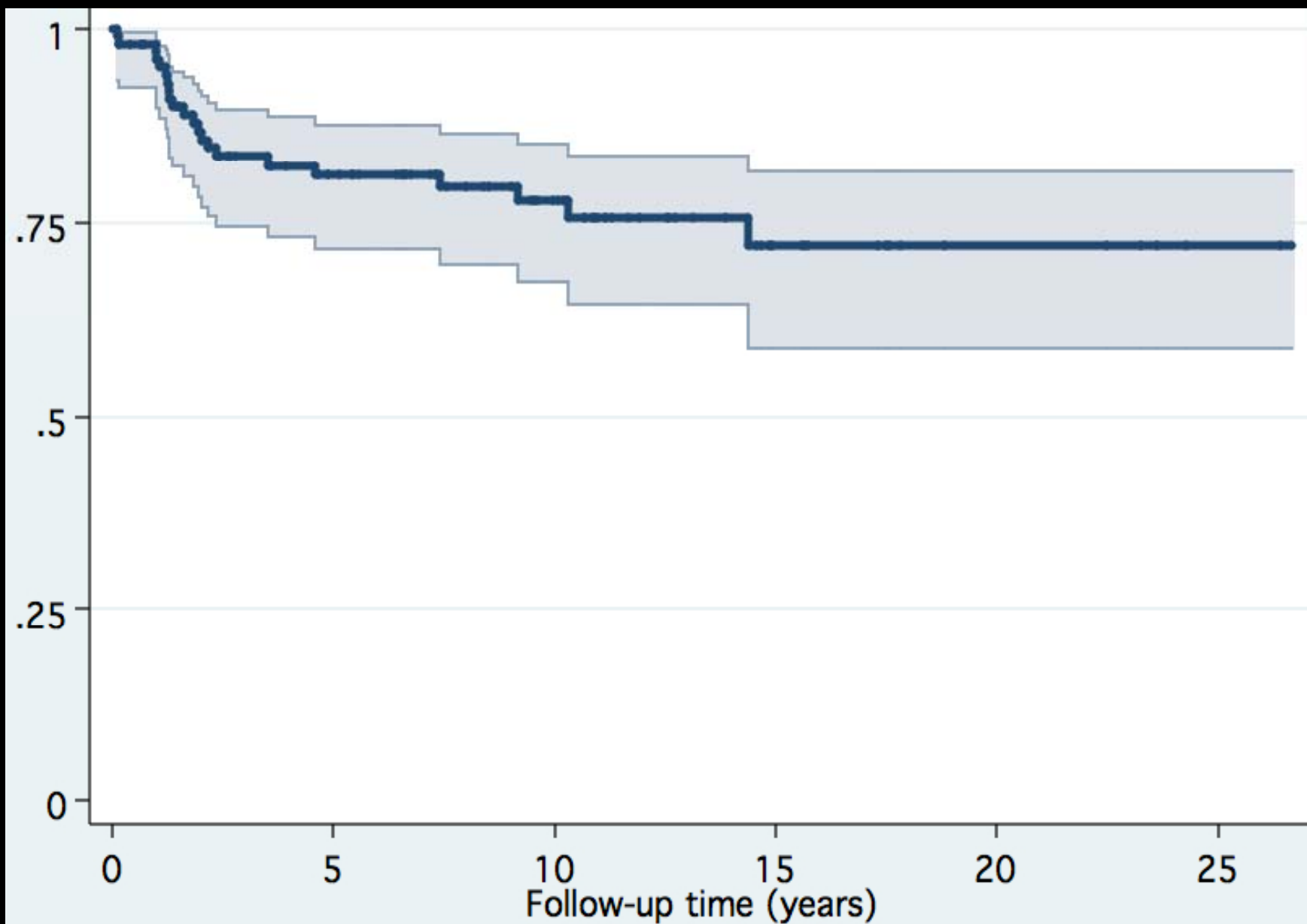
LC = 81 % 5 yrs.

= 78 % 10 yrs.

= 72 % 15 yrs.

20 yrs.

# LC: 100 Children with Chordoma of Cranial Base



# Conclusion

**Chordoma** and low-grade **chondrosarcoma** of the cranial base are locally invasive tumors with low metastatic potential.

They can be successfully treated by an interdisciplinary combined-modality strategy integrating:

(1) Cranial Base Surgery

(2) Proton Radiation Therapy

with the aim of maximizing tumor control and minimizing treatment-related morbidity.

# Treatment Strategy: Chordoma

## Cranial Base Surgery:

Gross total resection of chordoma if feasible with acceptable surgical morbidity.

Maximum debulking of chordoma to improve target geometry for postoperative proton RT.



# Treatment Strategy: Chondrosarcoma

## Cranial Base Surgery:

Biopsy to establish diagnosis

Limited tumor resection to improve tumor-related functional deficits

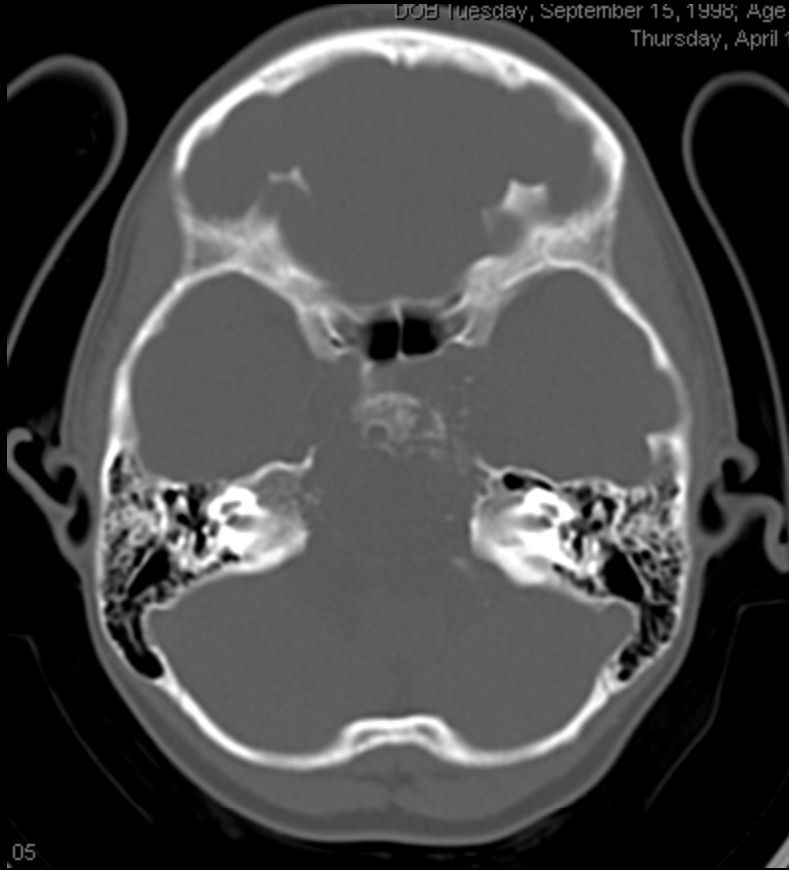
Partial tumor resection to improve target geometry for postoperative proton RT.

**No need for complete tumor resection of low-grade chondrosarcoma with potentially higher surgical morbidity**

# RT - Toxicity

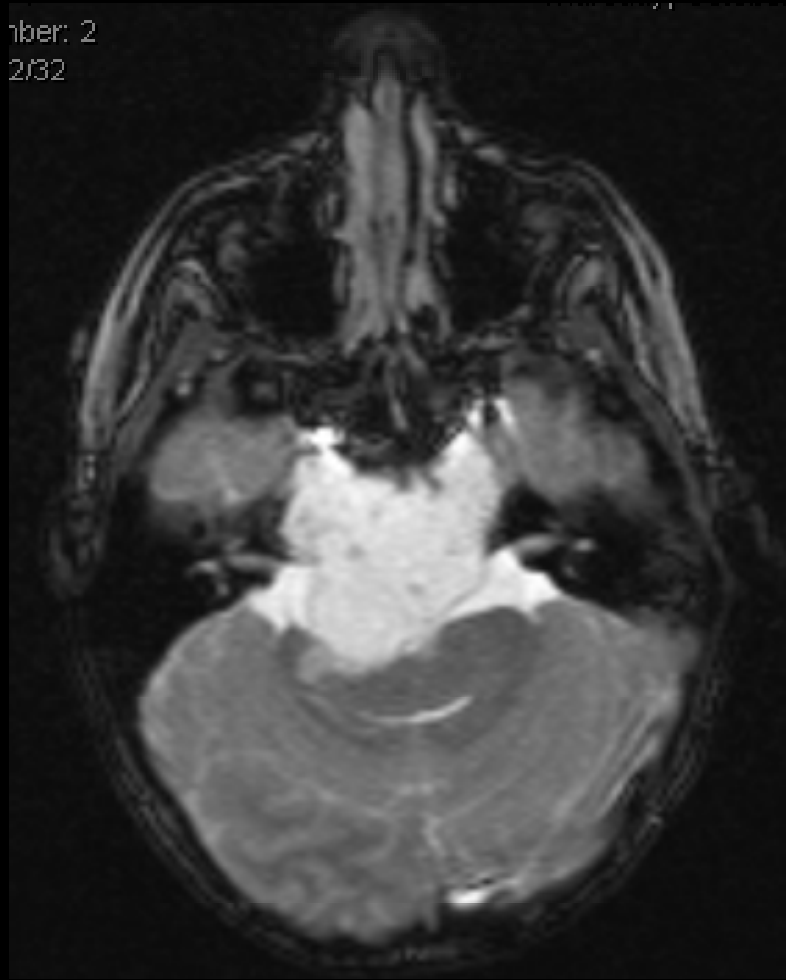
- Neuro-cognitive
- Neuro-endocrine
- Visual
- Audiologic
- CNs
- Cerebro-vascular
- Cranio-facial
- Osteoradionecrosis
- RT- induced tumor

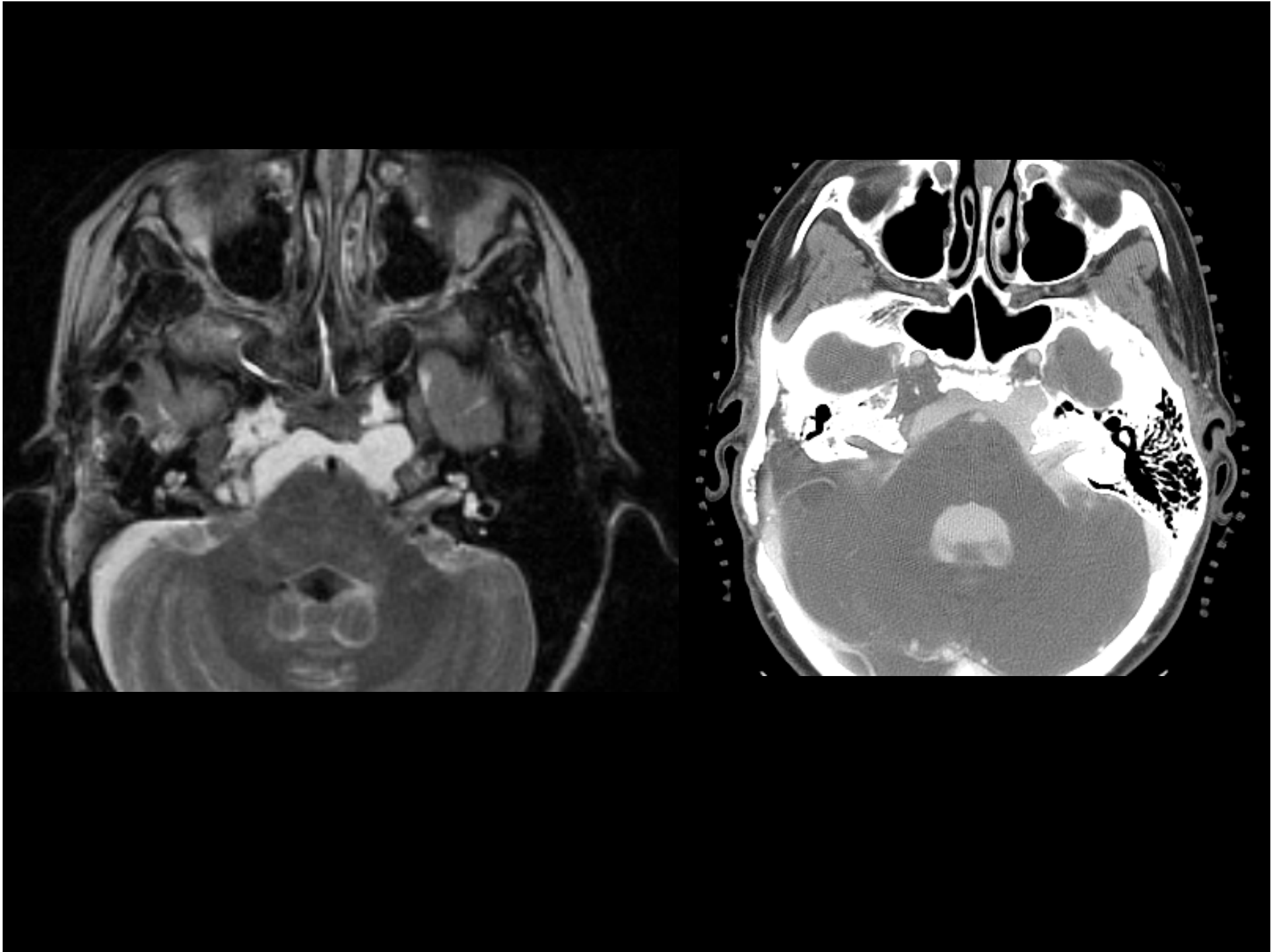
DOB Tuesday, September 15, 1998; Age  
Thursday, April 1

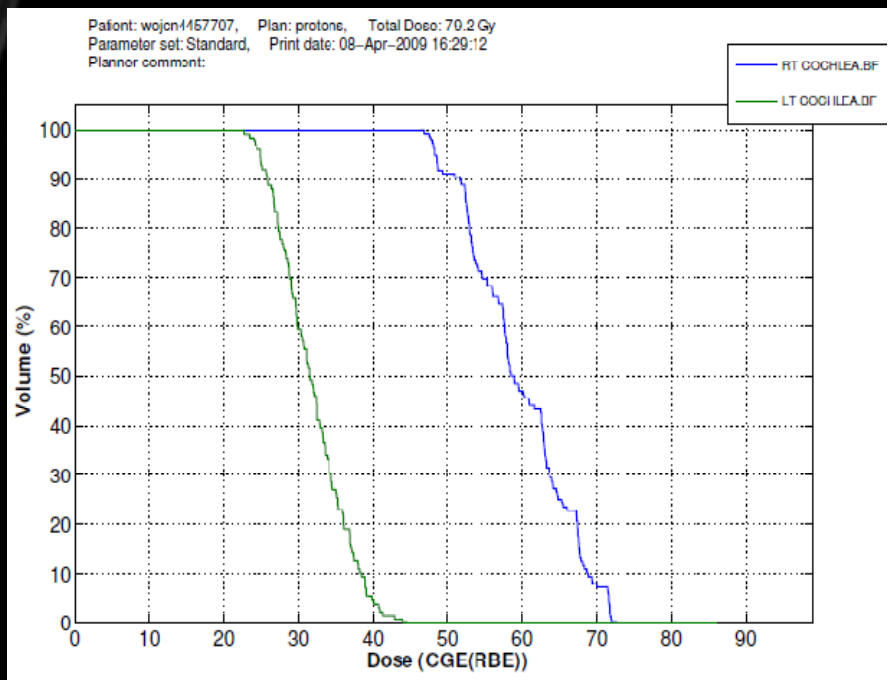
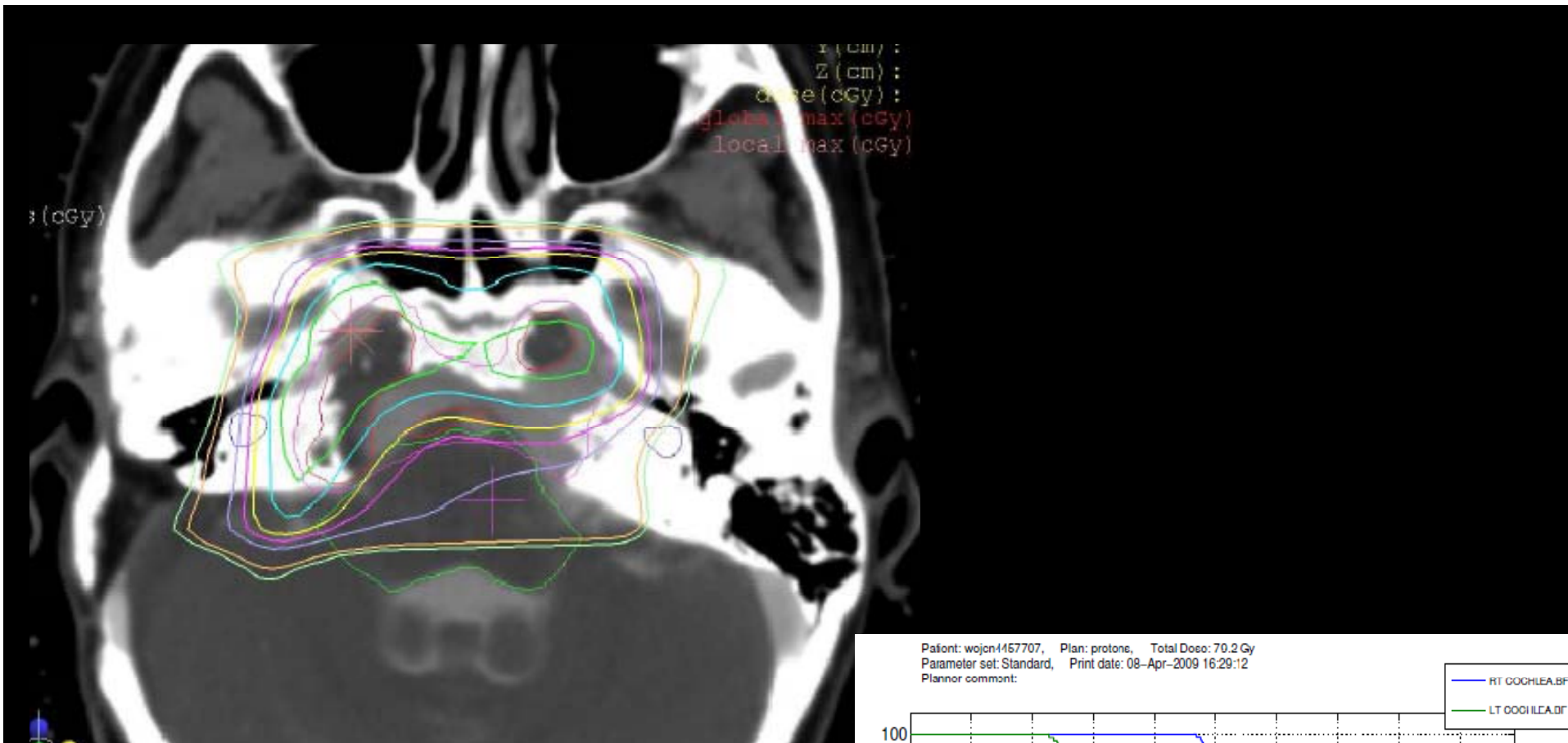


05

Number: 2  
2/32

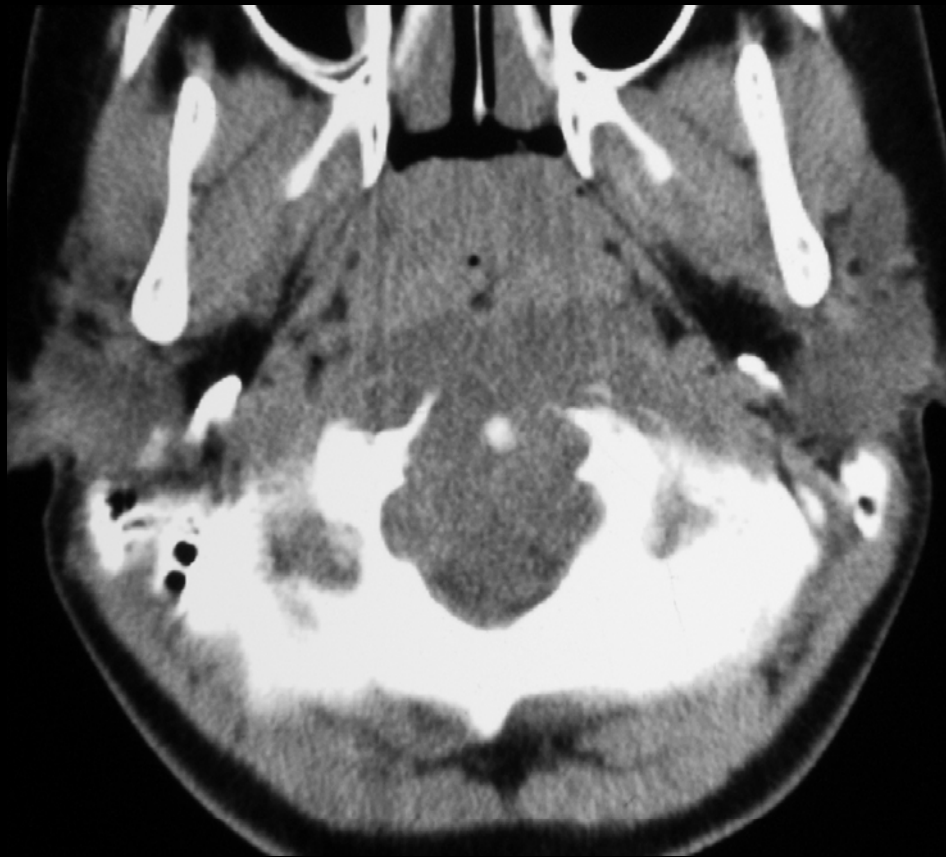




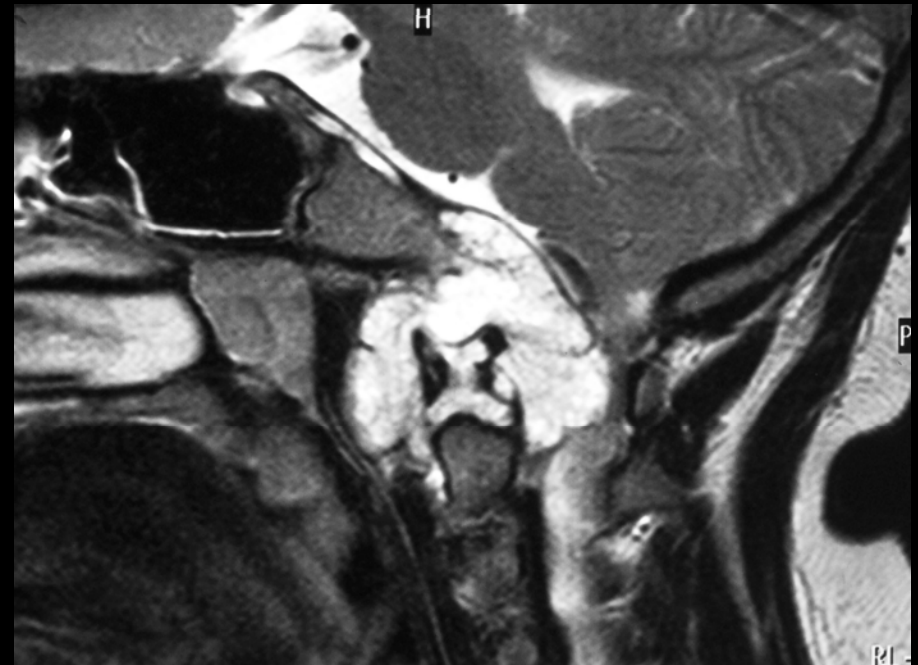
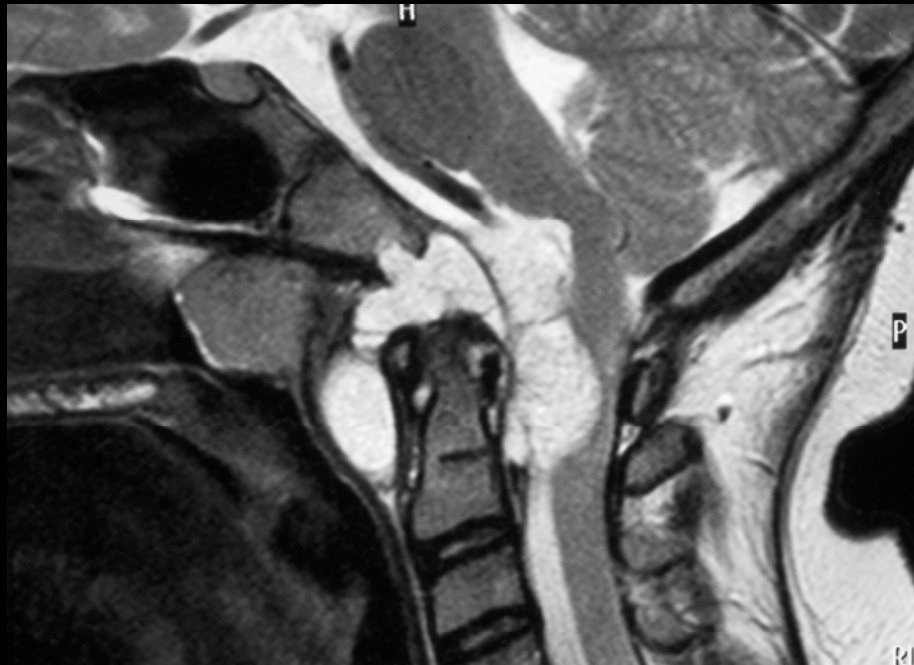


# Chordoma of Cranio-cervical Junction

11 y/o F, progr. rt.-sided weakness



# Chordoma of Cranio-cervical Junction



# Chordoma of Cranio-cervical Junction

- 12/22/06: Transoral-transpharyngeal biopsy: chordoma
- 01/27/07: Dorsal occipito-cervical (C3) stabilization
- 02/07/07: Part. transoral-transpalatal tumor removal, res. ant. arch C1, odontoidectomy
- 05/02/07: Part. tumor removal via rt. submental appr.
- 06/07/07: Part. tumor removal via lt. submental appr.
- 06-12/07: Gleevec (Imanitib mesylate) 400mg/m<sup>2</sup> q.d.



33



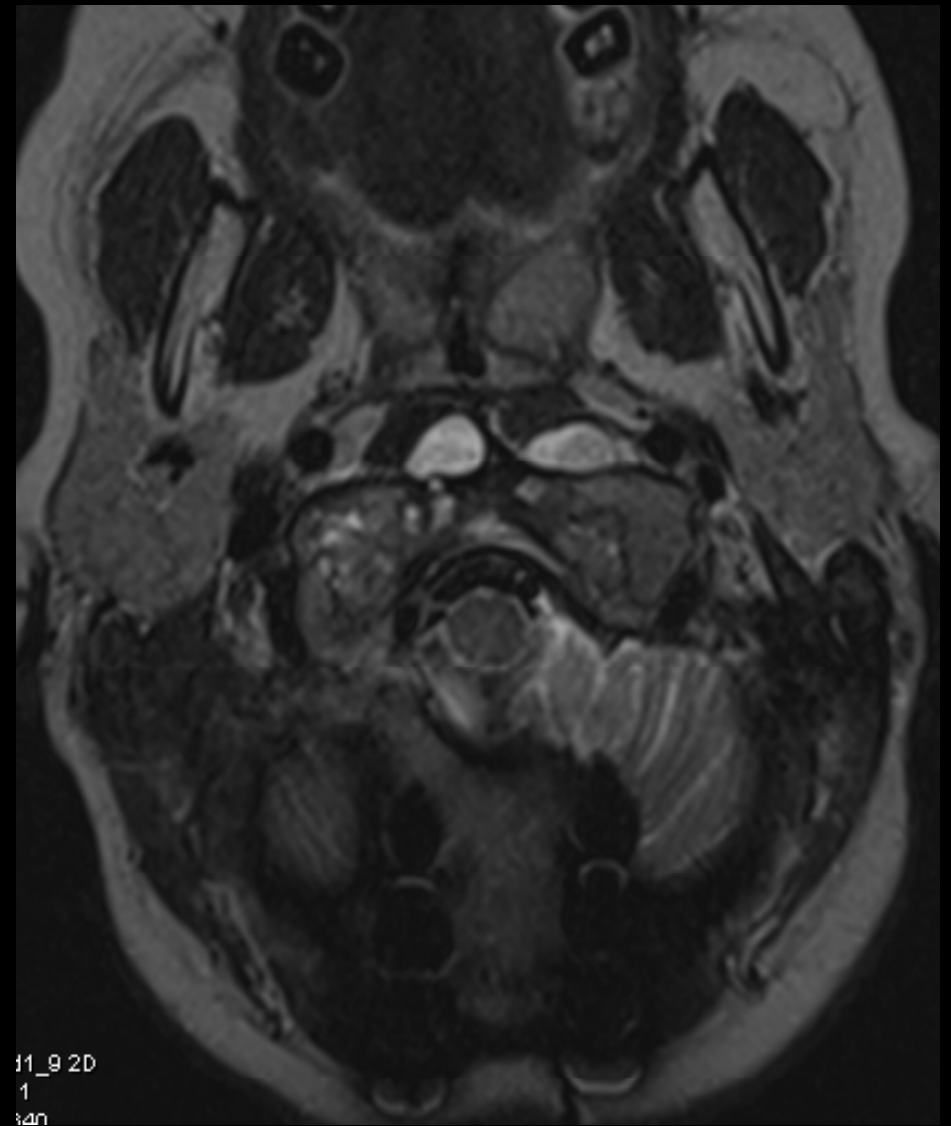
# Chordoma of Cranio-cervical Junction

Near total removal of intracranial-intraspinal tumor  
in 2 stages:

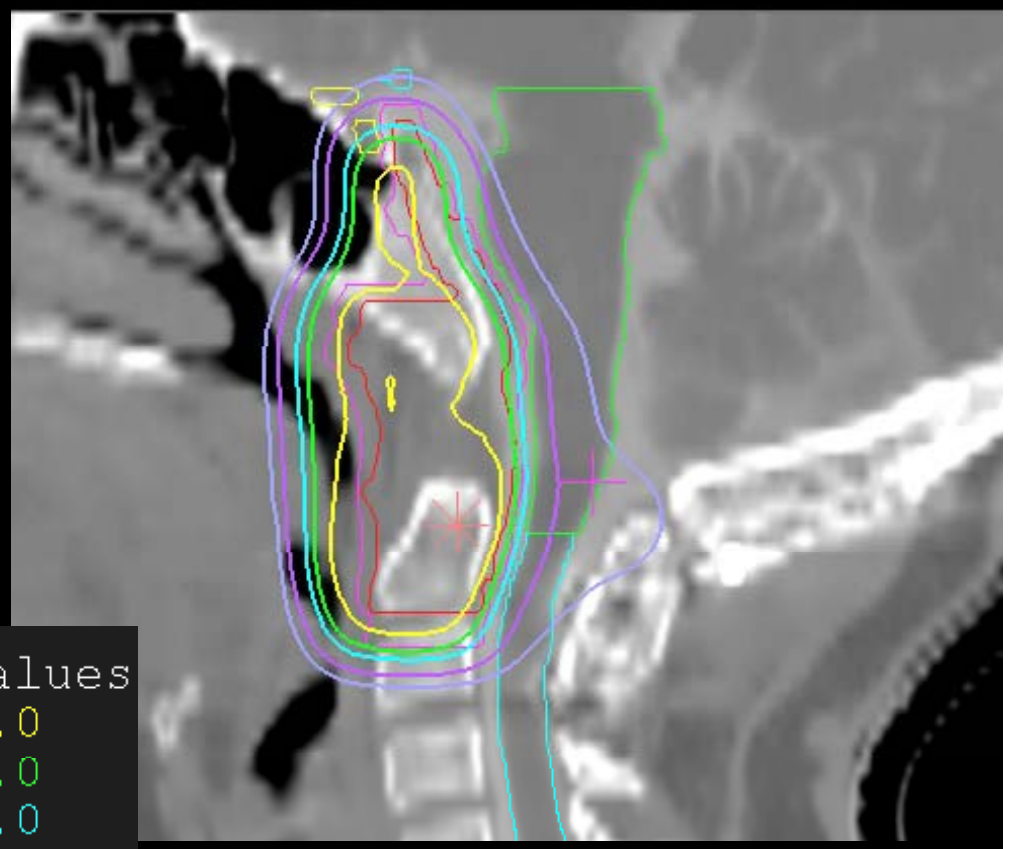
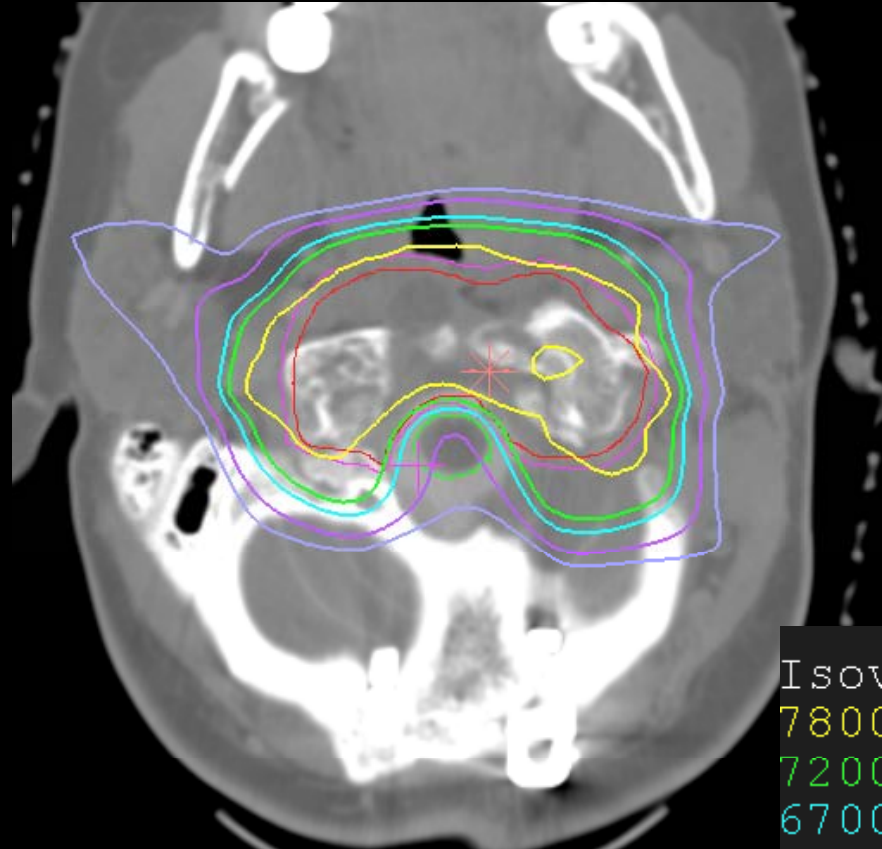
01/14/08: Lt. far lat. transcondylar appr.

01/29/08: Rt. far lat. transcondylar appr.

Postop: part. lt. CN XII palsy



11\_9 2D  
1  
:an



Isovalues  
7800.0  
7200.0  
6700.0  
5500.0  
4500.0

Thank you