Challenges of Retreatment

Allan F. Thornton

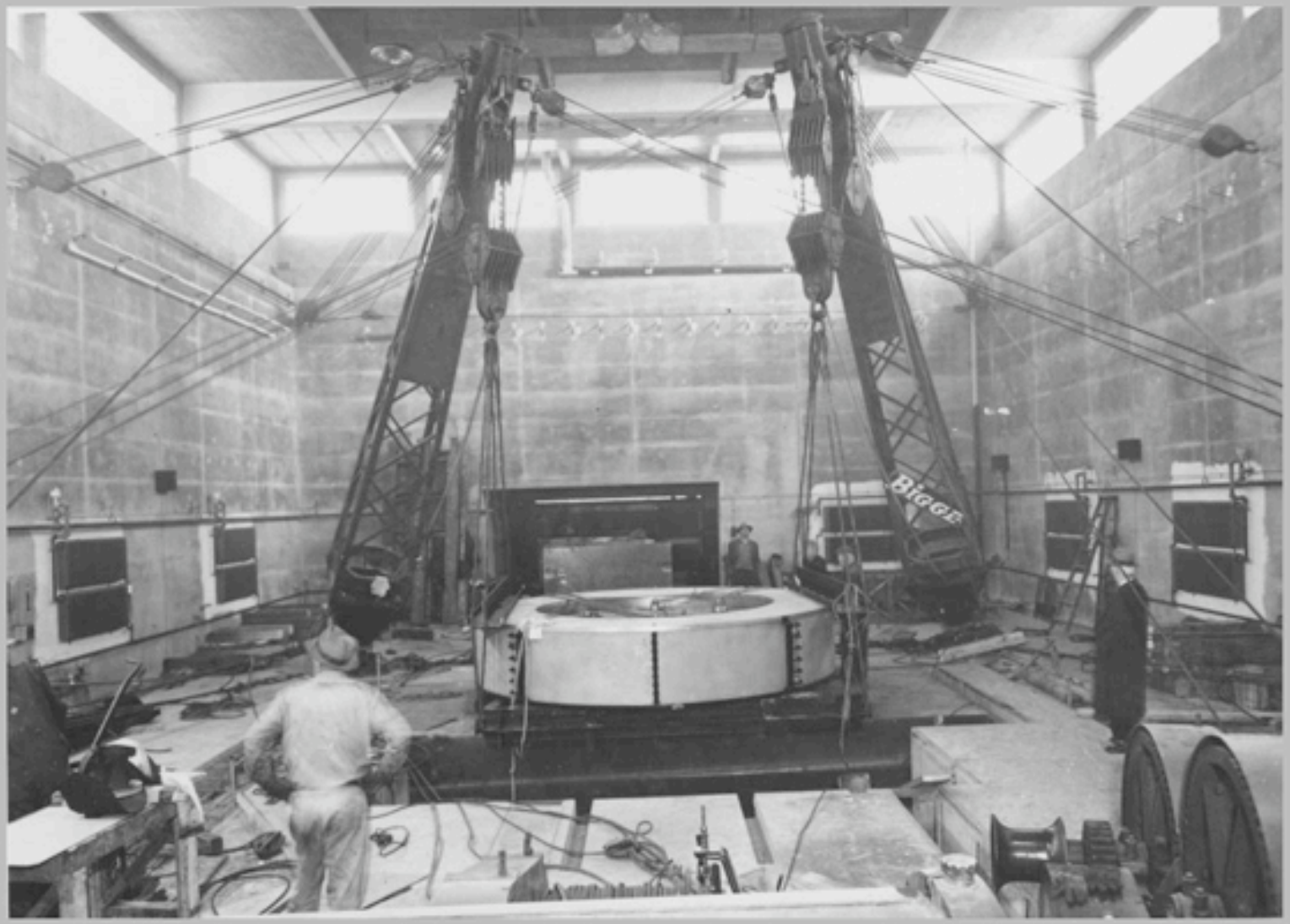
Midwest Proton Radiotherapy Institute

MPRI
MIDWEST PROTON RADIOTHERAPY INSTITUTE
On target for life and health

Harvard Cyclotron Laboratory

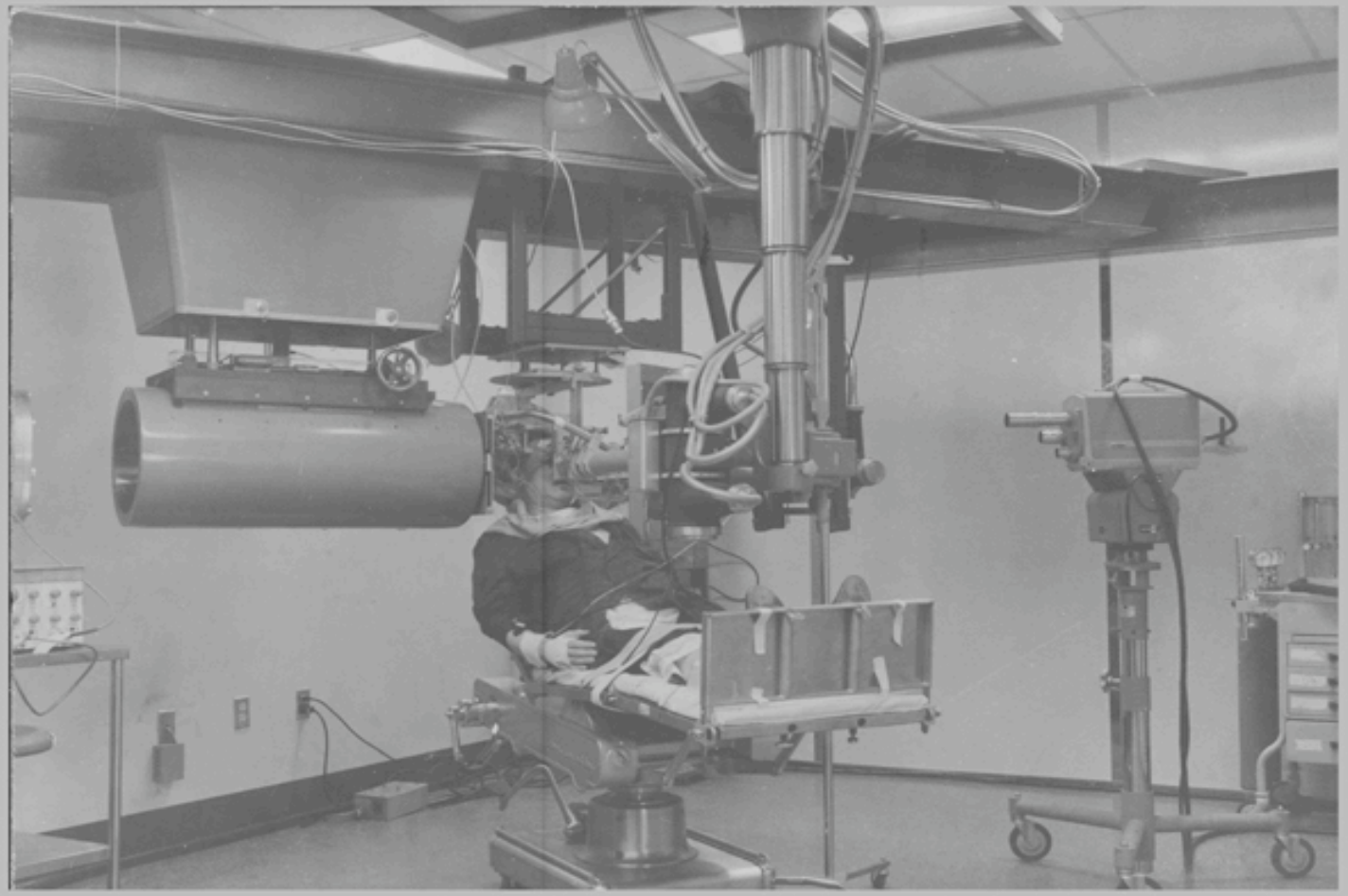
1946
to
4/11/2002

Cyclotron Buildings 1947

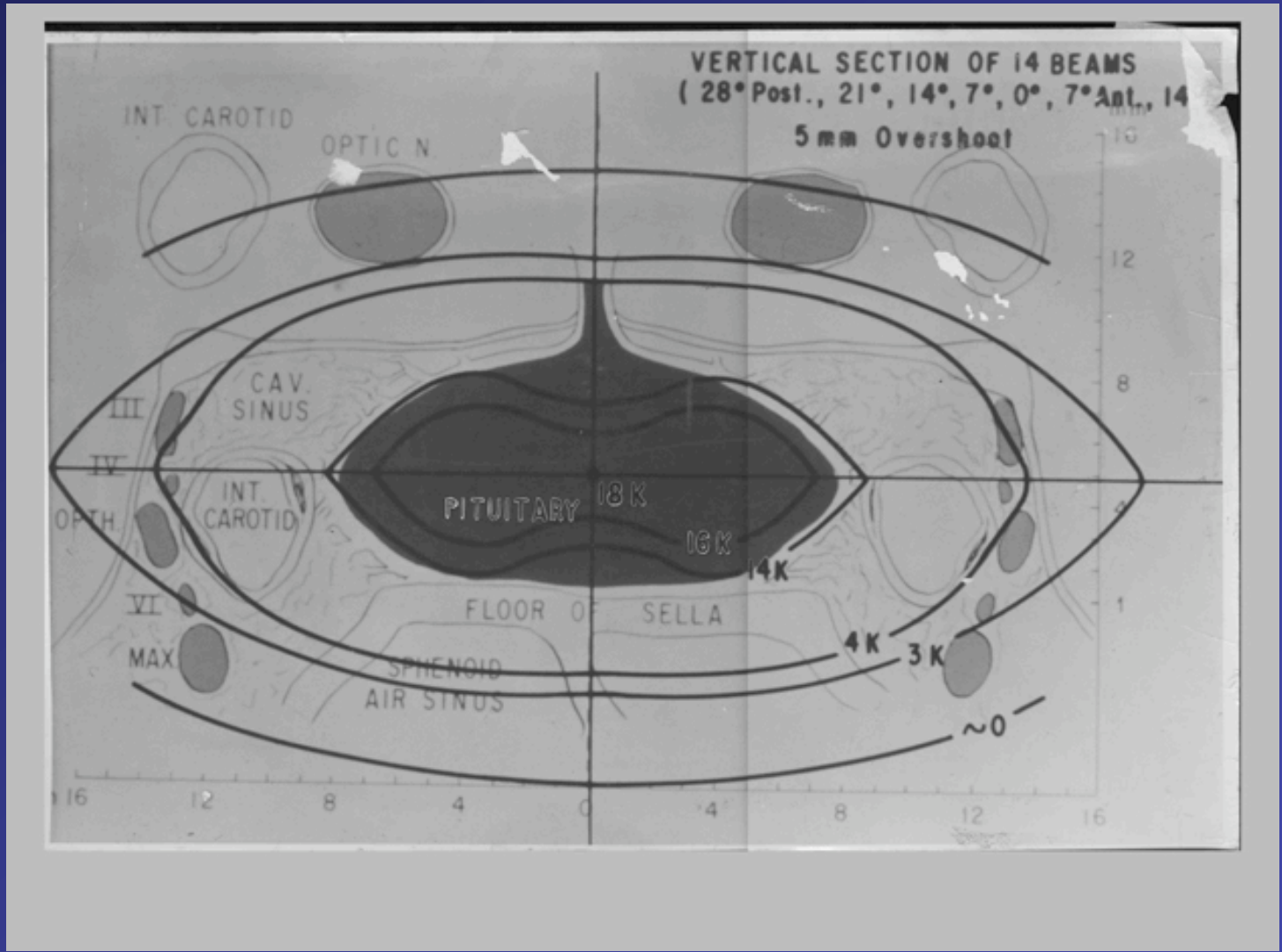


Coil being installed
Taken on Dec 10 1947

IGRT – circa 1965



Multiplanar Dosimetry c 1965



Clinical Challenges of Re-irradiation

- Usually at maximum tolerance for adjacent critical structures (chiasm, spinal cord)
- "Recall" phenomena – eg, skin, mucosa
- Concomitant chemotherapy often given for systemic control
- Debilitated patient – setup challenge

MPRI
MIDWEST PROTON RADIOTHERAPY INSTITUTE
On target for life and health

Goals of Proton Therapy in "Retreatment"

- Elimination of dose to adjacent critical structures previously tx
- Trajectory selection accounting for previous techniques
- Homogeneity optimal
- Hyperfractionation – but is it reproducible?

MPRI
MIDWEST PROTON RADIOTHERAPY INSTITUTE
On target for life and health

Nuances of Recurrence

- XRT – induced second tumor??
- Marginal failure about an adequate dose, but inadequate volume – aiming issue
- Insufficient dose, but adequate volume – difficult situation to re-irradiate
- Sufficient dose with adequate volume but with central failure – expect complications

Effects of Normal Tissues

- Wide range of complications possible depending on adjacent normal tissues
- Sarcomas/soft tissues vs nerve/cord vs skin/mucosa
- Do we really believe the linear quadratic model to hold for spinal cord with an alpha/beta of 2 for cervical and a differing value for lumbar cord of 4?
- Steep, steep portion of sigmoid curve we operate on for most re-irradiation of CNS tumors – should we have faith on a "safe" composite BED of <135Gy(2) for spinal cord?

Timing of Recurrence/Re-irradiation

- Personality of tumor - How long was local control established originally? >1yr or <1yr?
  - Reflects natural history/aggressiveness of tumor – Heidelberg/Dutch glioma retreatment series
  - If <1 year, was local control ever established??
- Separation duration of 2 irradiation courses: Spinal cord data suggest risk increases with <6 months between courses.

Open Your Eyes
(and those of the Patient and your Colleagues)

- They remember you for your complications, not your successes…… Dr. Suit, et al.
- Consent your patient carefully – they really do not believe the complications are possible, only success is likely. Have a family member present – do not rush consent.
- "Consent" your colleagues ahead of time – ie, the neurosurgeon that must re-resect the radionecrosis of your attempts.

Improve Your Odds of Success

- Hemoglobin, nutrition, hydration, diabetes – minimize the PLD and maximize repair of the normal cells
- Hyperfractionate? Ok, but do not compromise effective total dose in process.
- Volume reduction? Concentrate on GTV – use chemo/EGF modulators for adjuvant tx. Protons reign here.
- Concomitant chemo?? - Reduce variables – and normal tissue insults – avoid the temptation.
- Prolonged delivery?? – Pulsed reduced rate RT – UW
- Hyperbaric Oxygen – facilitator of microvascular repair in H&N – maybe CNS? - at 4-6 months post RT.

Literature Review

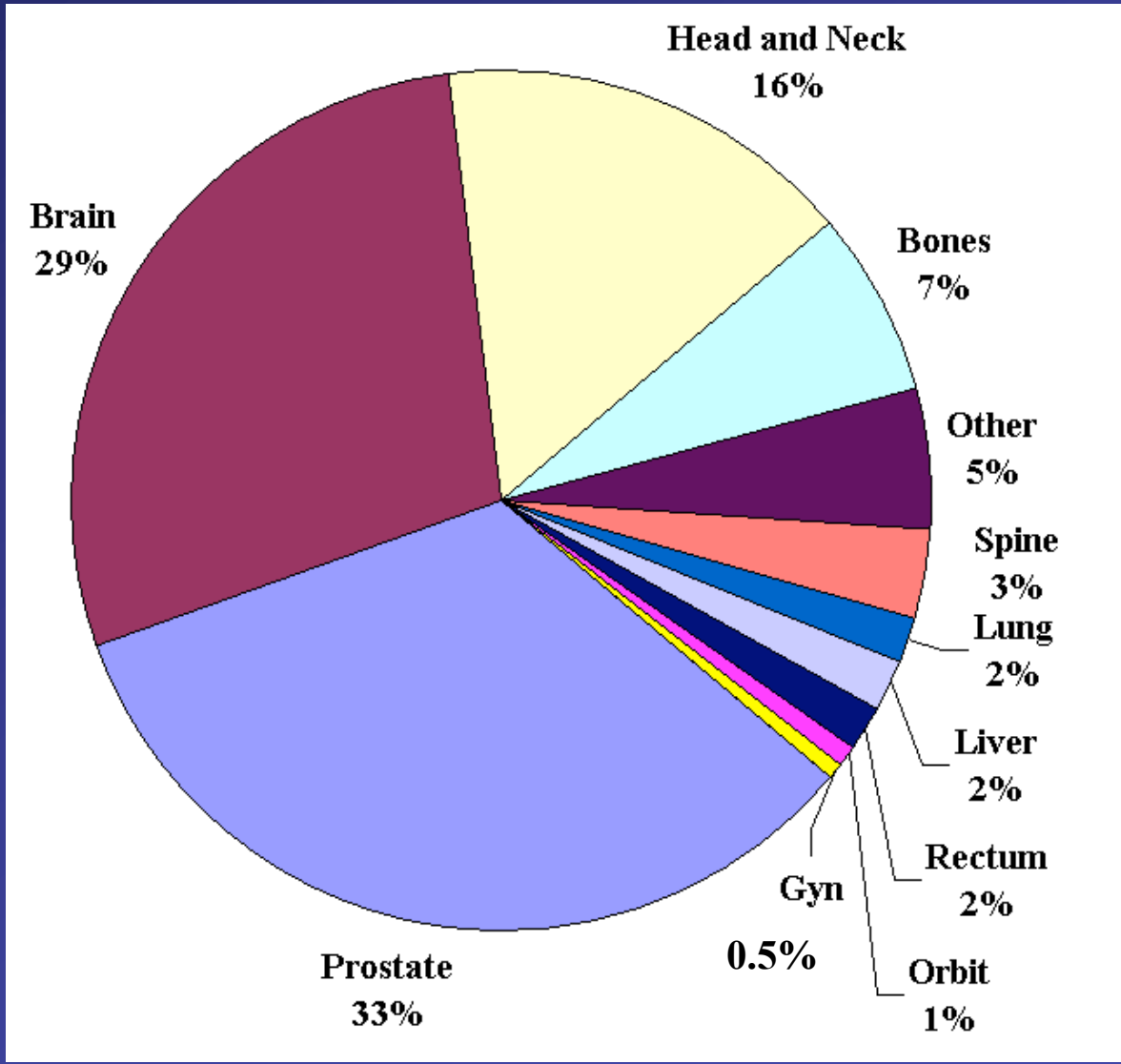
- 2 Particle re-irradiation papers: MGH ocular melanoma/proposed advantage paper for metastases
- 50+ publications 1998-2008
  - CNS: 17 (31%)
  - ENT: 19 (35%)
  - Breast: 6 (11%)
  - Rectal: 3 (6%)
  - Sarcoma: 3 (6%)
  - Metastases: 3 (6%)
  - Other (Skin, Lung): 3 (5%)

Proton Reirradiation for Ocular Melanomas MGH

- 70/5 Gy retx after 70 Gy/5
- ~4 year interval
- 63% local control/stability
- 55% eye retention rate
- 19% visual preservation rate
- Metastatic rate??

MPRI Patient Treatments – 5/08

- >425 patients treated
- 5% Retreatment cases



MPRI Recurrent Case Statistics

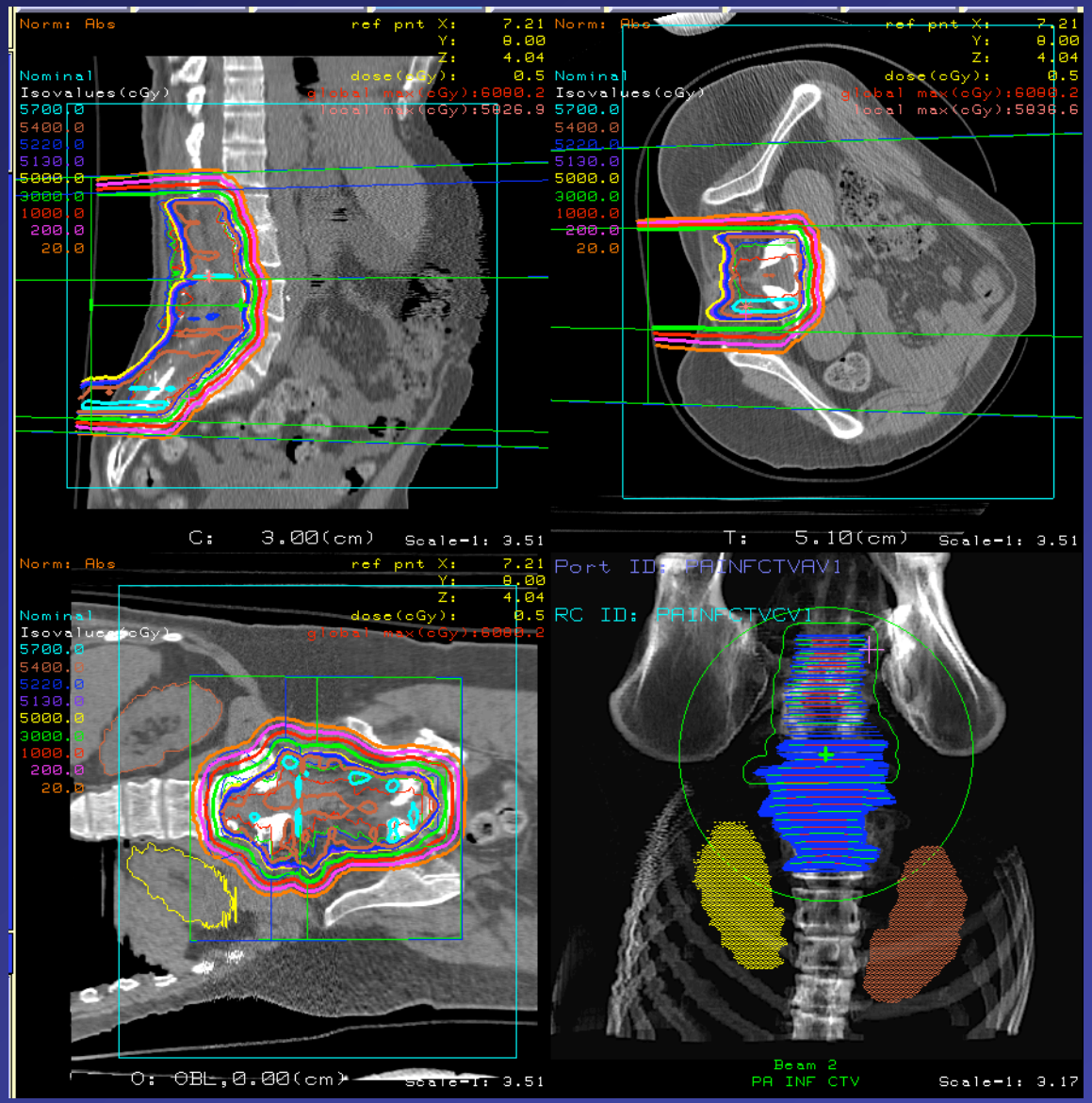
- 24 cases treated 4/04 to 5/08 (5%)
- Median OS = 1.7 yrs
- Local failure/progression rate = 28%
- Complications: 3/24 = 13%
- Case mix:
  - 30% base of skull
  - 20% head and neck/scalp
  - 10% vertebral column metastases retx
  - 25% brain/spinal cord parenchyma
  - 15% rectal/GI

Recurrent Caudal Ependymoma

- Previously treated 1971 @ age 12, L2-L3, 3900 cGy Co CNS axis PA SSD + 1050 cGy caudal boost
- Incomplete resection – age 12
- Recurrent 1985
- 3 resections all STR, now progressive disease, paraplegia
- Retreatment: 5400cGy/180cGy p+

MPRI
MIDWEST PROTON RADIOTHERAPY INSTITUTE
On target for life and health

Recurrent Caudal Ependymoma

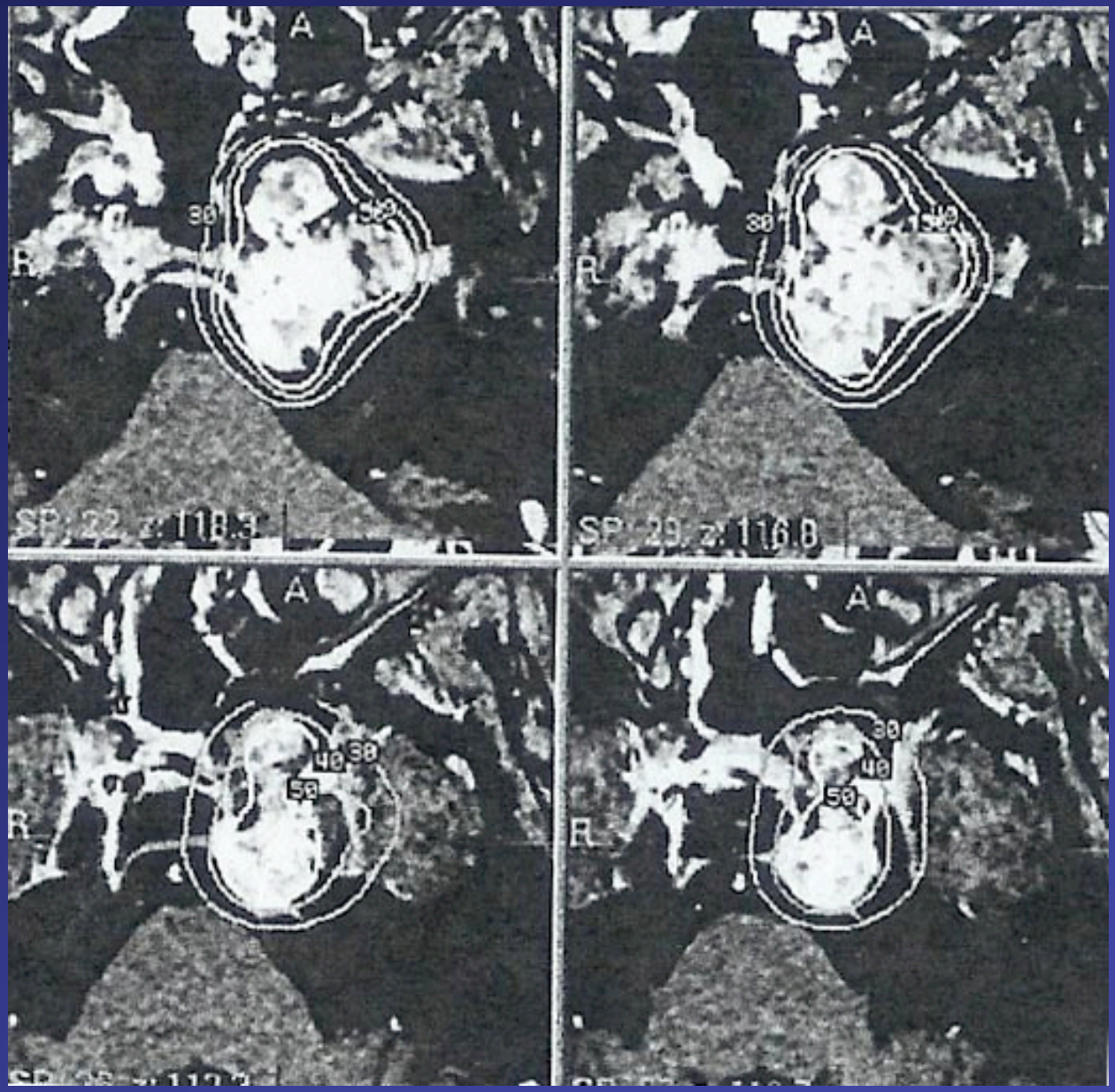


MPRI
MIDWEST PROTON RADIOTHERAPY INSTITUTE
On target for life and health

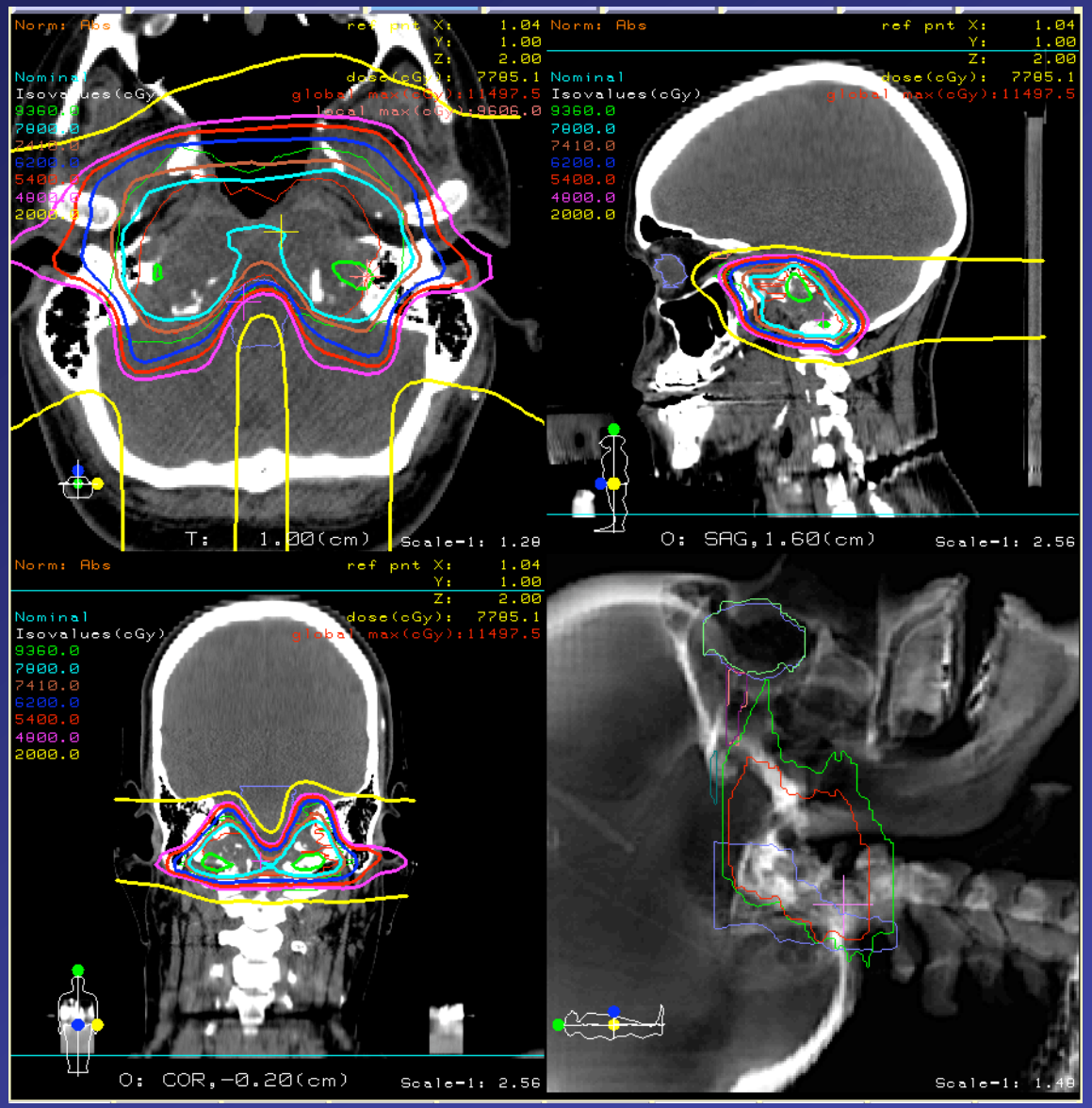
Recurrent Clival Chordoma

- 33 y/o dx 1996 with sellar/clival chordoma
- 1996-2005: 6 transphenoidal, endoscopic resections + 4 GammaKnife tx
- Multiple progressions at inferior margin
- Recurrence bilateral petroclival junctions and progression to top-C1
- Retreatment: 7800 cGY/180cGy p+

MPRI
MIDWEST PROTON RADIOTHERAPY INSTITUTE
On target for life and health


A
R
30
50
A
R
30
40
A
R
40
30
50
A
R
30
40
50

Recurrent Clival Chordoma



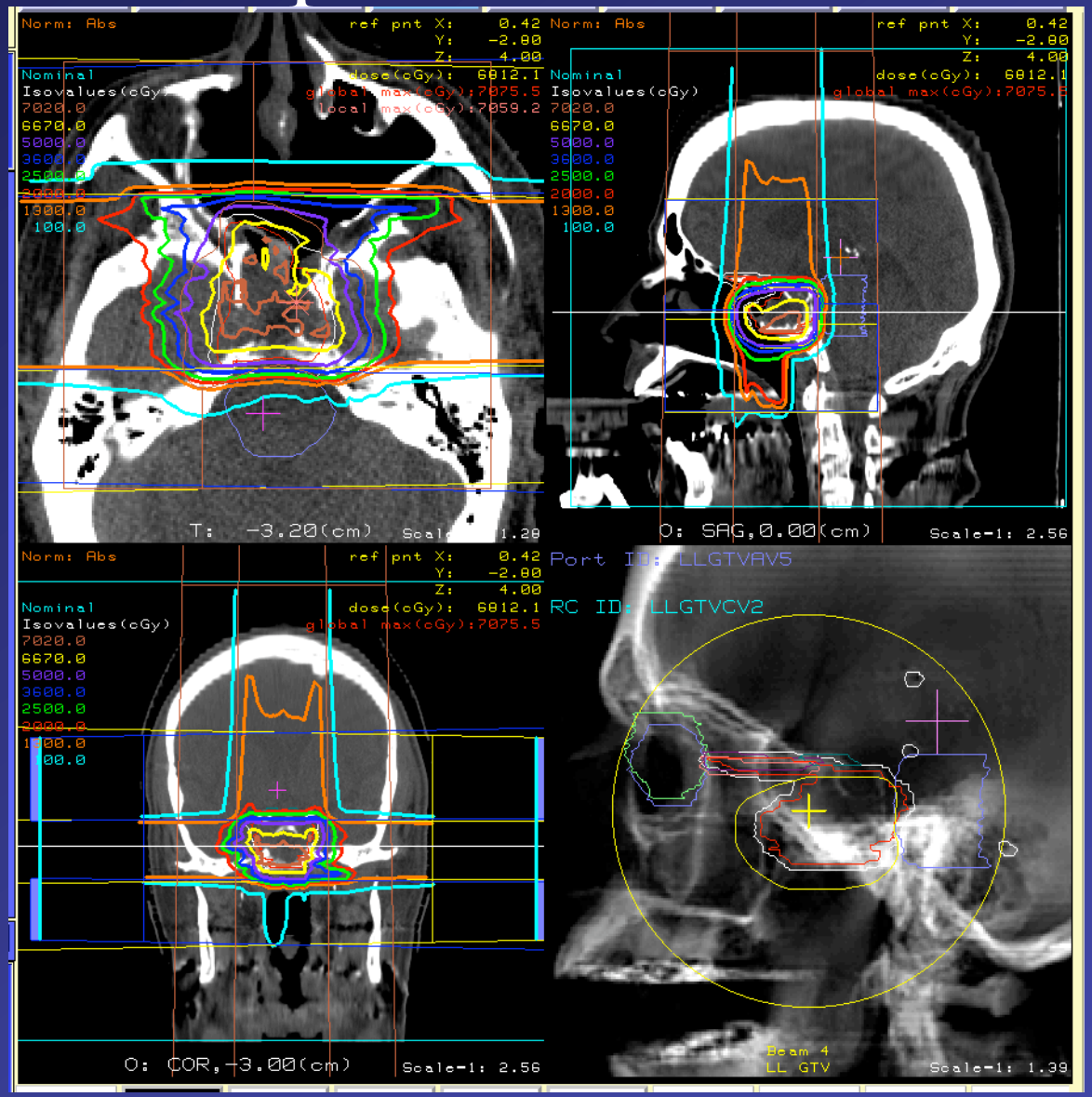
MPRI
MIDWEST PROTON RADIOTHERAPY INSTITUTE
On target for life and health

Recurrent Adenoidcystic Carcinoma Sphenoid Sinus

- 62 y/o Dx 2000 with ACC of Sphenoid STR
- 11/01: 5400/180 – traditional 3-field
- Progression into ethmoids and sella → bitemporal field loss, decreased color perception
- 2 additional STR (transnasal approach)
- Retreatment: 7200cGy/100cGy BID p+

MPRI
MIDWEST PROTON RADIOTHERAPY INSTITUTE
On target for life and health

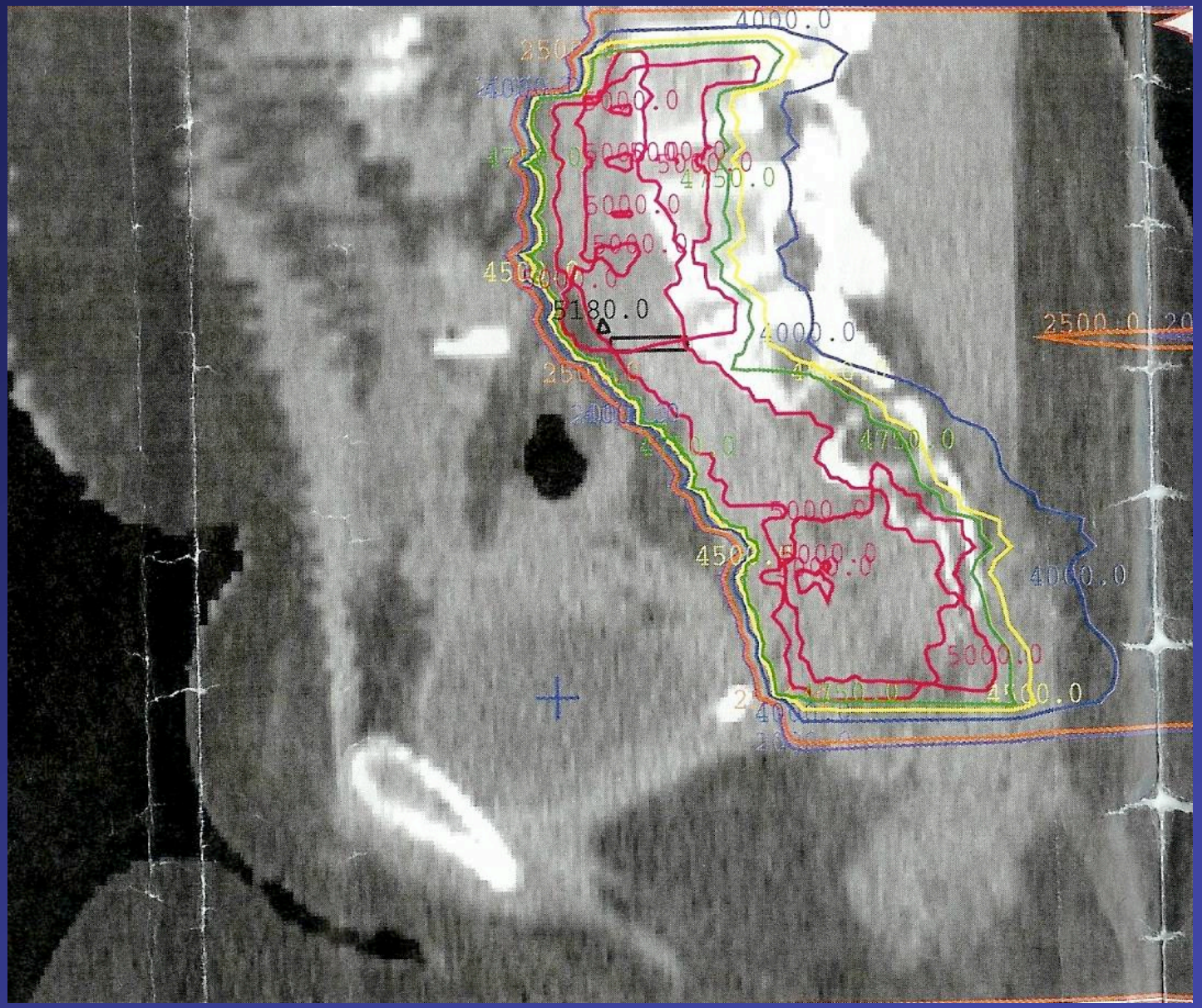
Recurrent Adenoidcystic Carcinoma Sphenoid Sinus

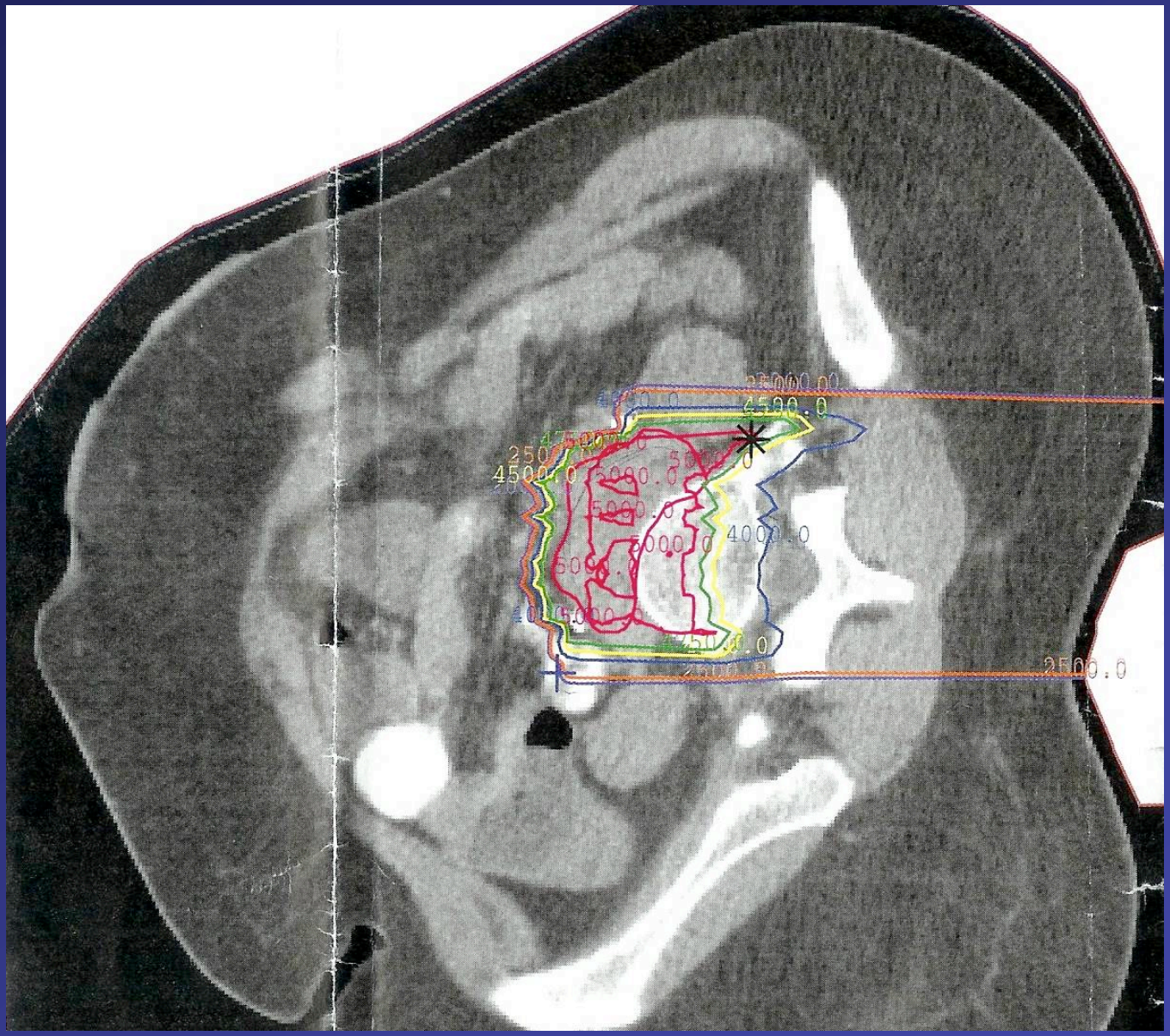


MPRI
MIDWEST PROTON RADIOTHERAPY INSTITUTE
On target for life and health

Clinical Case – D.O.

- 32 YO African female IU student with recurrent rectal carcinoma, s/p full photon radiation and chemotherapy – requiring 100mg MS/hour for pain – still teaching and studying for PhD
- Referred by BMG Radiation Oncology
  - Received 55Gy of proton re-irradiation
  - No dose delivered to bowel or spinal cord
  - At 7 months, tumor 90% regression, complete pain relief
  - Survived 2.3 years after re-irradiation, finished PhD.


4000.0
5180.0
4000.0
2500.0
4000.0
5000.0
4750.0


4500.0
4500.0
4000.0
2500.0

Conclusion
(Retreatment Appraisal Tips)

- Choose your neighborhood carefully:
  - In-field, marginal, suboptimal dose, XRT induced?
- Who are your neighbors? – location, location: are you at the peak (glioma-chiasm/cord), or a little lower (sarcoma-soft tissue)
- Realistic goals: Cure vs durable palliation
- Check market history: <1yr since previous treatment – what is the tumor behavior??
- Resale strategy: Nutrition, hyperbaric, surgical consults
- The paperwork: Full consent, open dialogue, reflection
- Protocol only?

MPRI
MIDWEST PROTON RADIOTHERAPY INSTITUTE
On target for life and health