MD Anderson Cancer Center

Proton Therapy for Pediatric Patients

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PTCOG 54, San Diego CA
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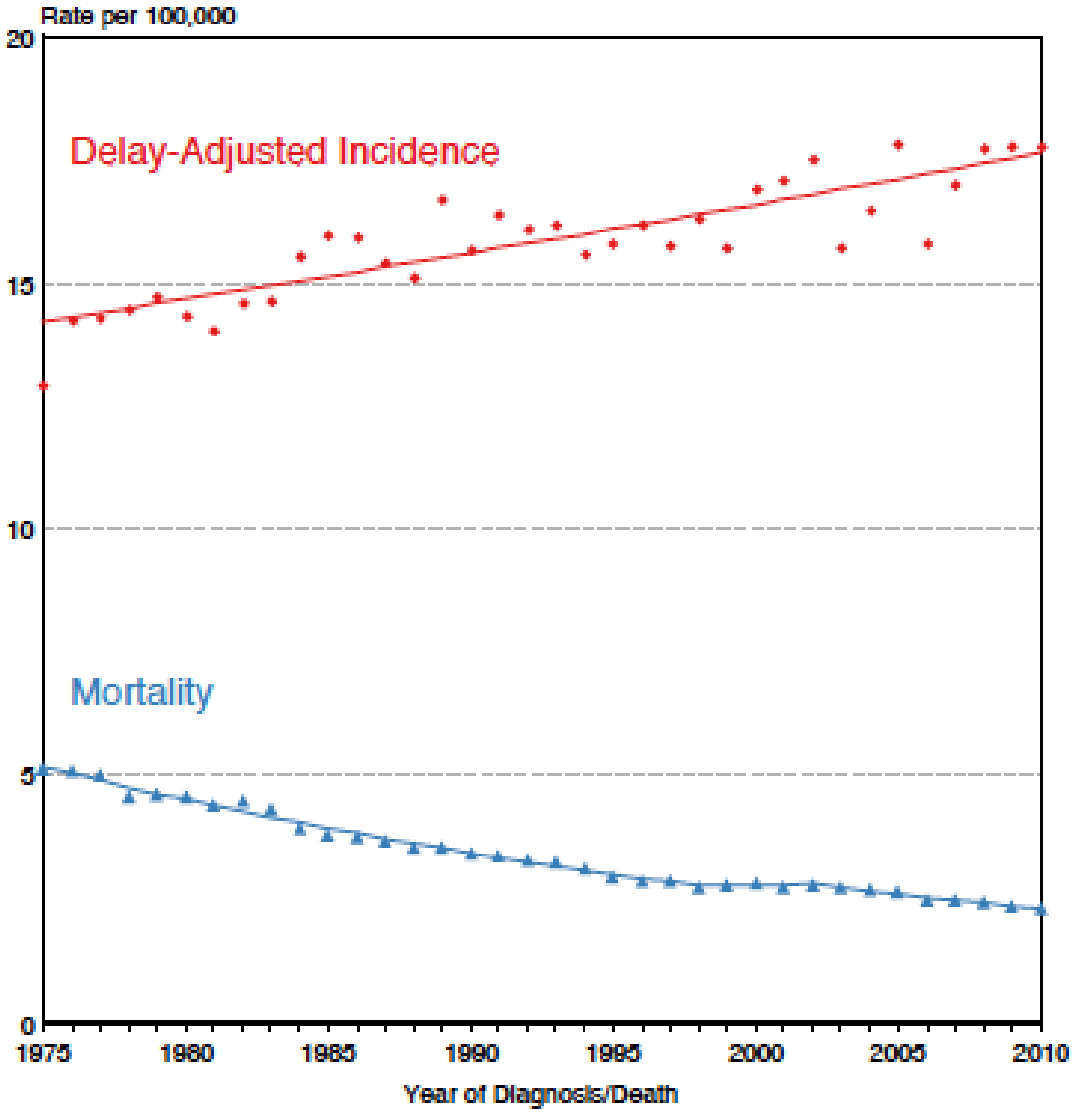
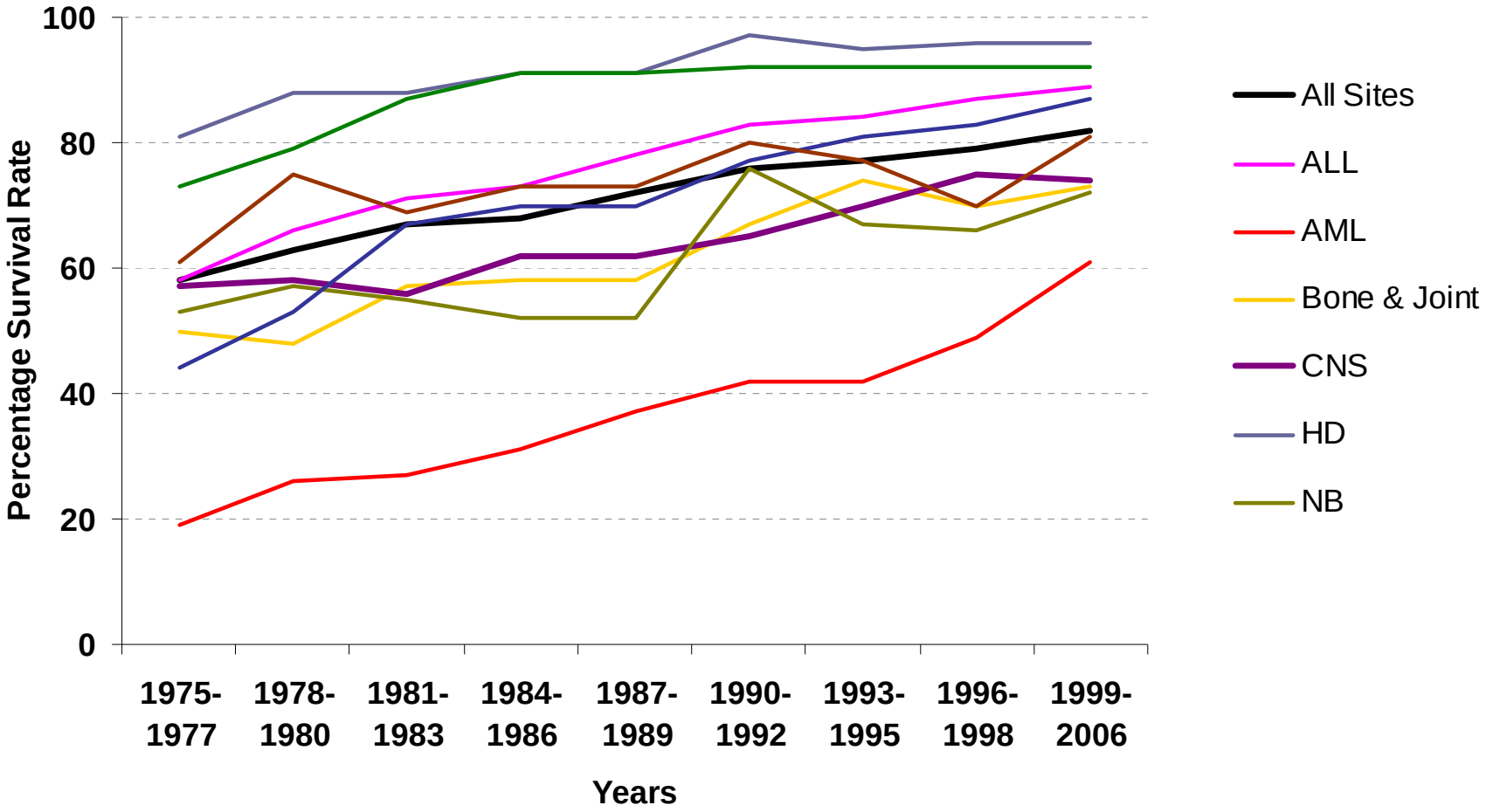
PTCOG

SEER Delay-Adjusted Incidence and US Mortality
All Childhood Cancers, Under 20 Years of Age
Both Sexes, All Races, 1975-2010



Cancer Survival Trends <15 y.o

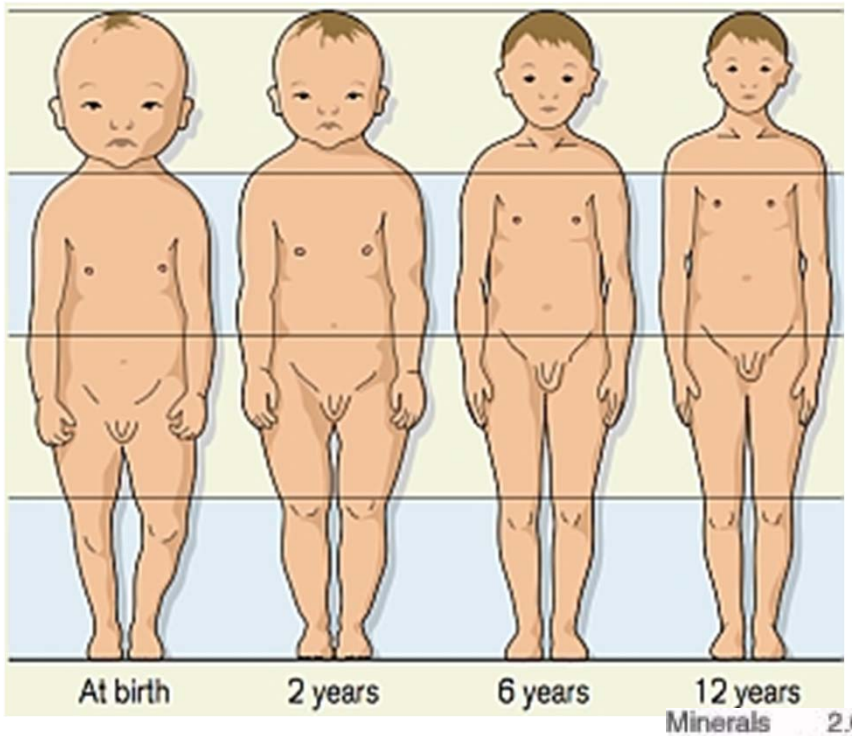


RT is needed to treat many tumors effectively
RT is associated with long term survival

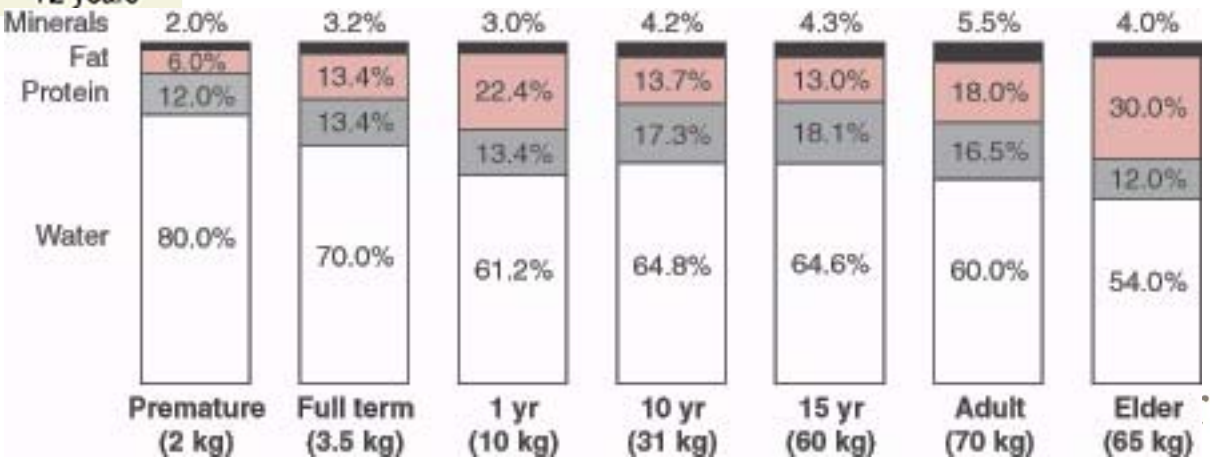
AGE	<5	5-9	10-14	15-19
1	ALL 58	**CNS** **32**	**CNS** **25**	HD 32
2	**CNS** **36**	ALL 30	ALL 18	GCT 31
3	NB 27	**STS** **8**	HD 12	**CNS** **20**
4	Wilms 18	Wilms 6	**STS** **11**	**STS** **16**
TOTAL	200	110	117	202

Children Are Not Little Adults

Growth and Development



- Organ vulnerability
- Body proportions & physiology



Radiation in Children

- Radiation is not good for any normal tissue
- Radiation is worse for children
- Radiation has been shown to effect:
  - Neurocognition
  - Neural development
  - Normal tissue growth and function
  - Rate of secondary malignancies

Selected Late Effects of Low Dose Radiation

• **Fertility**		
– Testis	2-3 Gy	permanent azospermia
– Ovaries	12-15 Gy	difficult fertility
• **Cardiovascular**		
– Heart	2.5-3 Gy	increased CAD
– Vascular	1-4 Gy	stroke & heart disease
• **Vision**		
– Eye	0.5-2 Gy	Cataract
– Eye	5-12 Gy	Double vision, dry eye

Shimizu et al, BMJ 2010;340:b5349

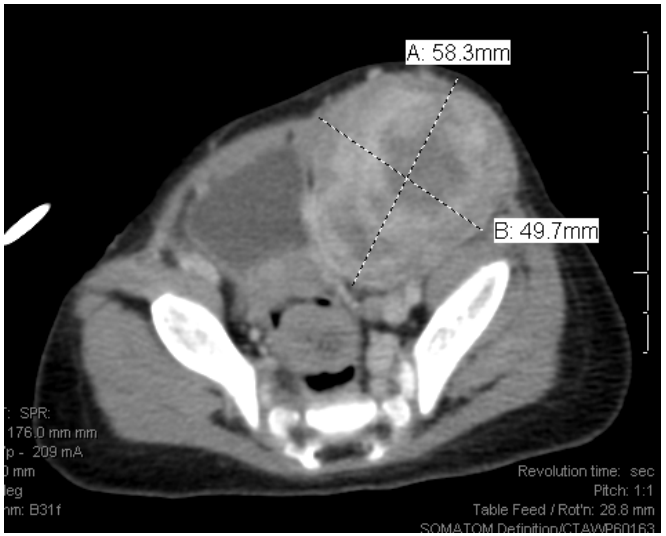
Carr et al, IJROBP 2005 842-850

BUT…

- Radiotherapy is necessary to treat many tumors effectively
- Radiation is associated with long term survival

Pediatric Radiotherapy Issues

- Large variety of tumors
- Every body location
- Patient Sizes vary
- Tumor size varies relative to patient size
- Tumor radiosensitivity varies
- Often need concurrent chemotherapy



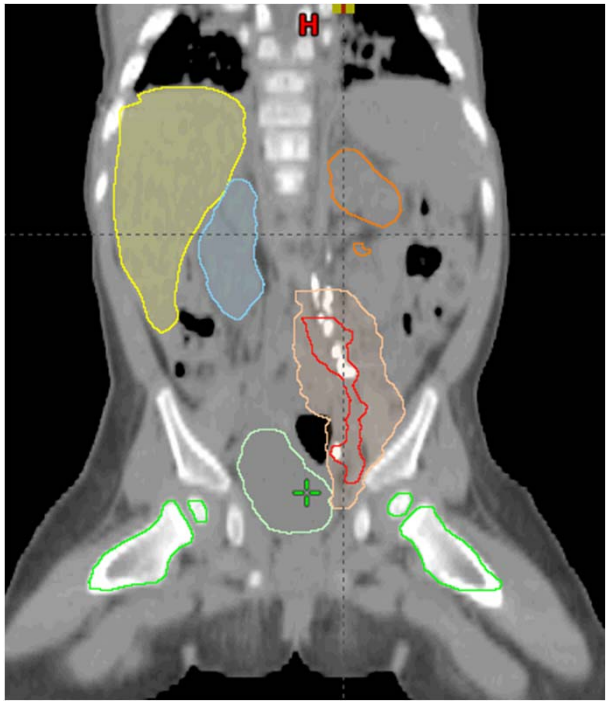
10 mo old RMS

Pelvic mass
6 x 5 x 8.5 cm

Had biopsy, chemo, surgery

Now RT and chemo

Discuss with oncologist, surgeon, anesthesia, nursing…



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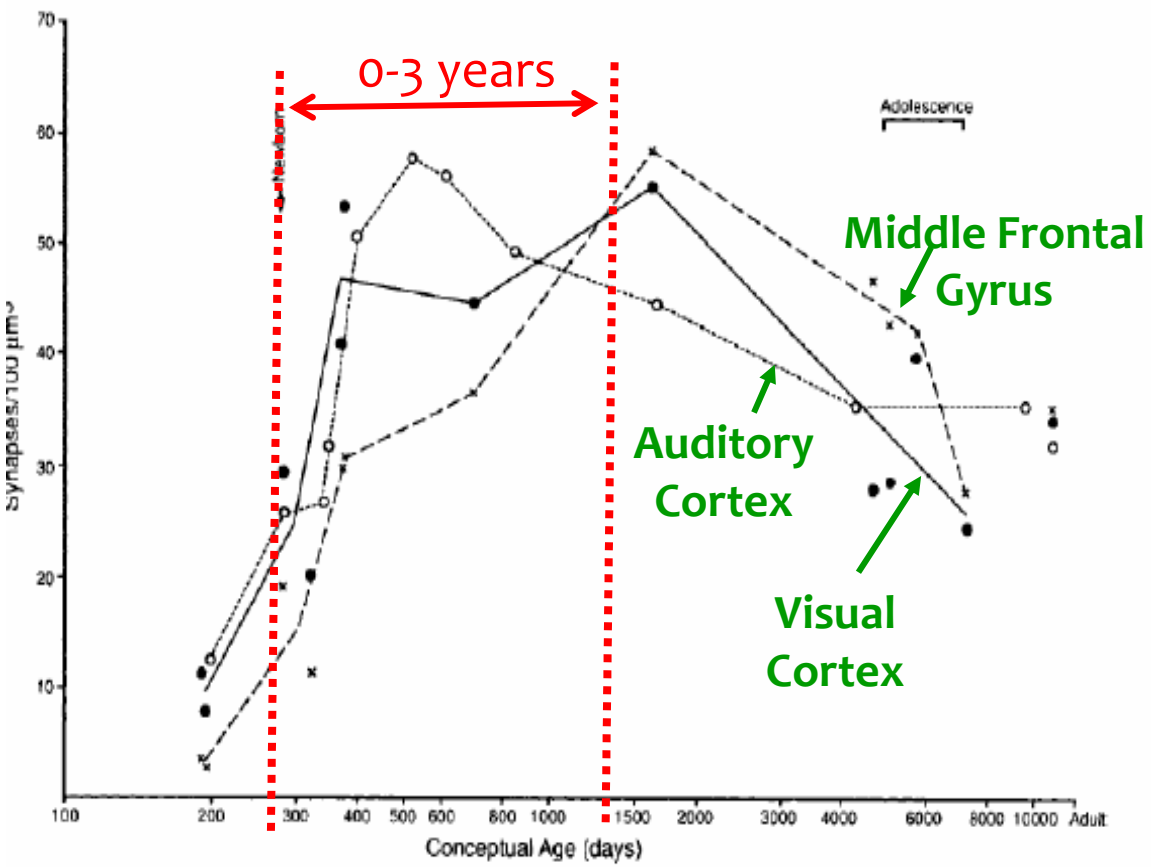
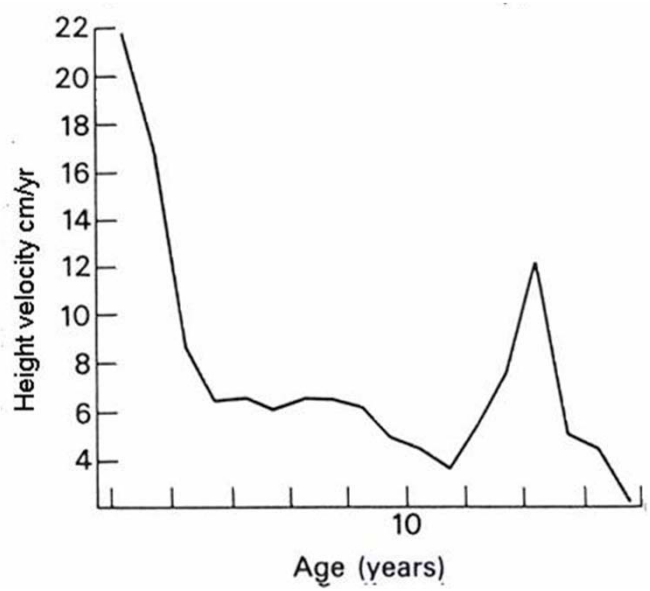
Development Varies with Age

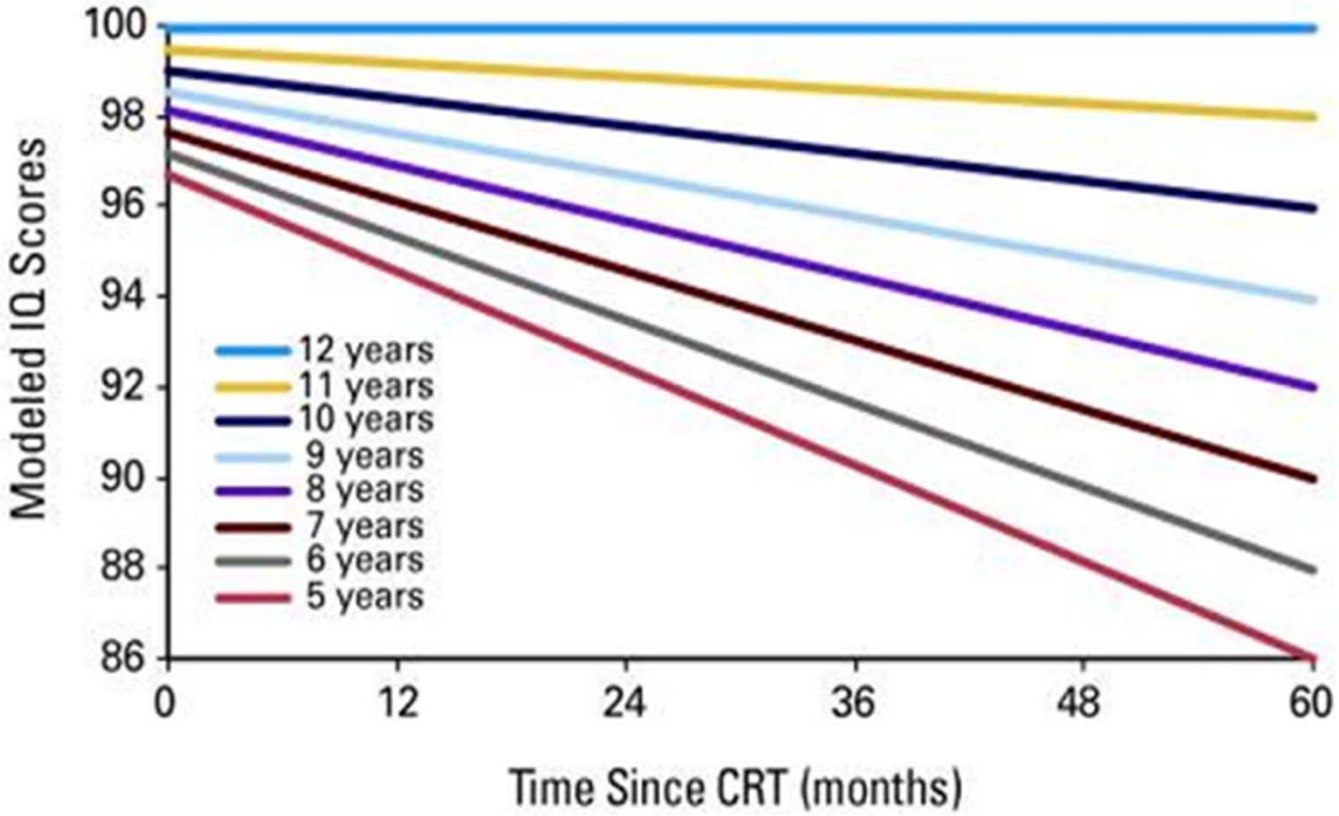
BRAIN



HEIGHT



IQ changes vary with age and time



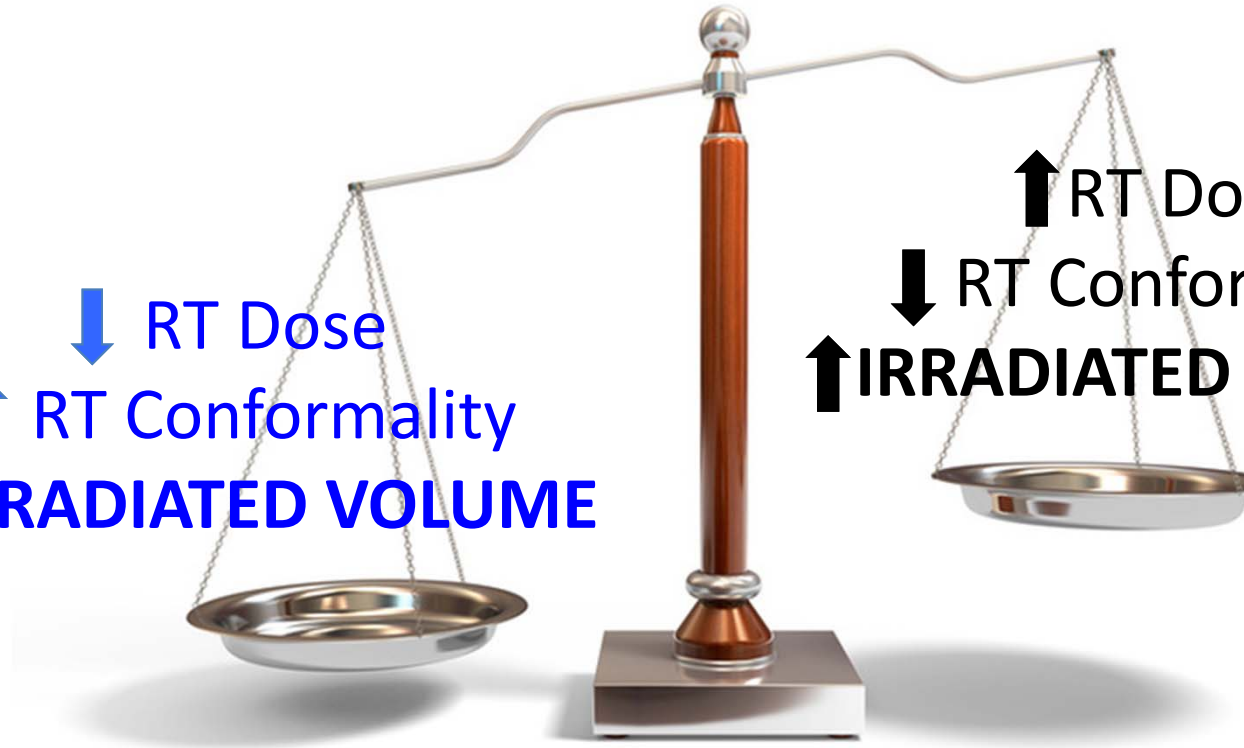
IQ outcomes in patients treated for LGG with RT

Merchant et al, JCO 27(22) 2009

Long Term Sequelae of Cranial RT

- Neurocognitive – **volume**, **dose**
- Endocrine – Pituitary/hypothalamic **dose**
- Growth – GH, bone **dose**, T4, nutrition
- Hearing – Cochlear **dose**
- Vascular – Moya moya
- Leukoencephalopathy – **volume**, **dose**
- Secondary Malignancy – Age, genetics, tumor, RT **volume**, **dose**

SO HOW DO WE BALANCE THESE ISSUES?



⬇ RT Dose
⬆ RT Conformality
⬇**IRRADIATED VOLUME**

⬆ SURVIVAL
⬇TOXICITY

⬆RT Dose
⬇ RT Conformality
⬆**IRRADIATED VOLUME**

⬆ TOXICITY

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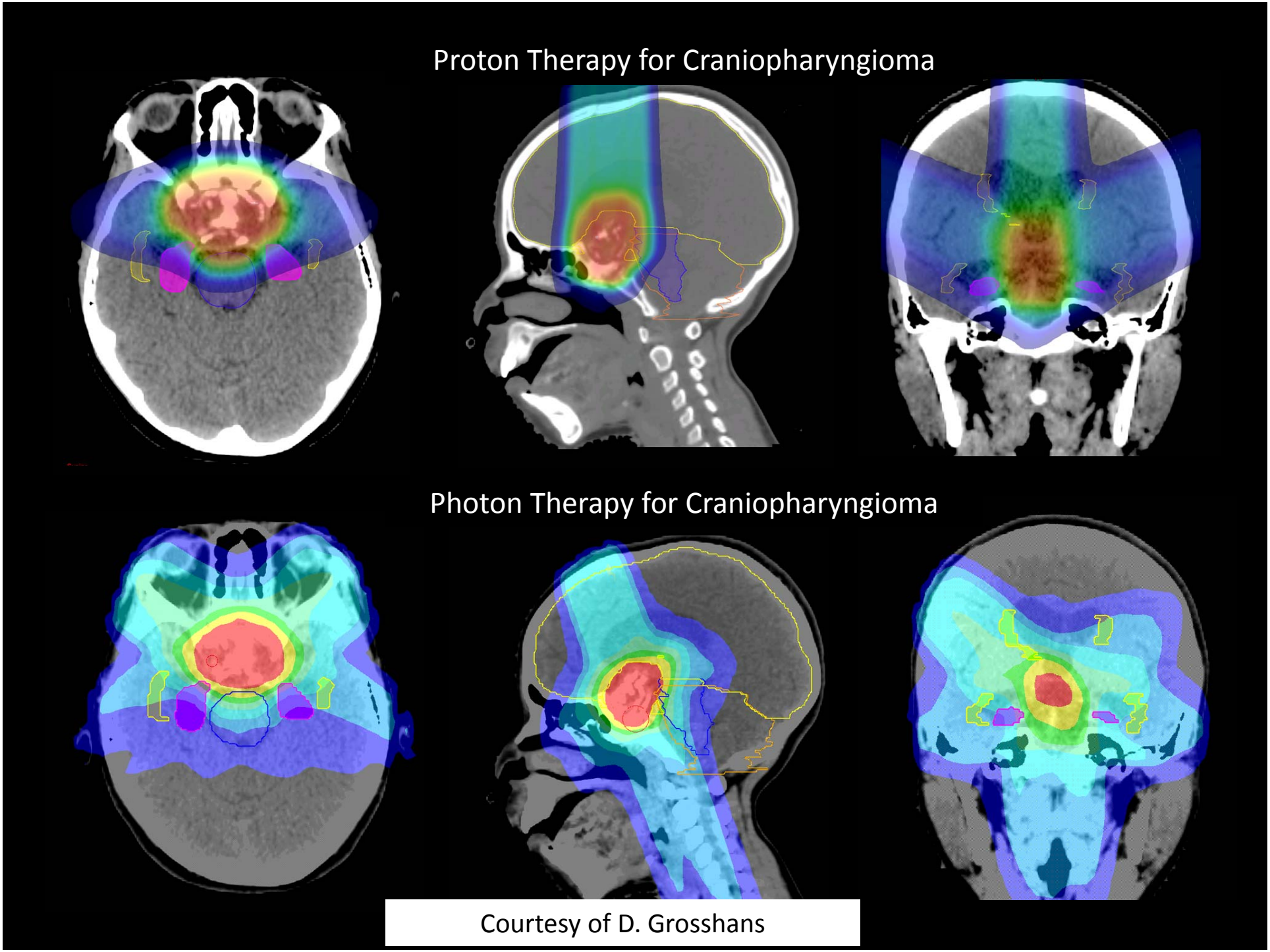
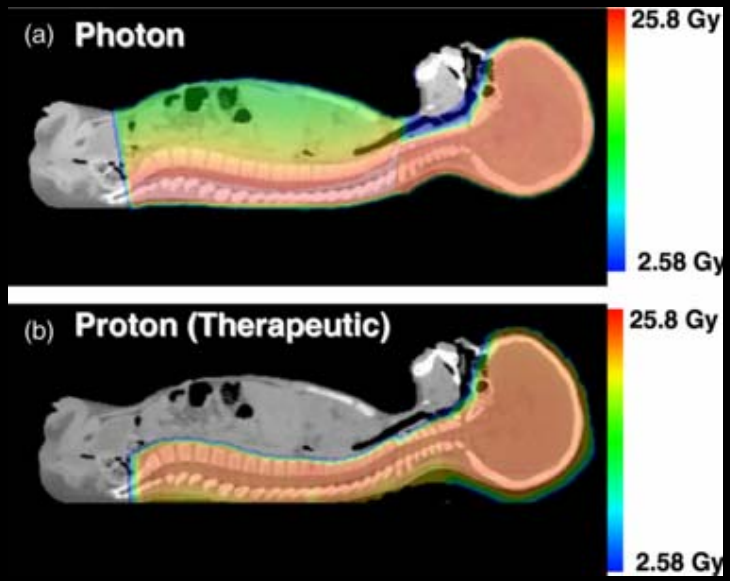
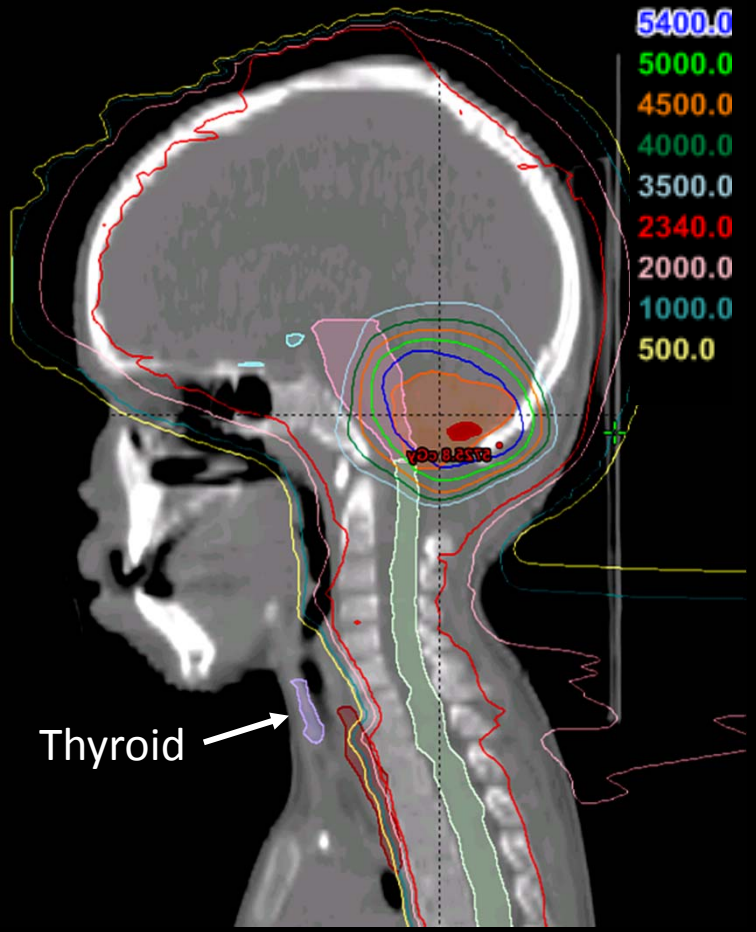

Proton Therapy for Craniopharyngioma
Photon Therapy for Craniopharyngioma
Courtesy of D. Grosshans

Proton CSI for Medulloblastoma

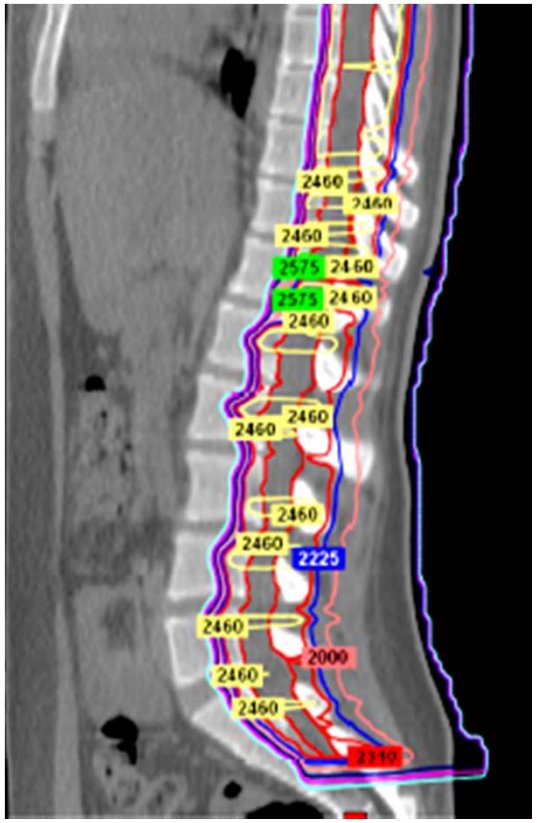
Organ	Mean Dose (Gy)	Maximum Dose (Gy)
Thyroid	0	4
Testis	0	0
Pituitary	24	24
Hypothalamus	25	30
Esophagus	9	25





Uncertainties

- Proton therapy more sensitive to setup and density changes
- Need to have excellent physics support
- Need to have excellent set up and dedicated team
- Need to understand the differences between x-ray and proton planning



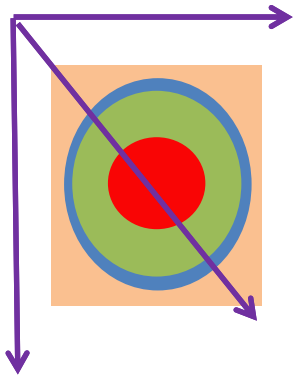
Learn from others

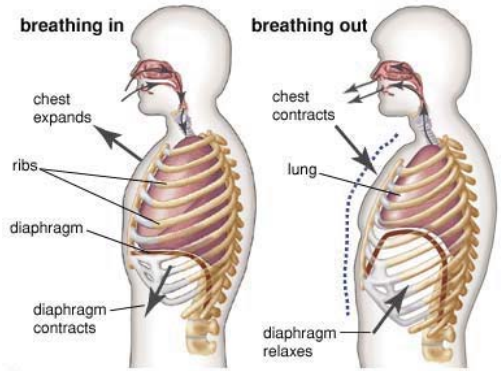
- Pediatric radiation oncologists need to learn from adult experience

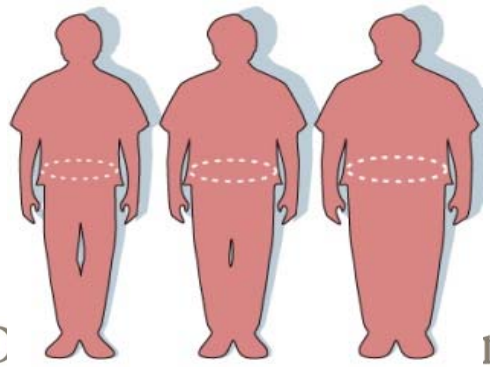
- We have to BEG, BORROW and STEAL techniques and adapt them to pediatric needs

Radiotherapy Dimensions

- 1,2,3rd dimension
  - Tumor delineation
  - Patient external set up
  - Beam orientation, planning…
- 4th dimension
  - Intrafraction motion
    - Breathing, patient set up, bowel motion
- 5th dimension
  - Interfraction changes
    - Patient set up, patient changes, tumor changes





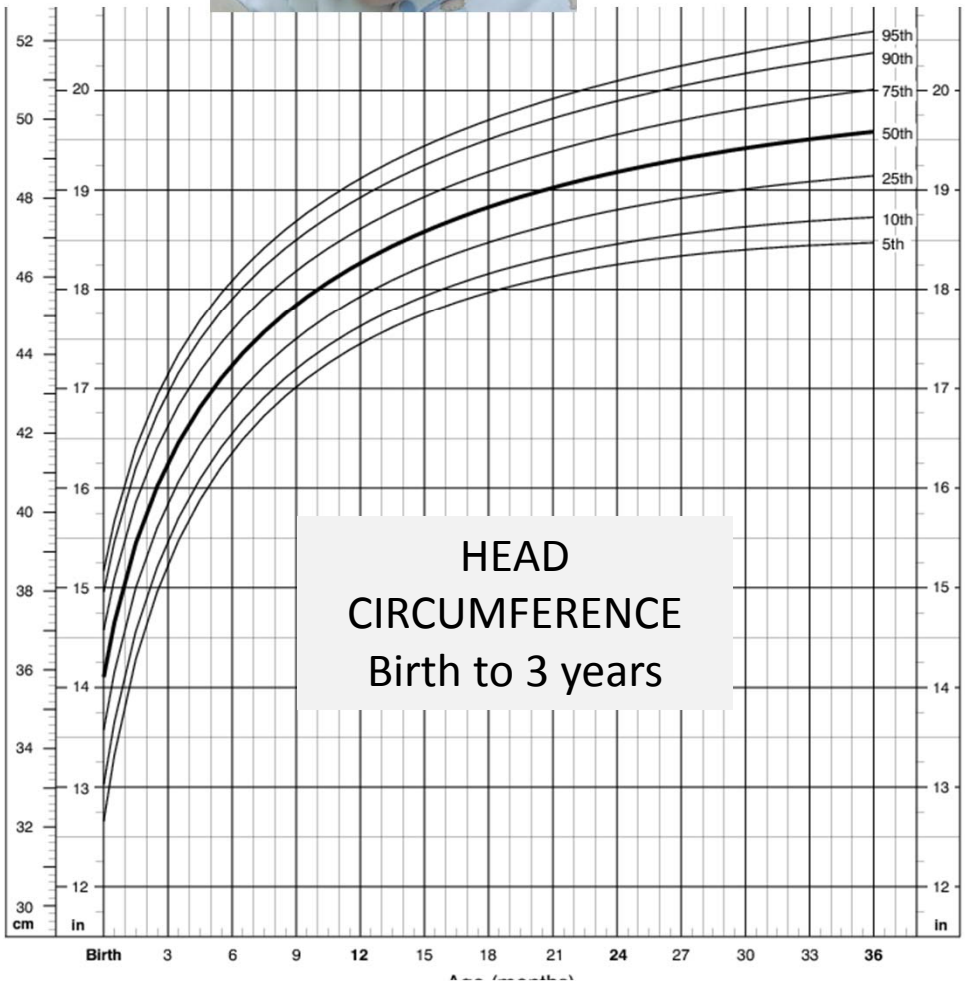



Child Life Specialist

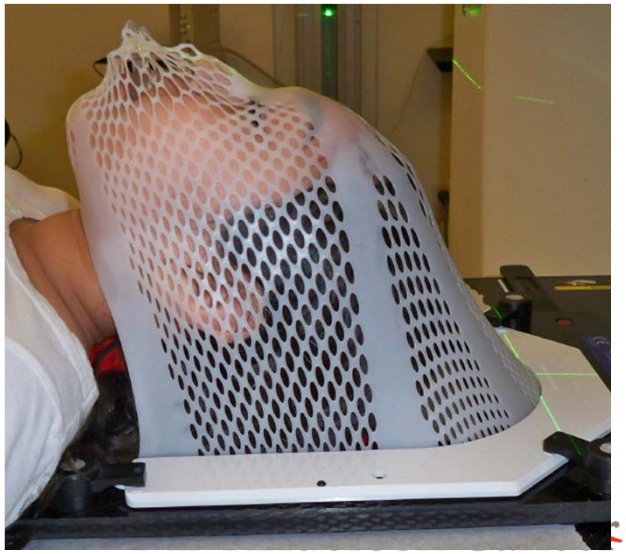
Anesthesia

- No endotracheal tube or LMA
  - Setup supine
  - Airway access
- Specialized team
  - Anesthesiologist
  - CRNAs
- 50% of our children require sedation

External Immobilization



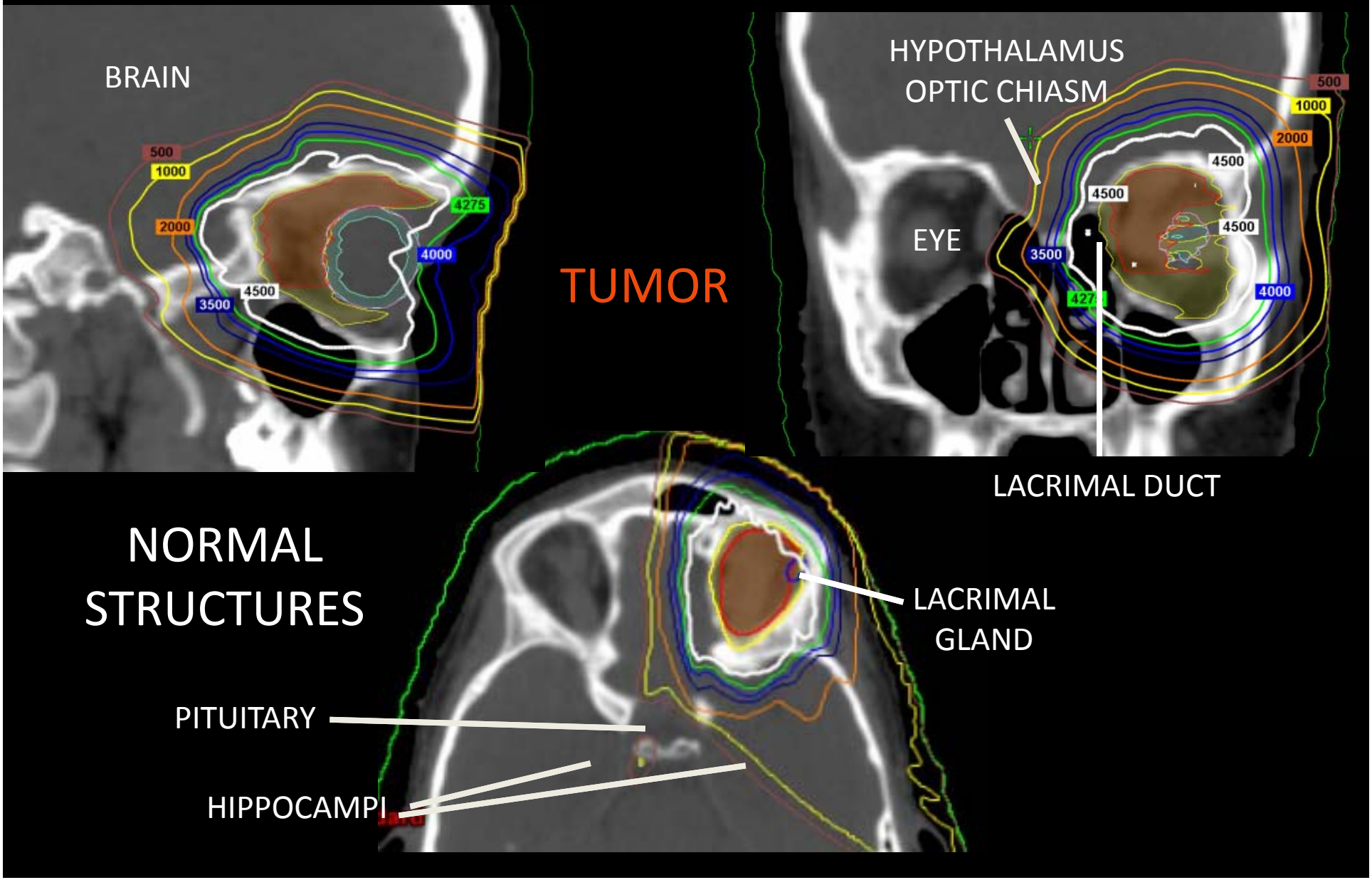
HEAD CIRCUMFERENCE
Birth to 3 years



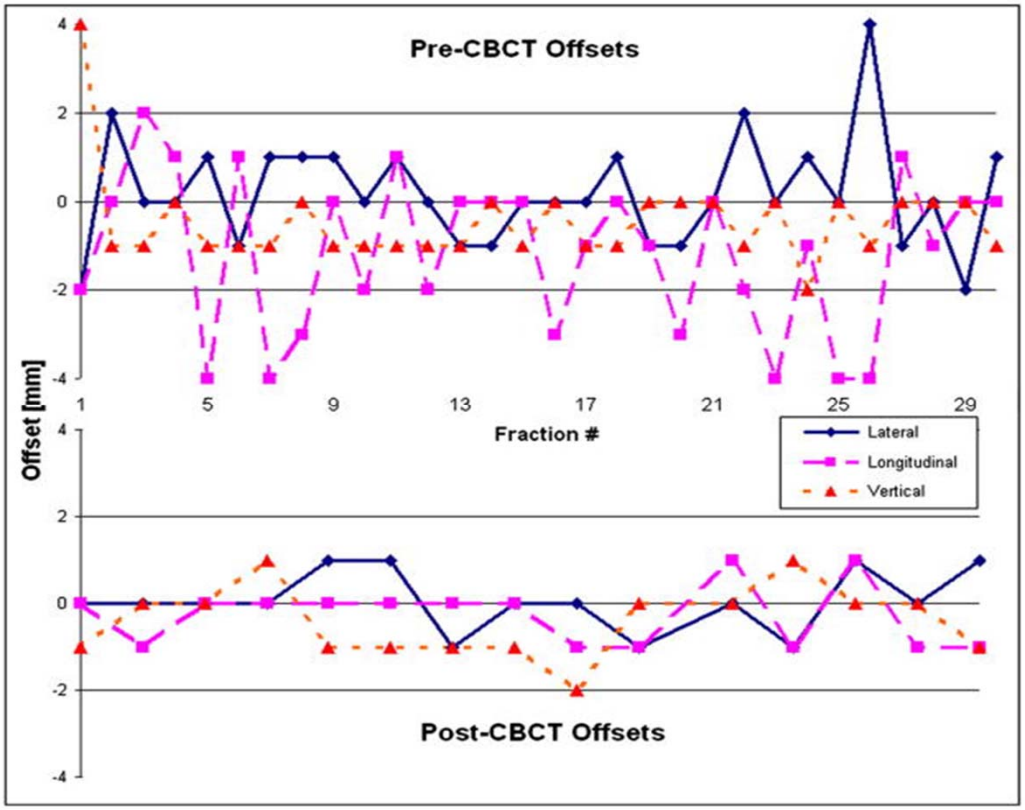
Center

CNS &
Head and Neck

ORBITAL RHABDOMYOSARCOMA



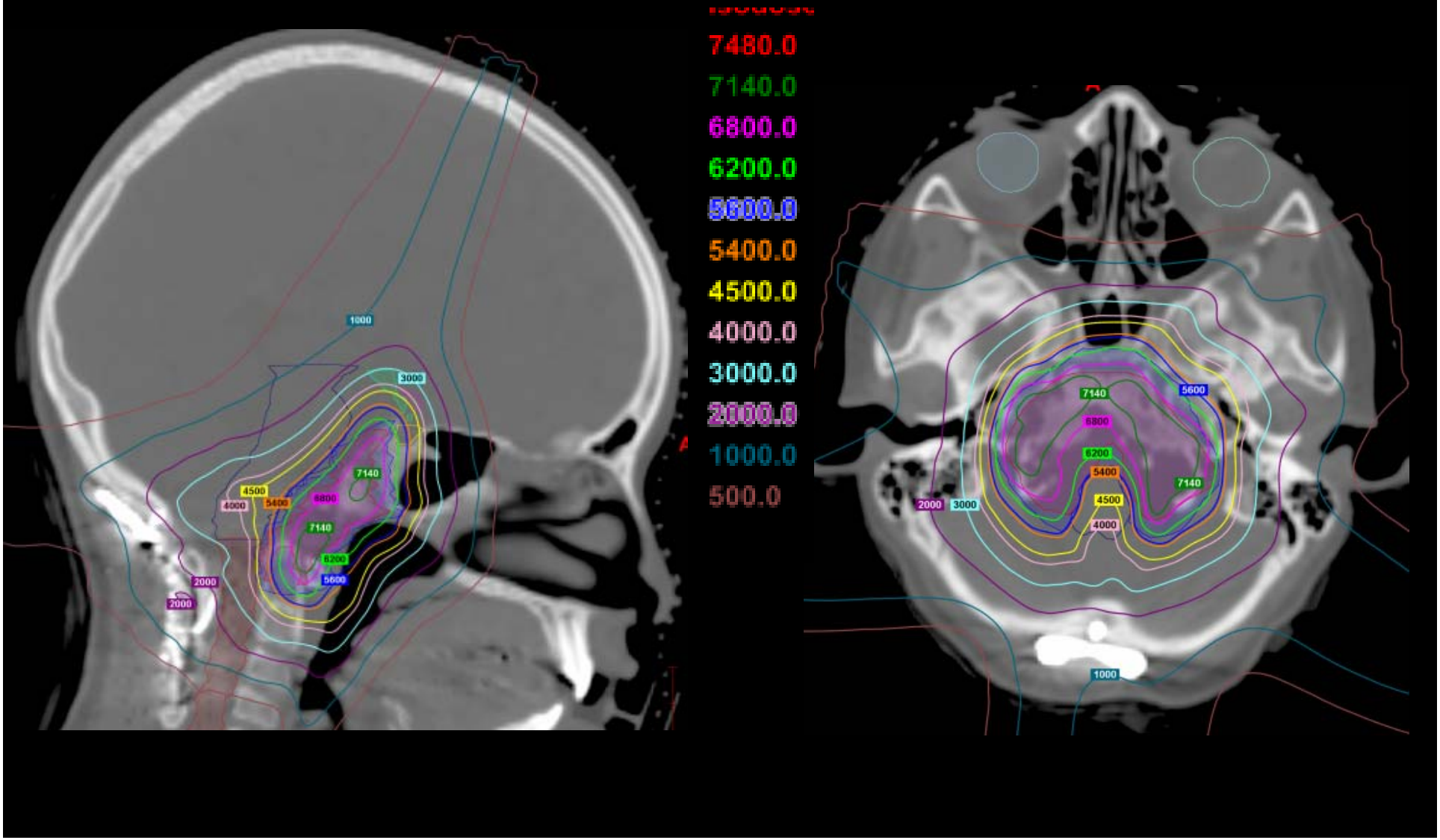
PTV Determination- CNS & H/N



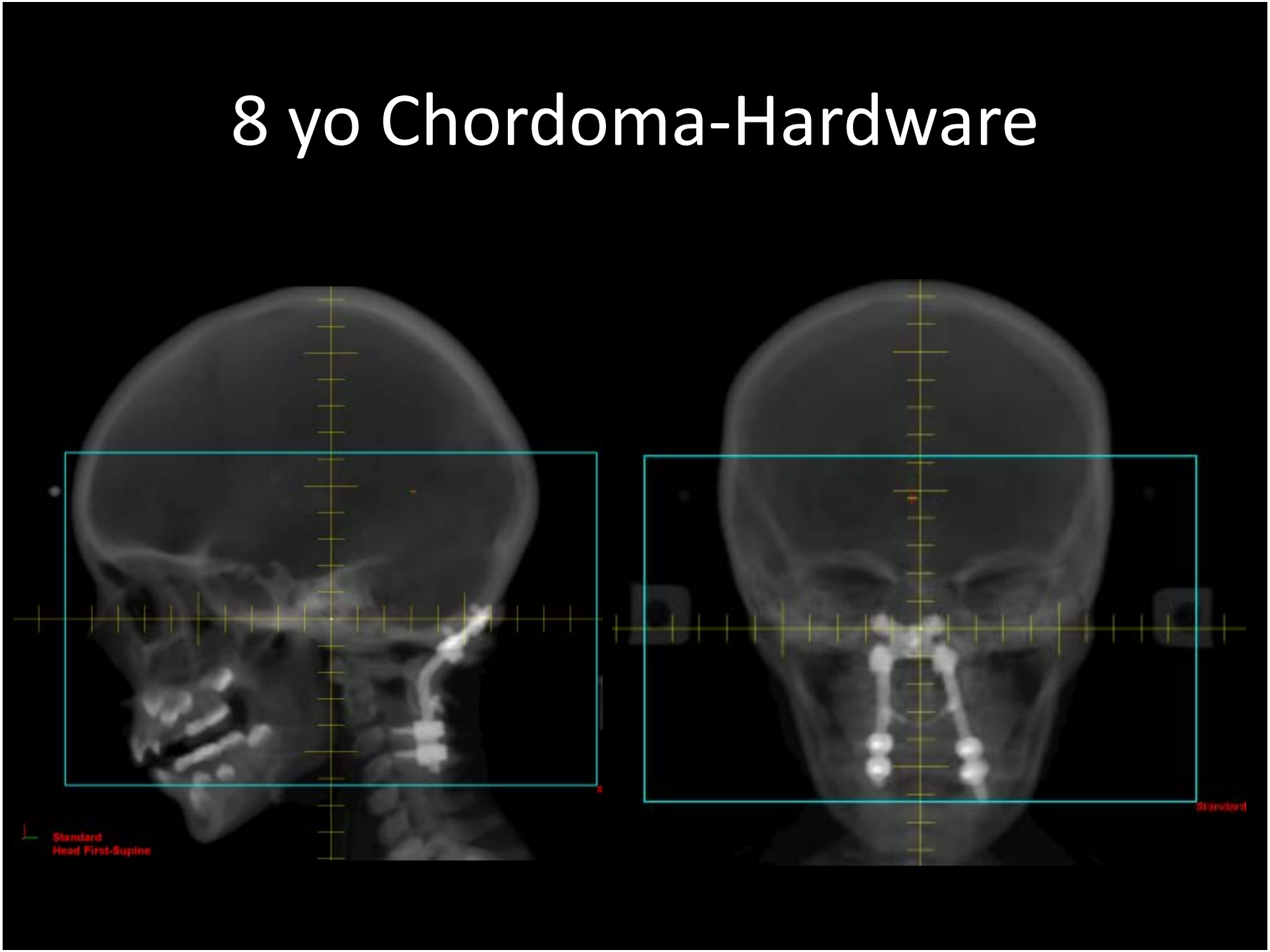
- 100 patients
  - 83 brain, 17 head/neck
- Daily cone beam allows 2 mm PTV
- Weekly cone beam allows 3.5 mm PTV

Beltran et al, IJROBP, 79 (4) 166-74, 2011

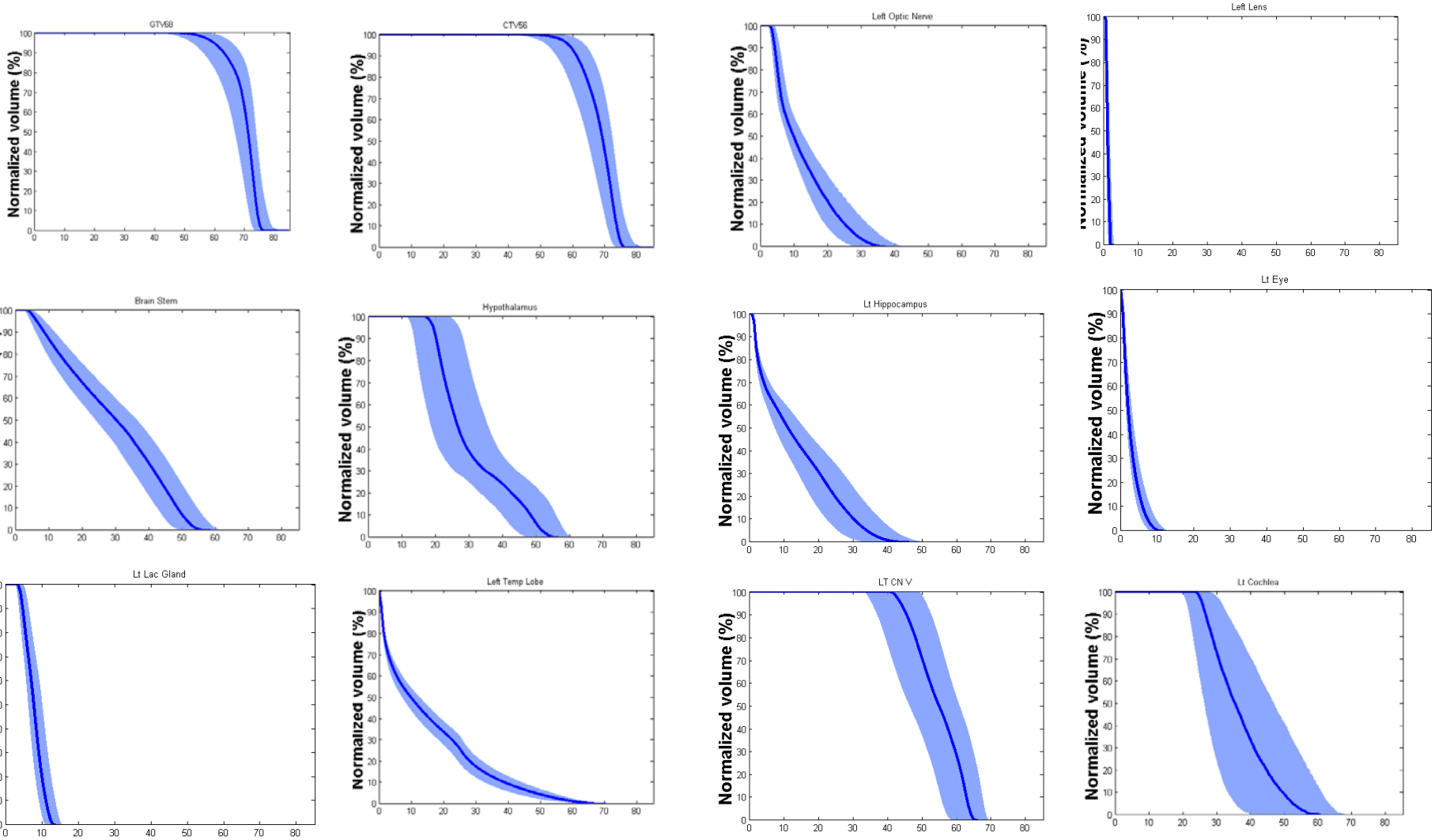
8 Year Old With Chordoma



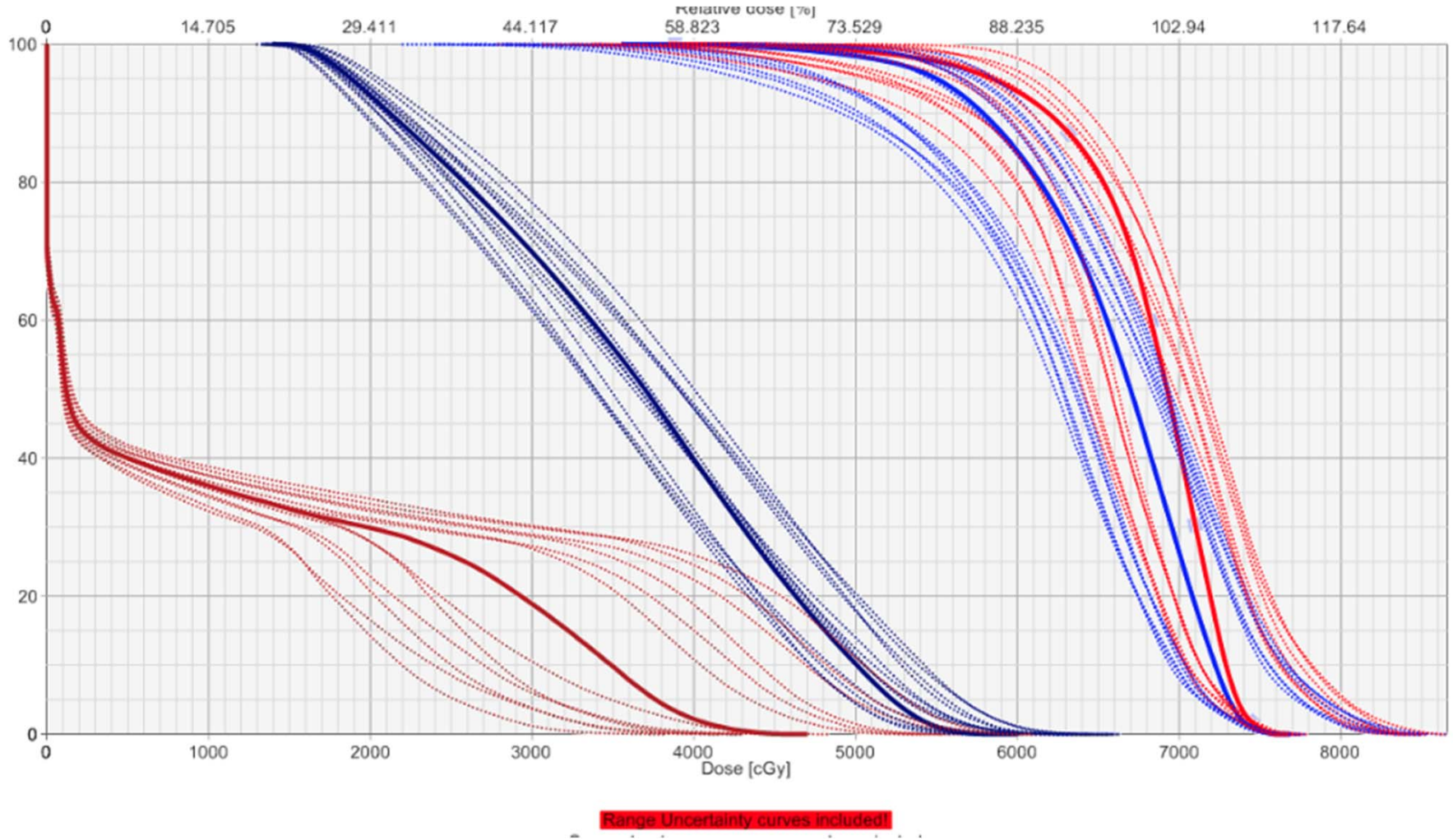
8 yo Chordoma-Hardware

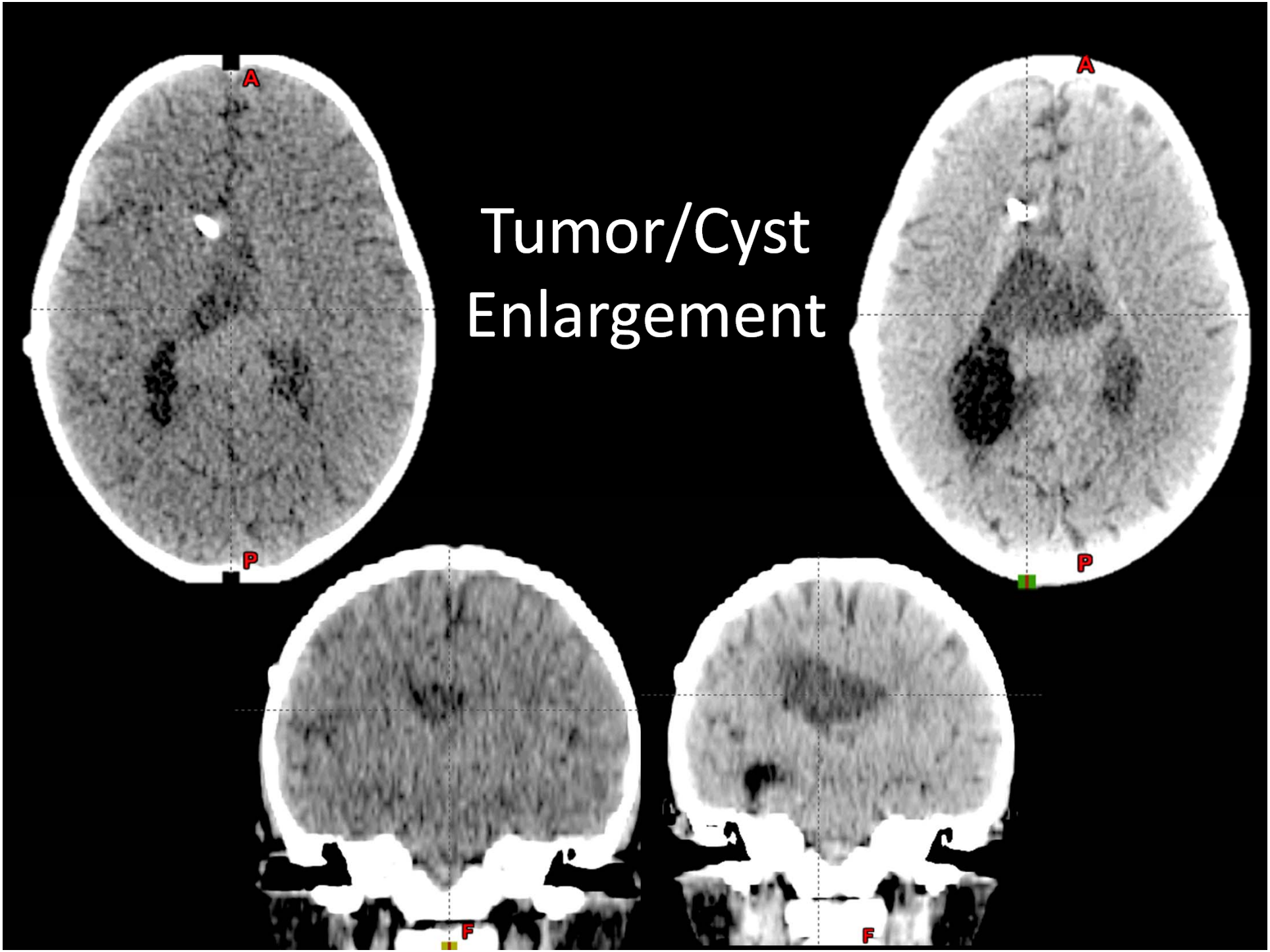


Robustness Evaluation

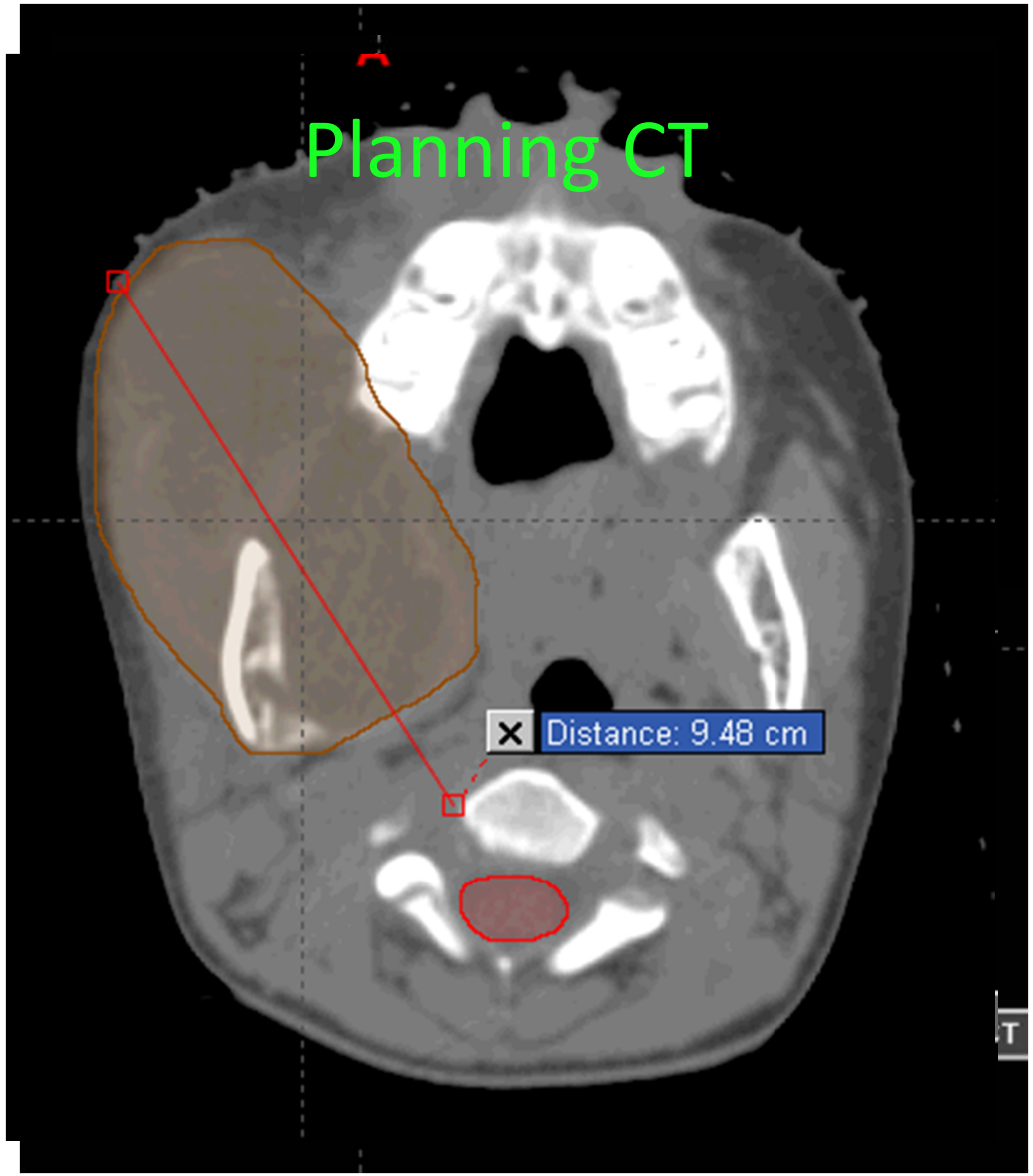


Robustness Evaluation



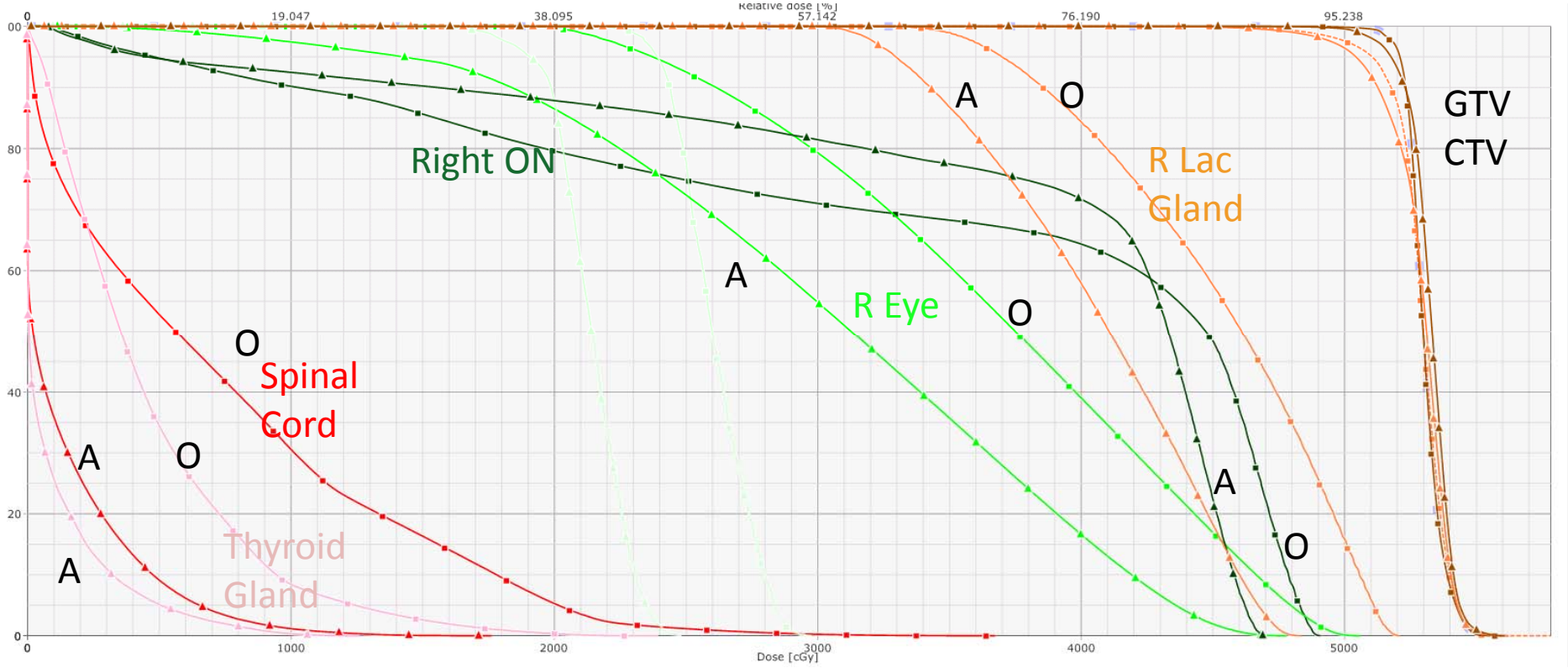

Tumor/Cyst
Enlargement
A
P
A
P
F
F

RMS
Tumor Changes



- 10 yo patient with large growing mass
- Started RT with chemo
- After 9 days, tumor visibly shrinking
- Adaptive plan to reduce dose to spinal cord

Adaptive Plan



A : Adaptive Plan; O : Original

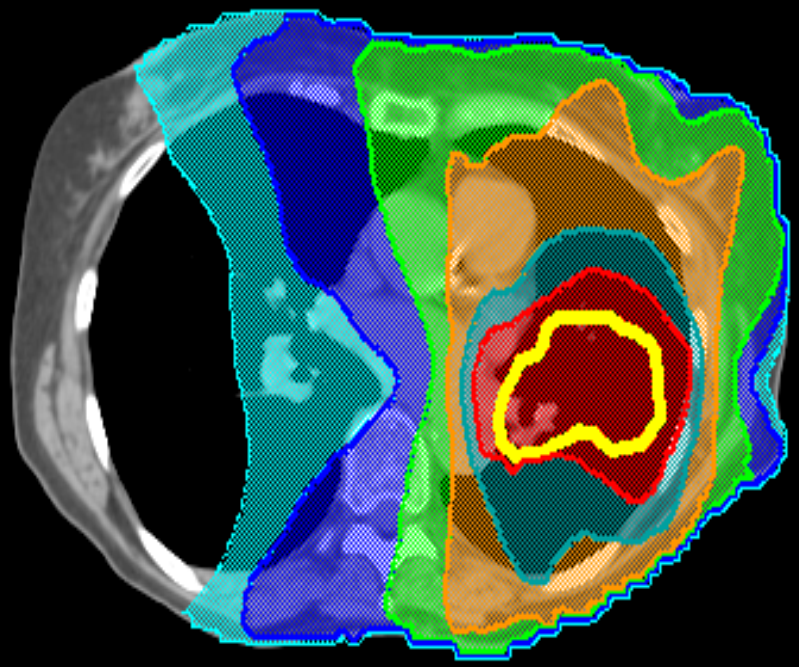
Thorax

Thorax
Organs at Risk

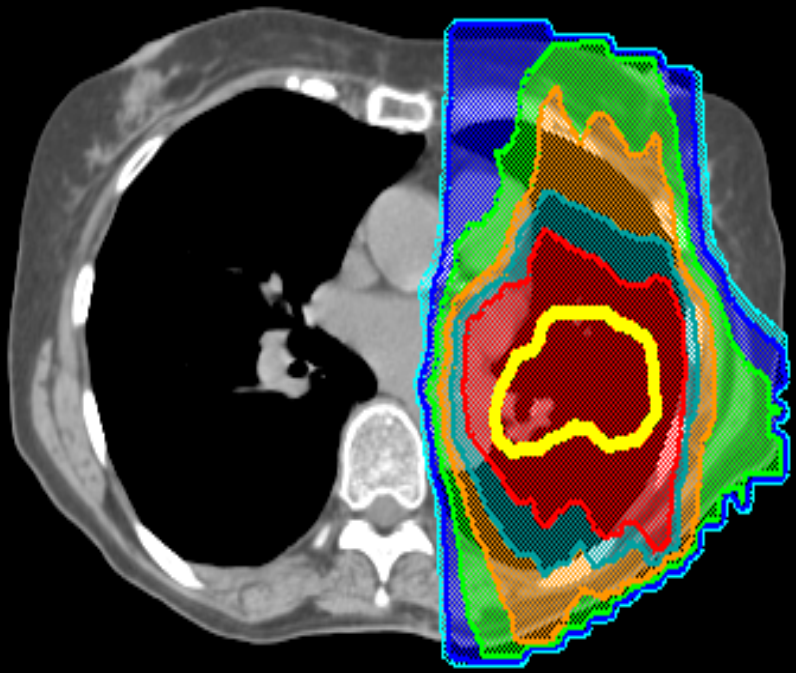
- Thyroid gland
- Lungs
- Heart
- Esophagus
- Spinal Cord
- Brachial plexus
- Breast tissue

Thoracic Tumors

IMRT



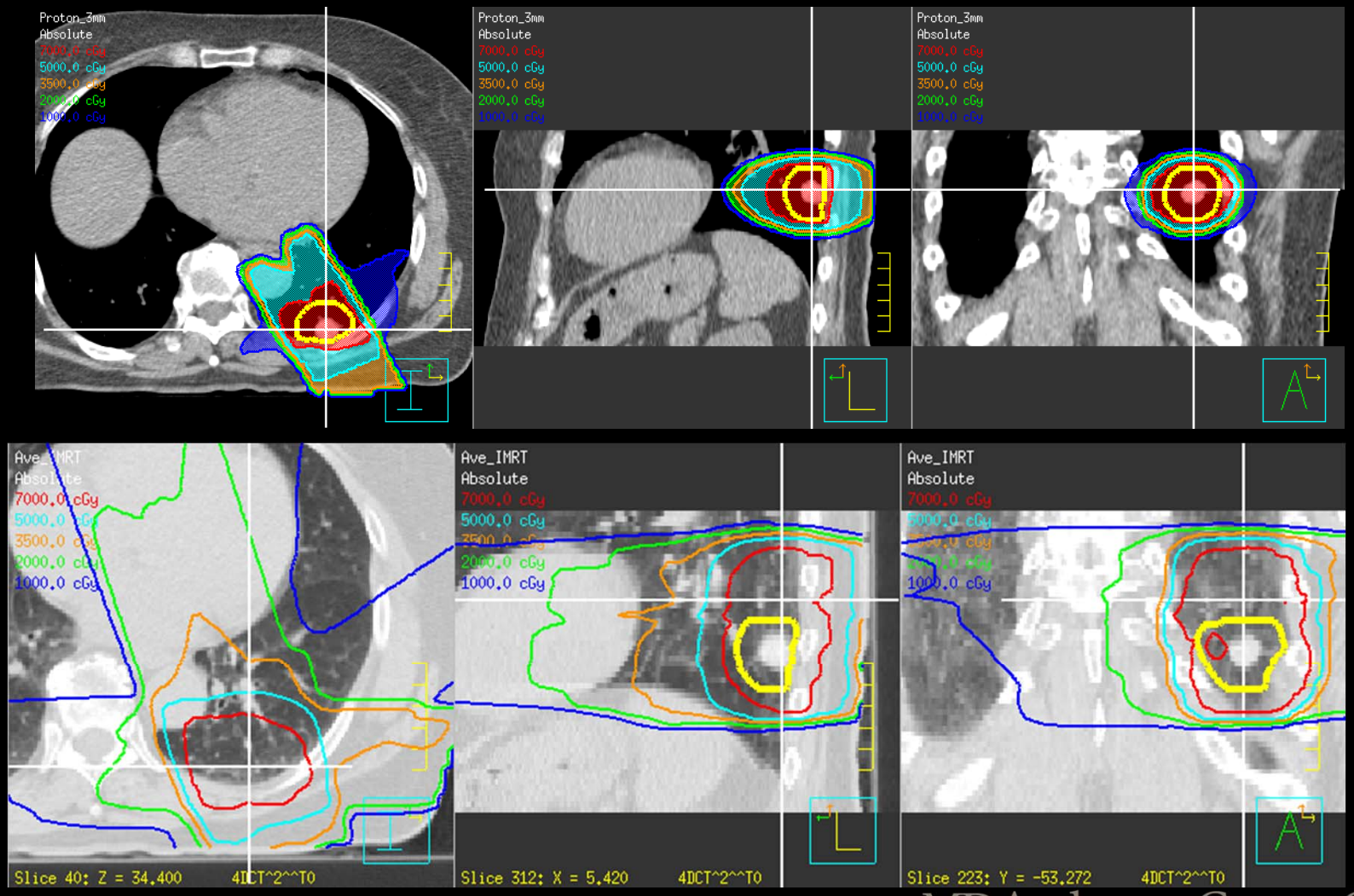
Proton



Lower dose to heart, cord and contralateral lung

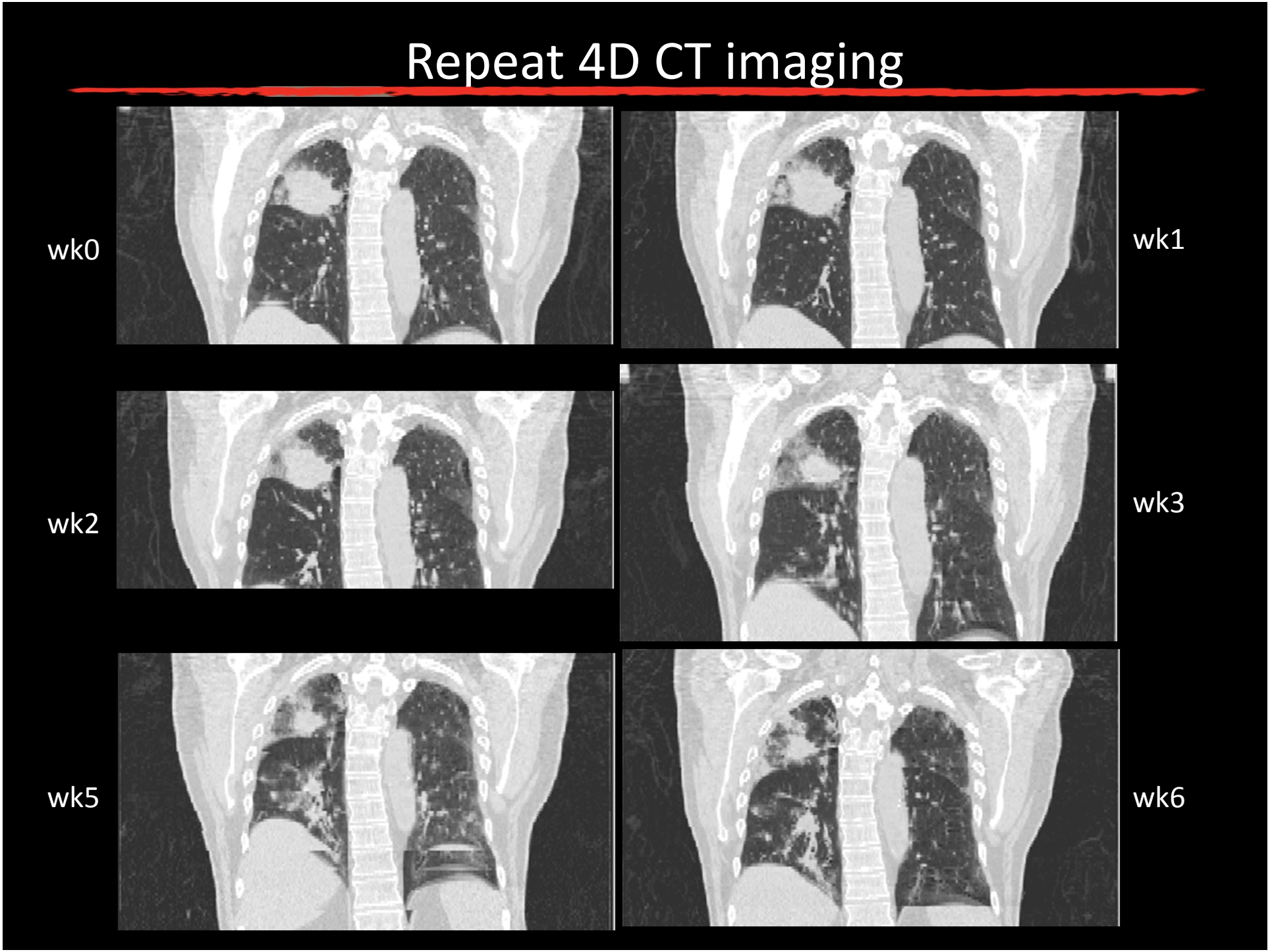
Chang et al, IJROBP 65:1087-96, 2006

The Moving Target

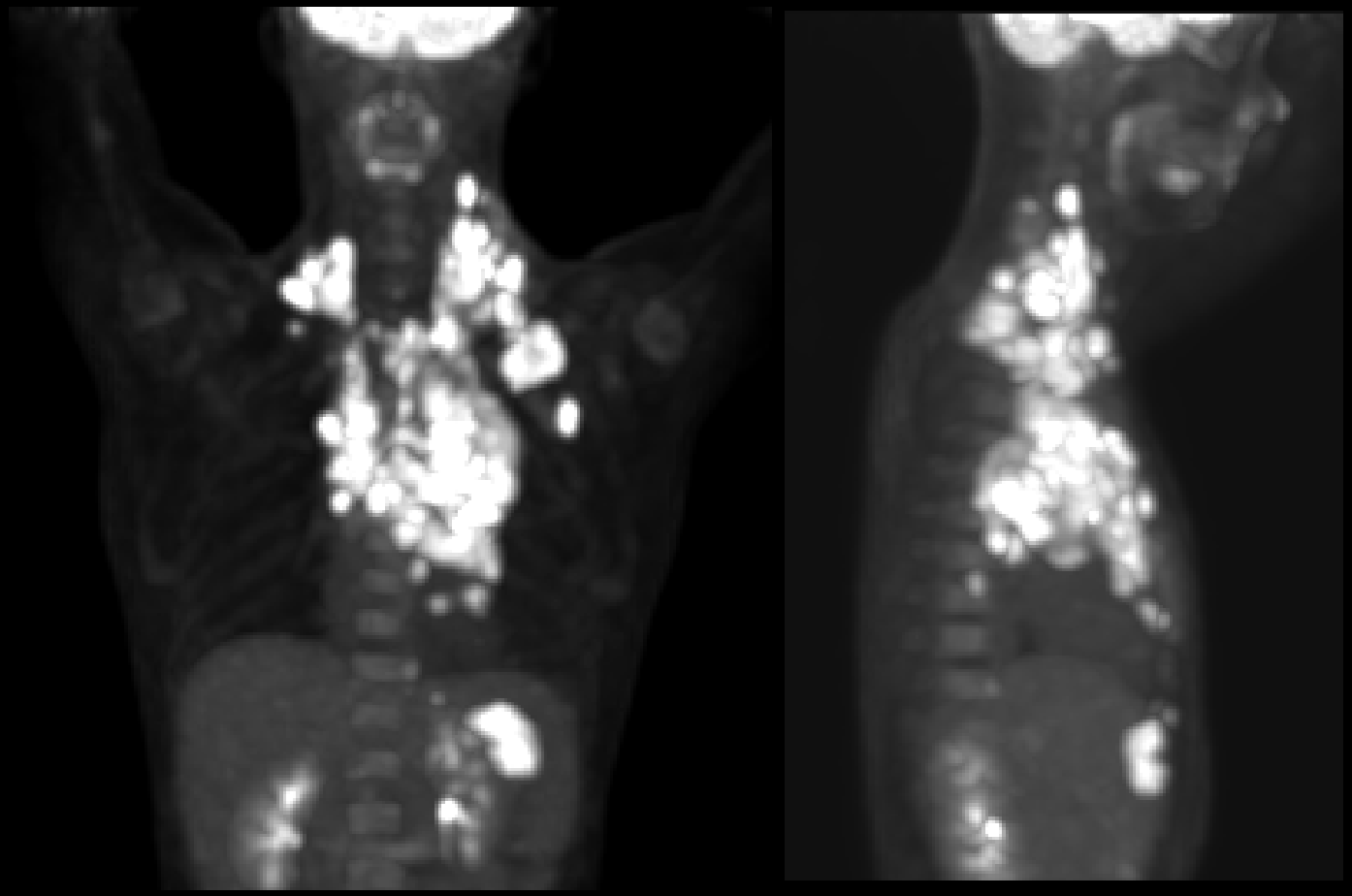


Courtesy of J. Chang

Repeat 4D CT imaging

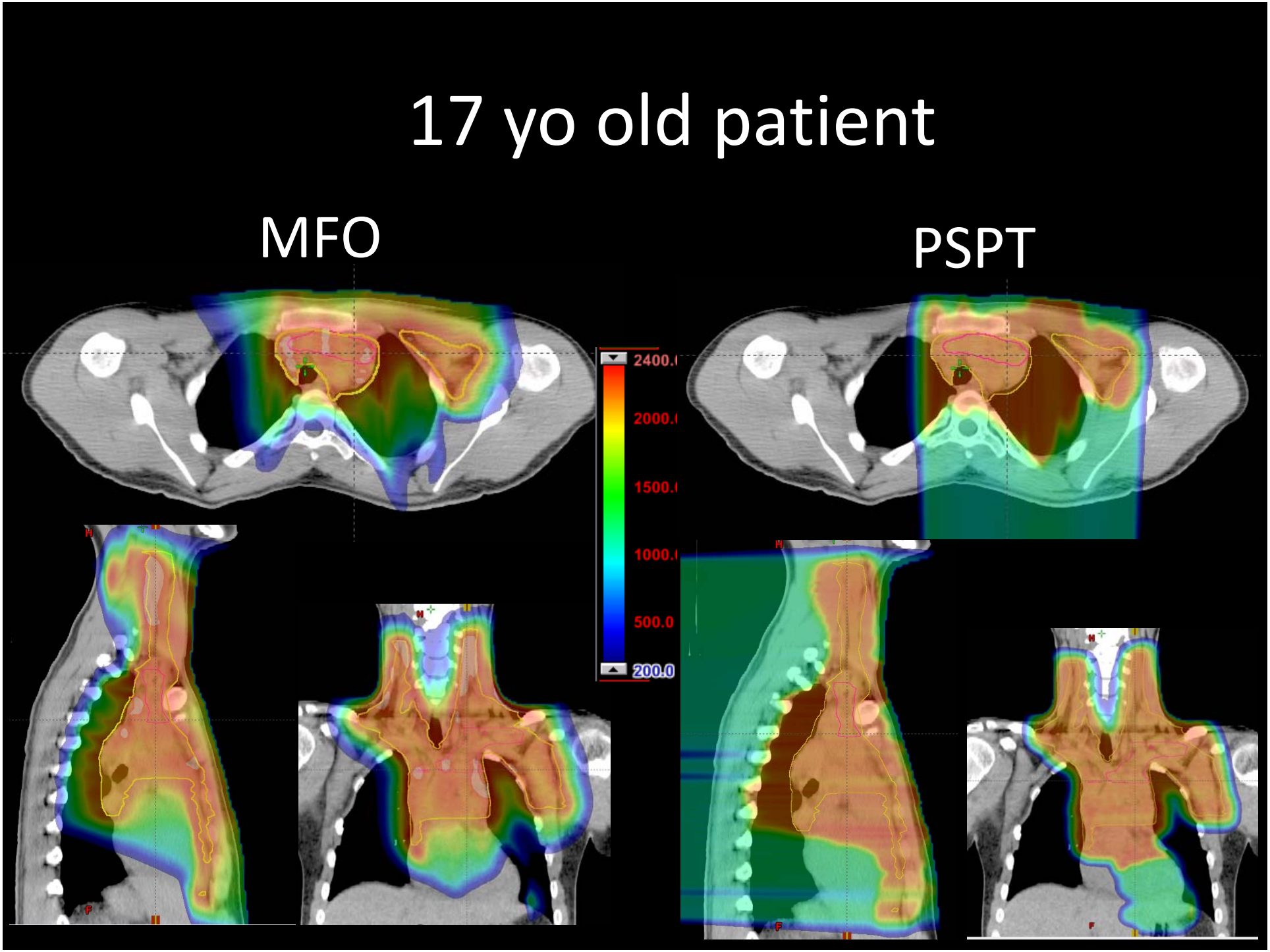


17 yo old patient

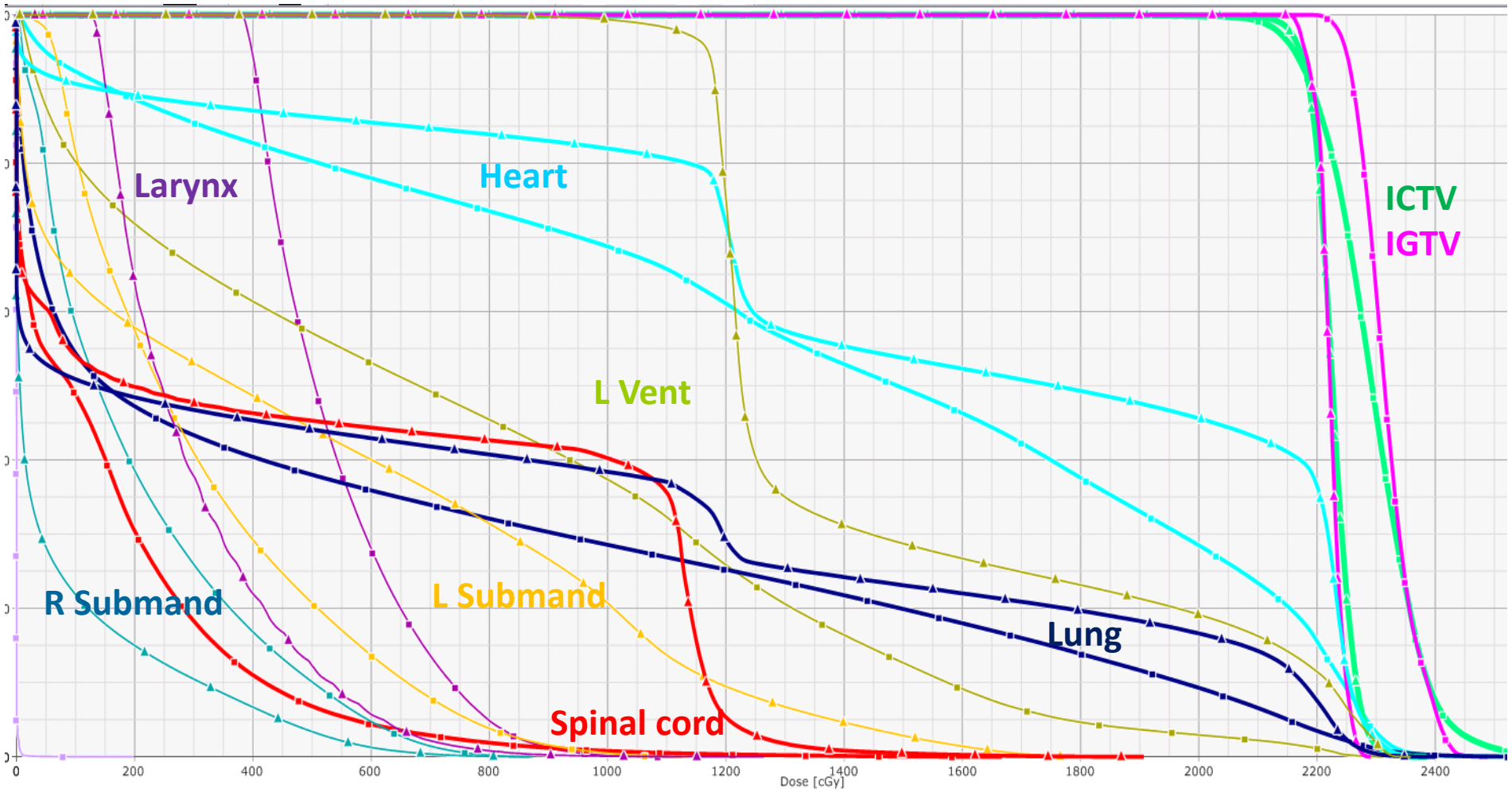


- Stage II bulky nodular sclerosing Hodgkins Lymphoma
- Very good response after 2 cycles of chemotherapy

17 yo old patient

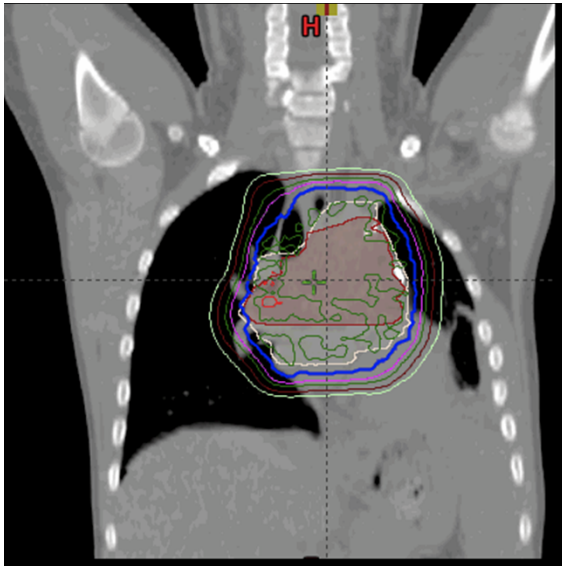


17 yo old patient



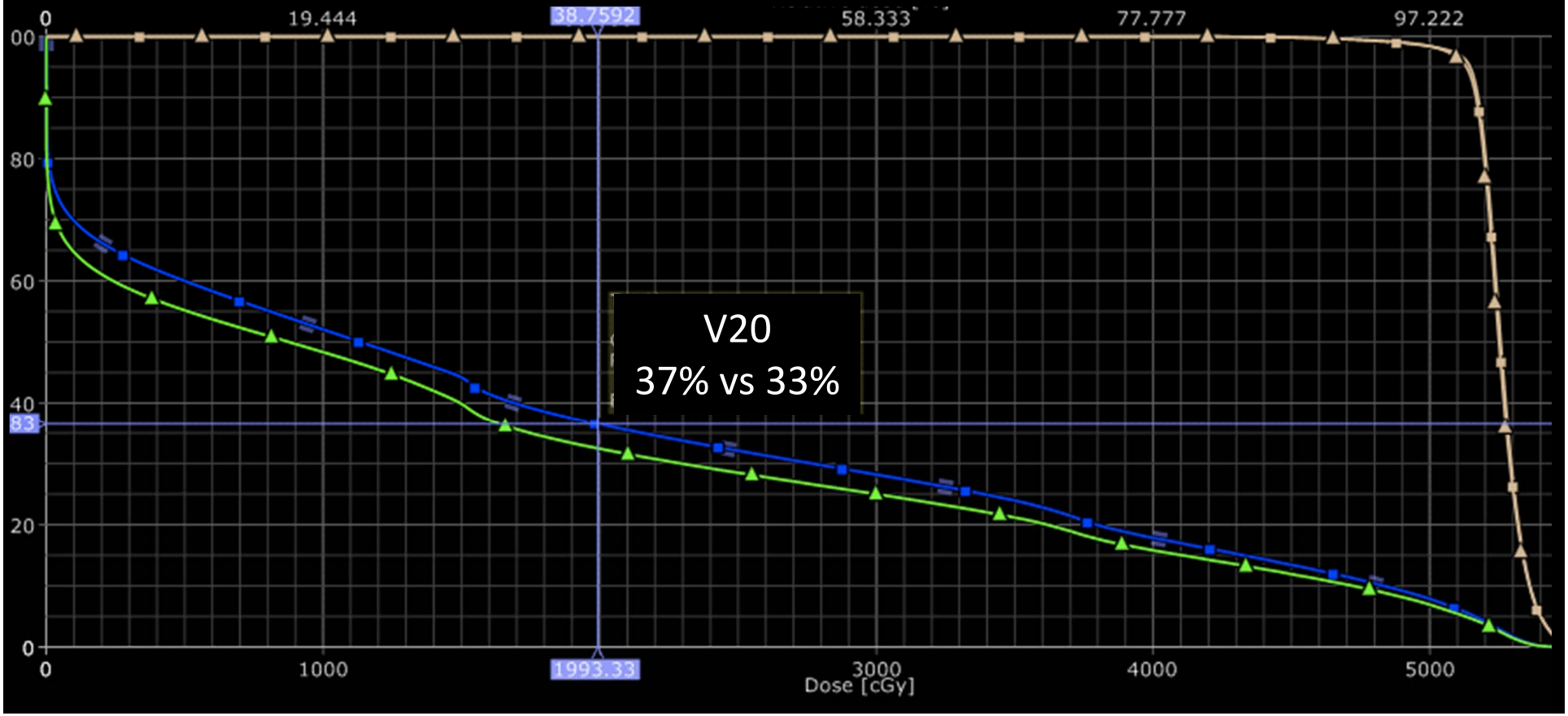
Internal Motion

- Have to consider internal motion
  - Respiratory movement
  - Bowel gas
  - Bladder filling
  - Organ motion
- Consider ITV, respiratory gating, tumor tracking to customize volume to patient's need
- Watch patient status, measure what can be measured: bladder filling, abdominal distension, breathing pattern

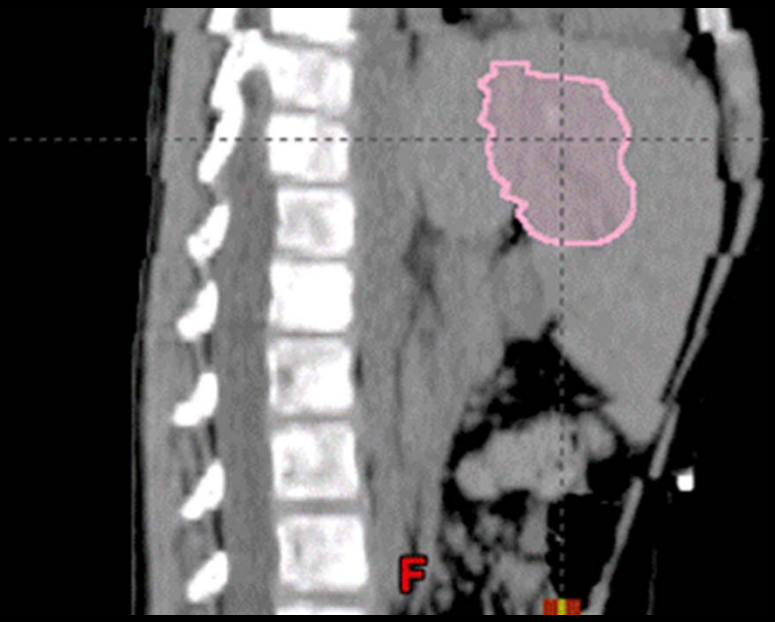


Mediastinum

-10 year old patient with Li Fraumeni
-Mediastinal recurrent ACC

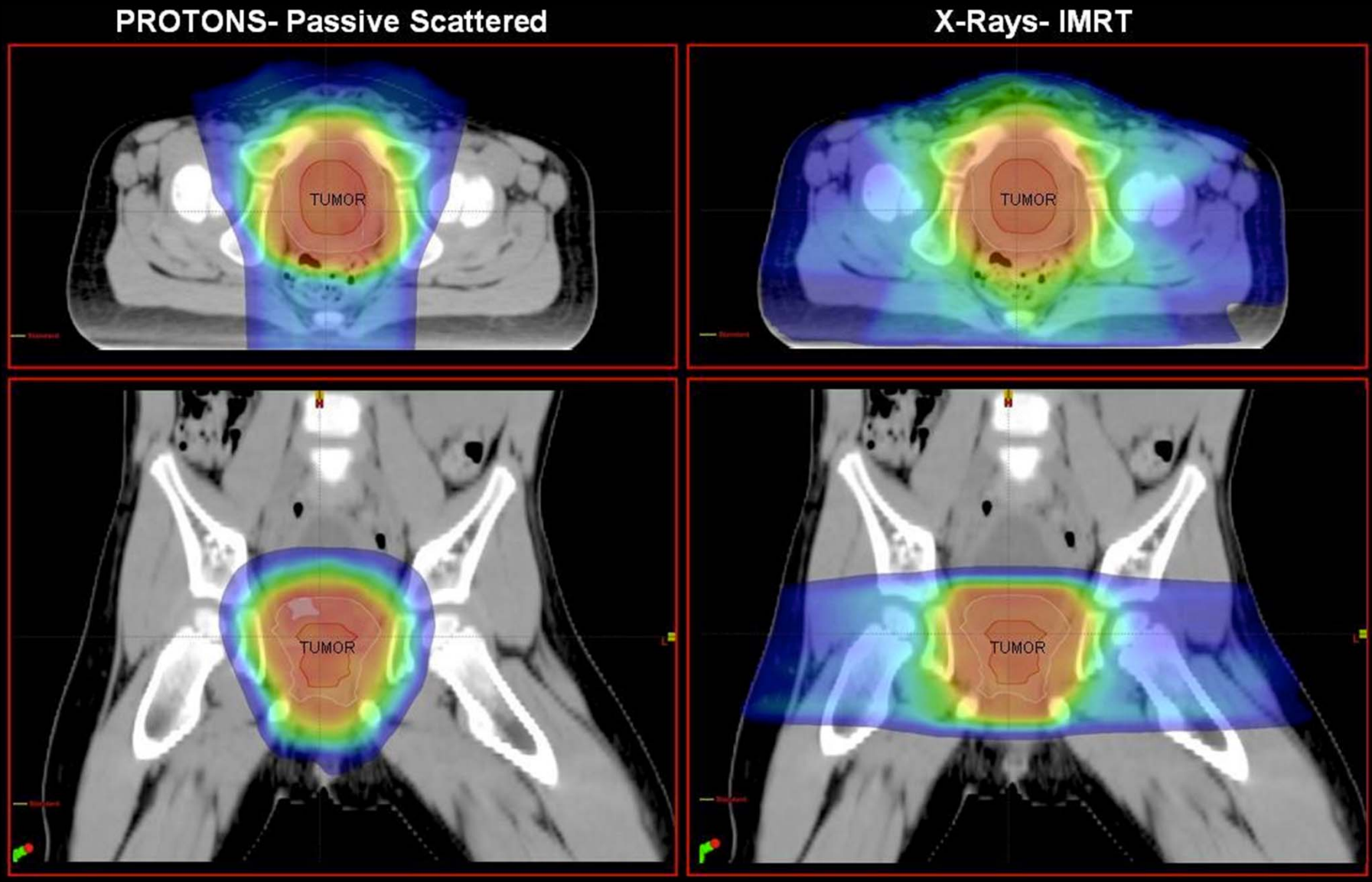


Liver Target and Abdomen

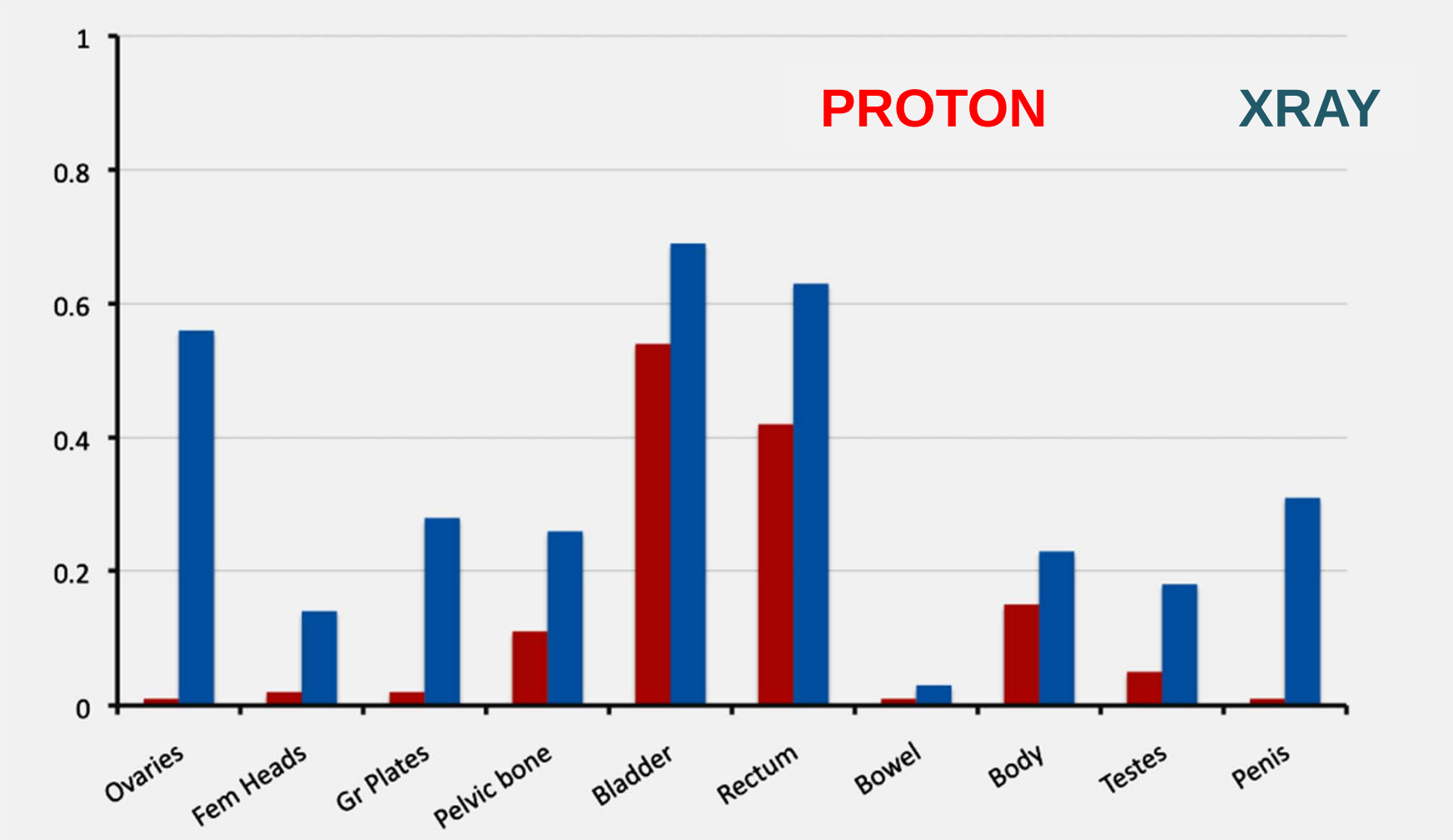


Pelvis

Pelvic Tumors



Central Pelvic Tumors



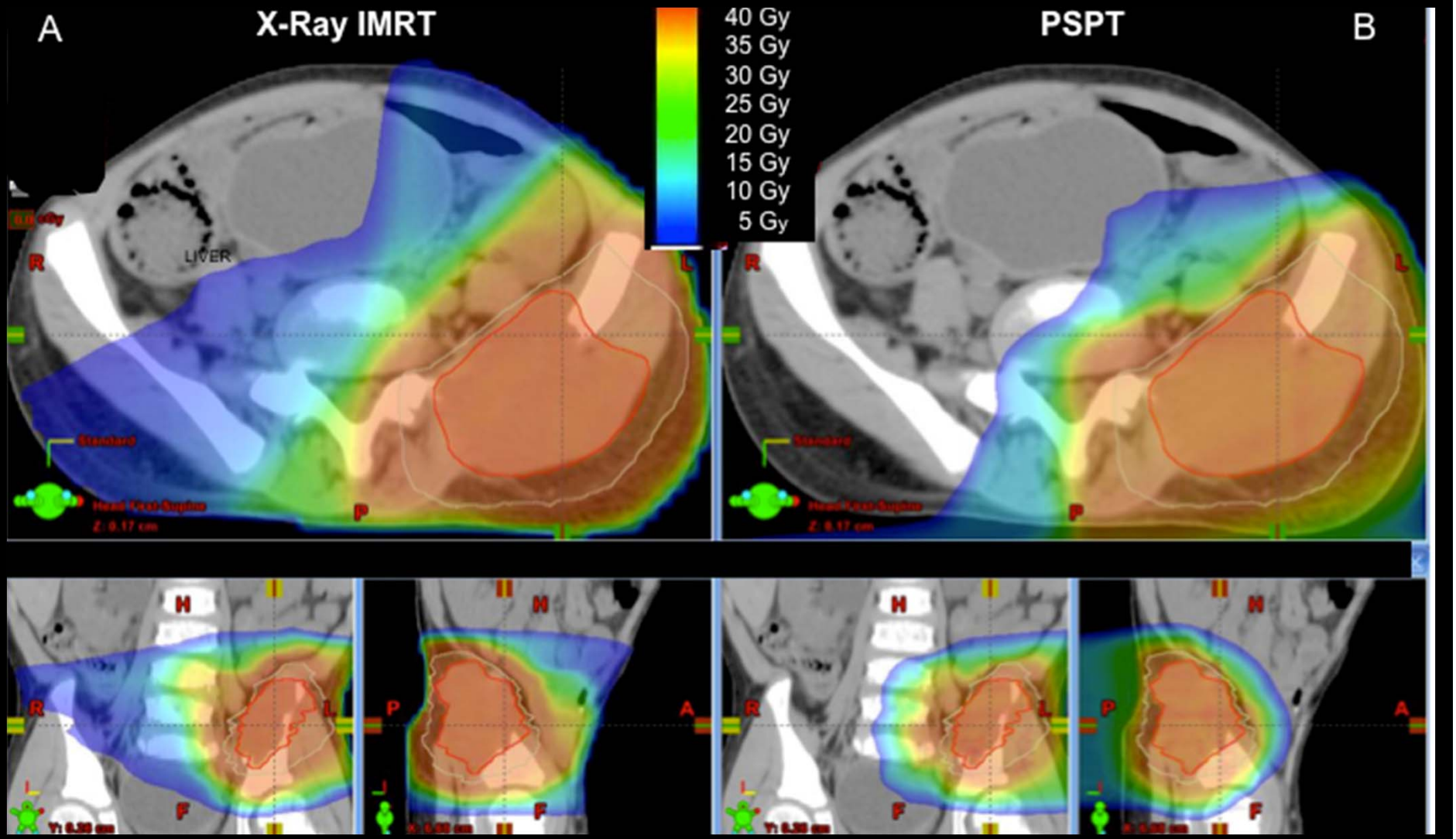
Pediatric Bladder/Prostate RMS

- 7 patients
  - Proton vs IMRT plan comparison
    - Significant median dose reduction
  - Median follow 27 mo
    - 5/7 had intact bladders, NED

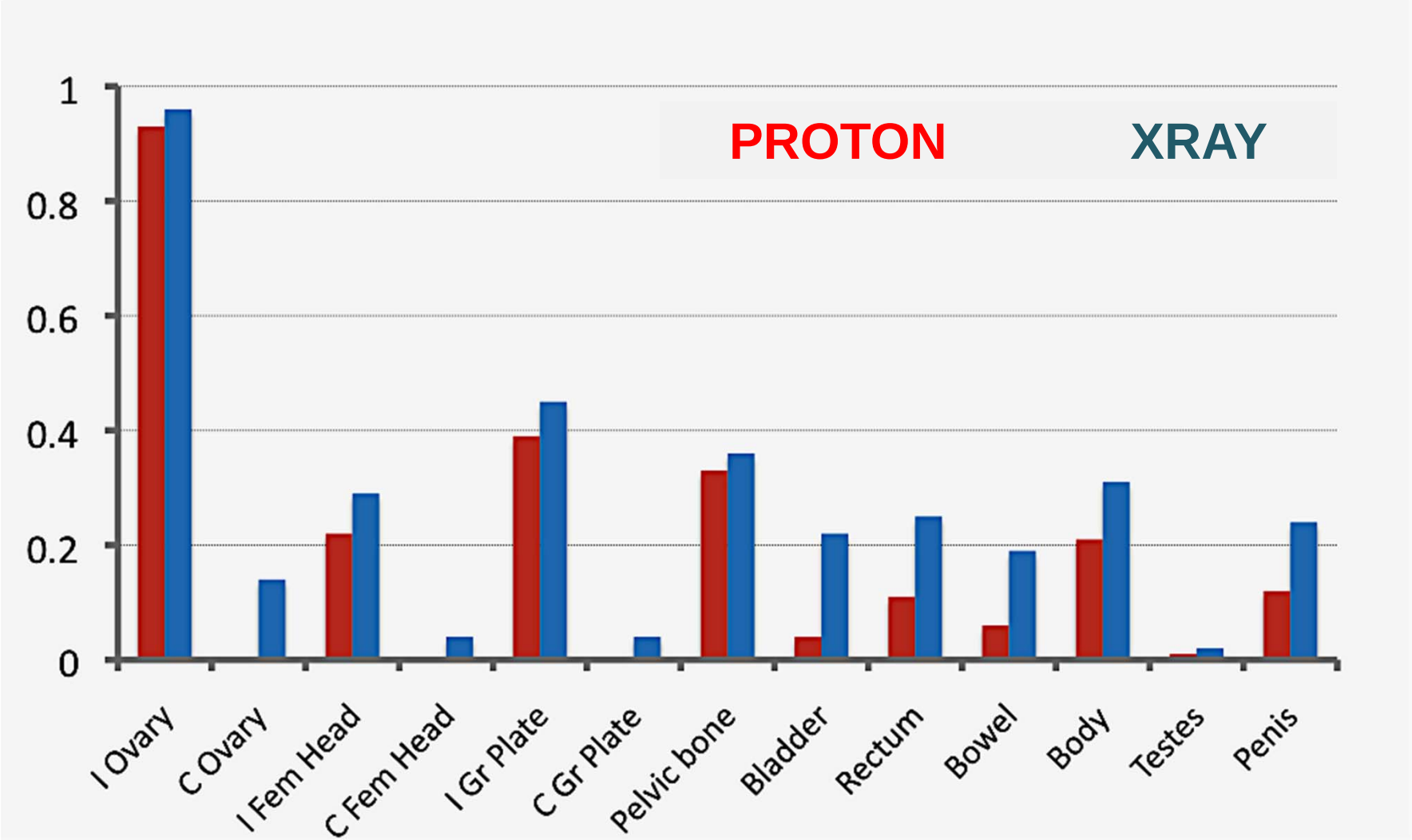
Organ	Proton	IMRT
Bladder	25.1	33.2
Testes	0	0.6
Femoral Heads	1.6	10.6
Growth Plates	21.7	32.4
Pelvic Bones	8.8	13.5

Cotter et al, IJROBP 81, 1367-1373, 2011

Lateral Pelvic Tumor



Lateral Pelvic Tumors



Patient Changes

- Weight gain
  - Steroids
- Weight Loss
  - Change in separation
  - Noted in head and neck patients
- Active nutritional surveillance and management

Ongoing Issues

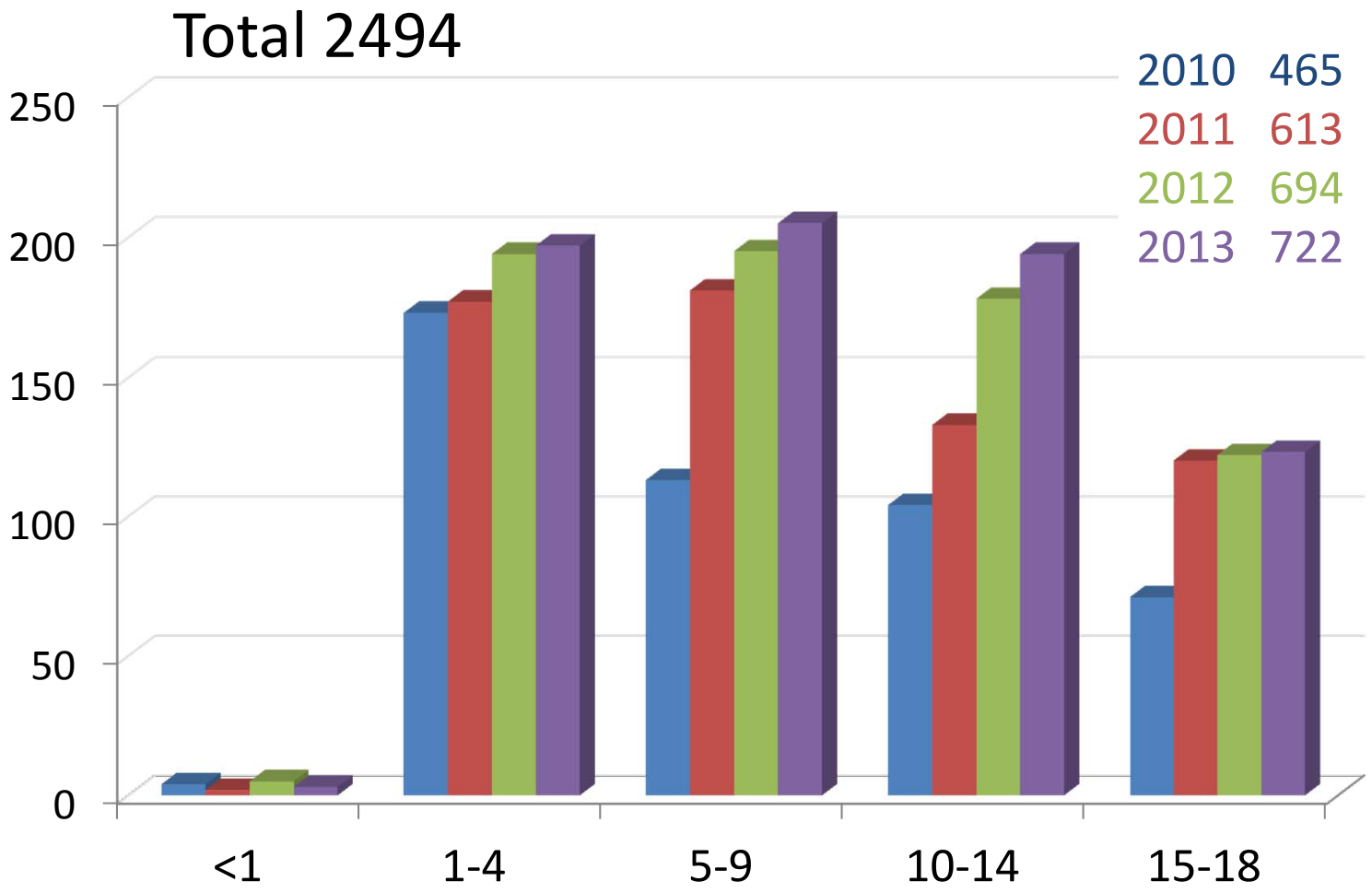
- Efficiency of daily set up
- Dose of daily CBCT, KV imaging
- Can surface mapping techniques help
  - Vision RT
- Incorporate MRI delivery?
- Be aware of all of these issues

Pediatric Experience

Pediatric Experience In North America

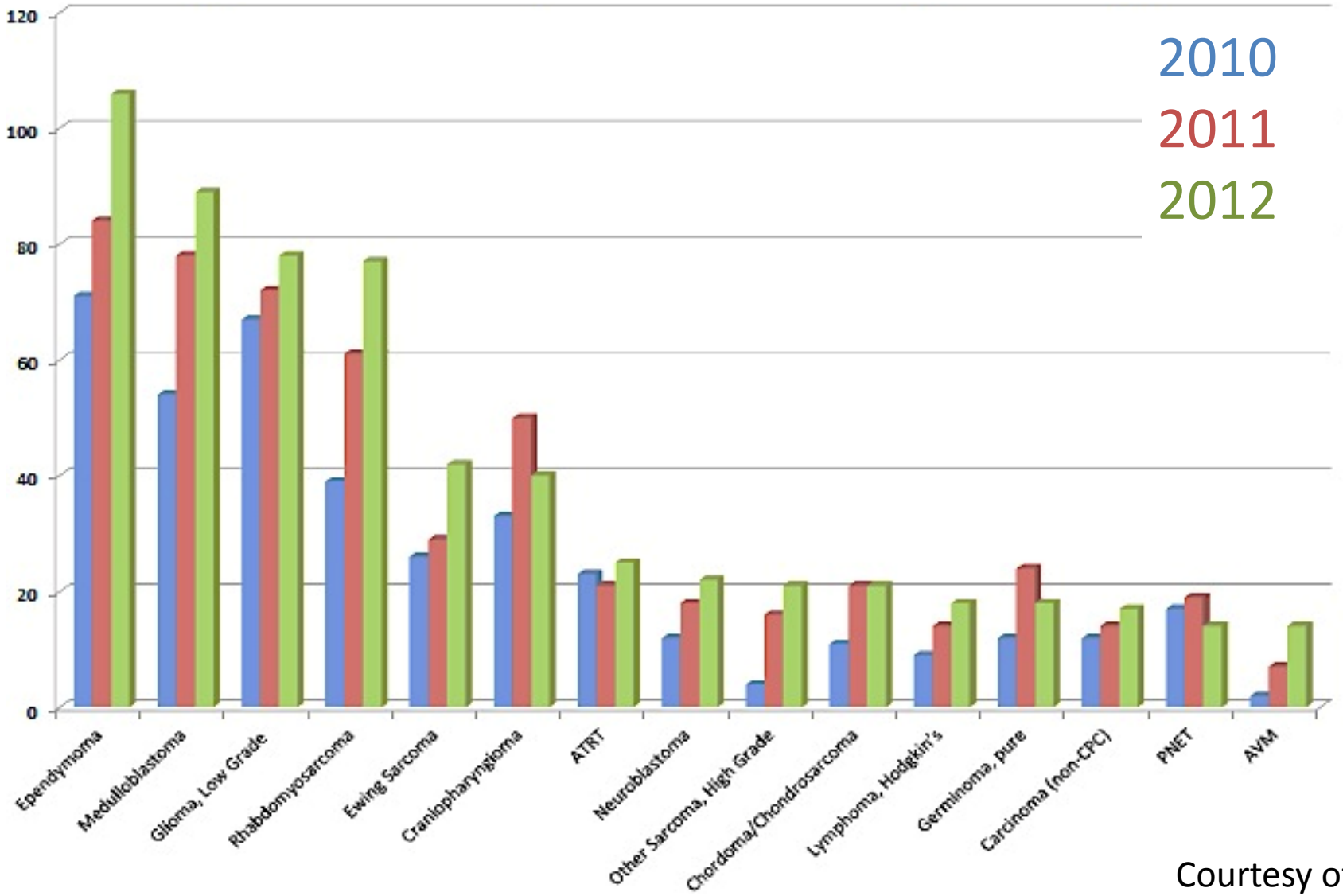
- Increased acceptance of proton therapy for children
- Proton therapy allowed as treatment modality in co-operative groups
- Pediatric Proton Foundation (PPF) has collected treatment patterns of children annually for past three years

Patient Age at Treatment



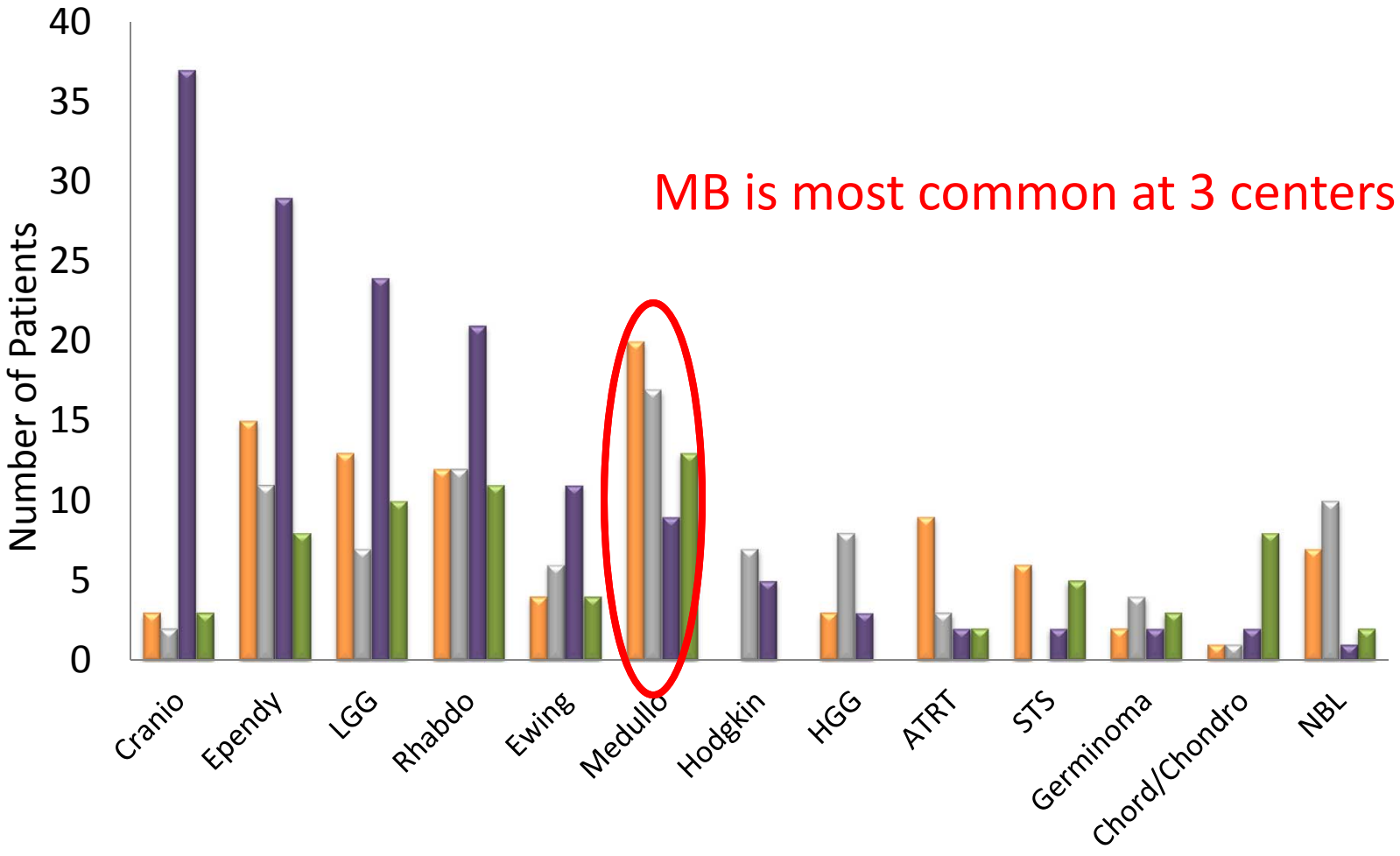
Courtesy of PPF

Top 15 Diagnosis



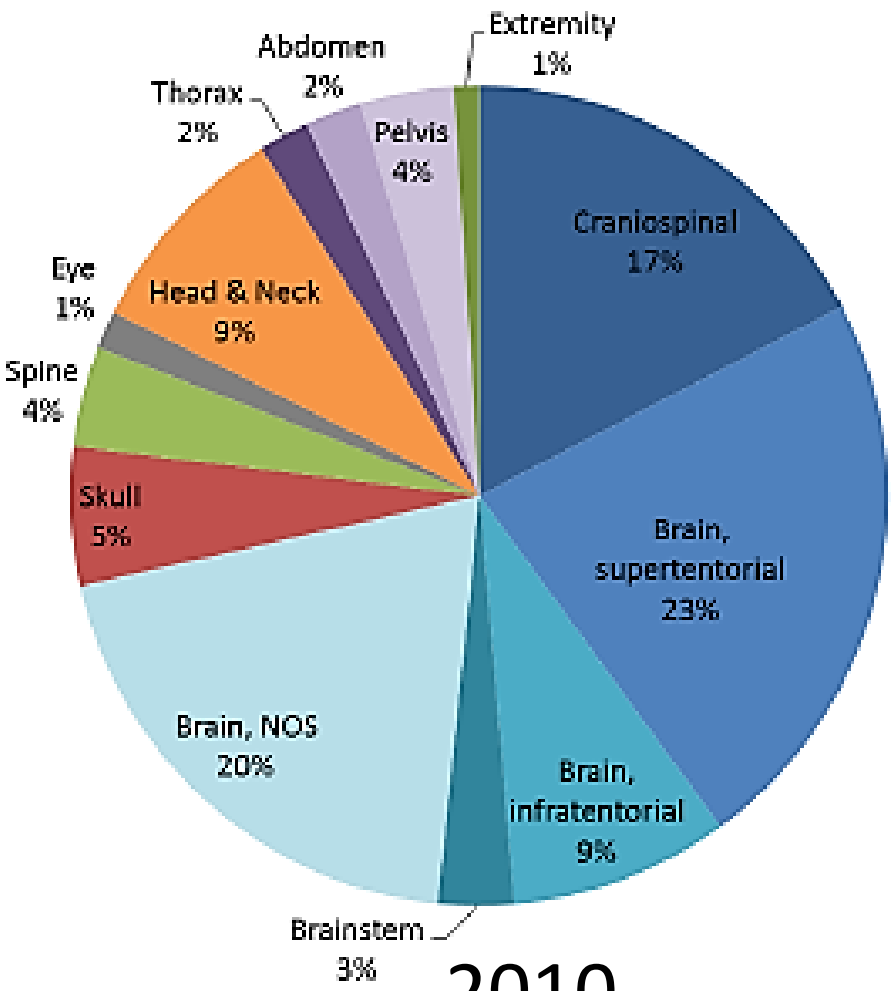
Courtesy of PPF

Variation Between 4 Programs 2013

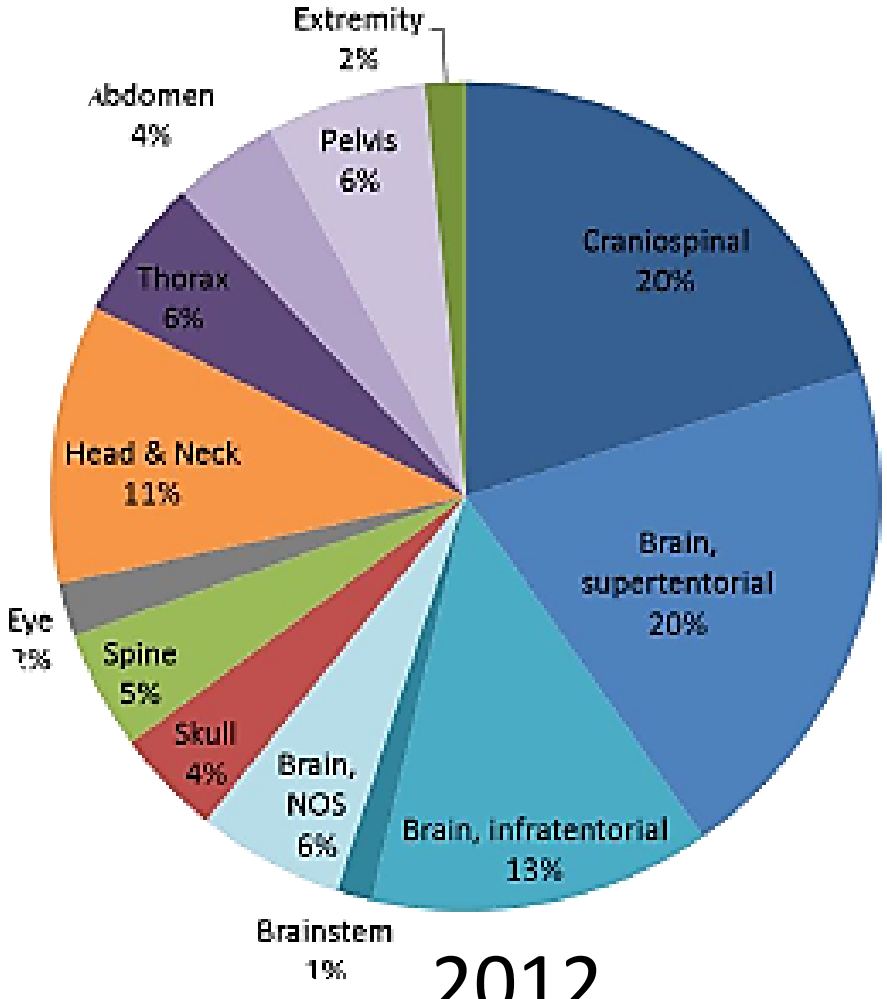


Courtesy of PPF

Treatment Location



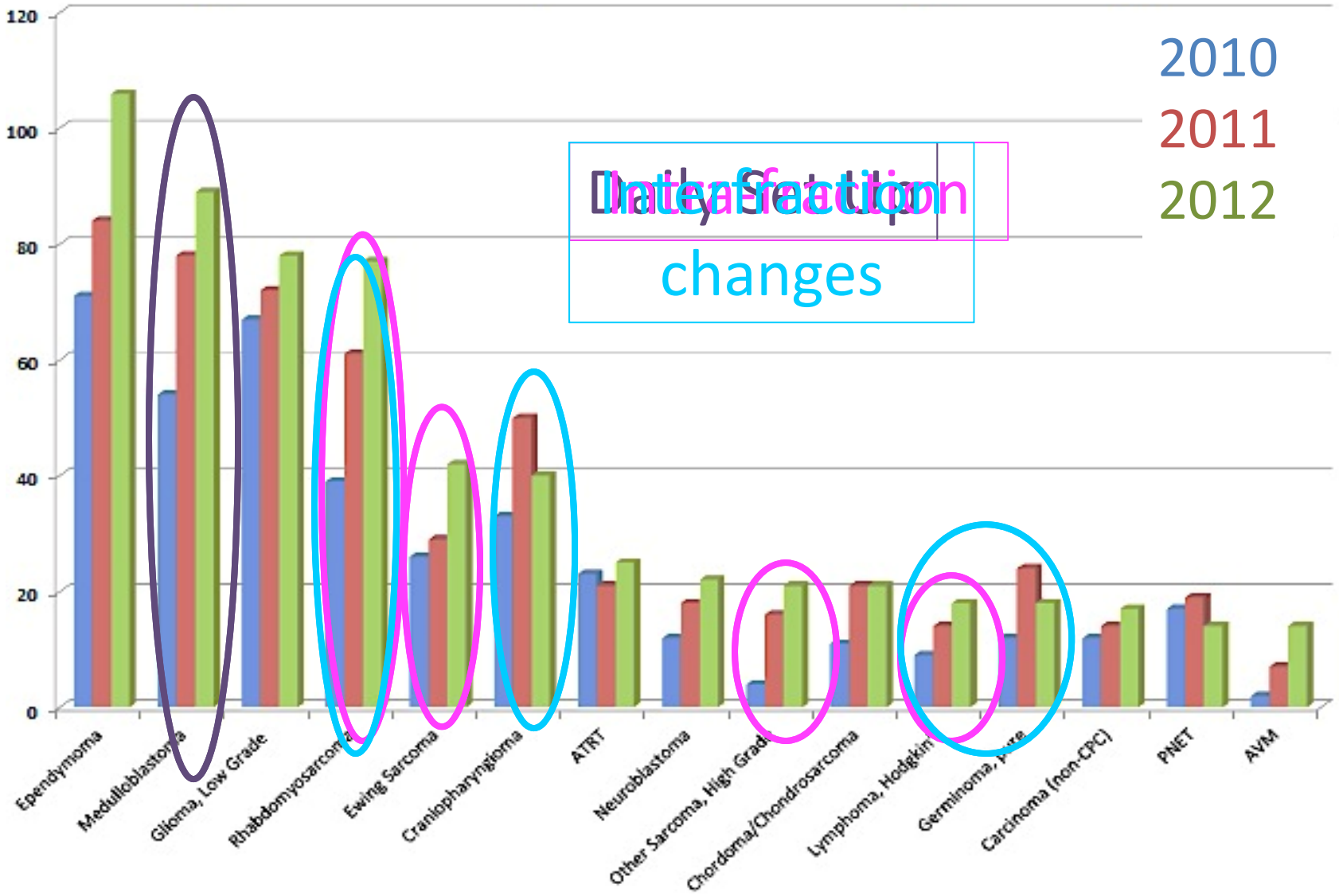
2010



2012

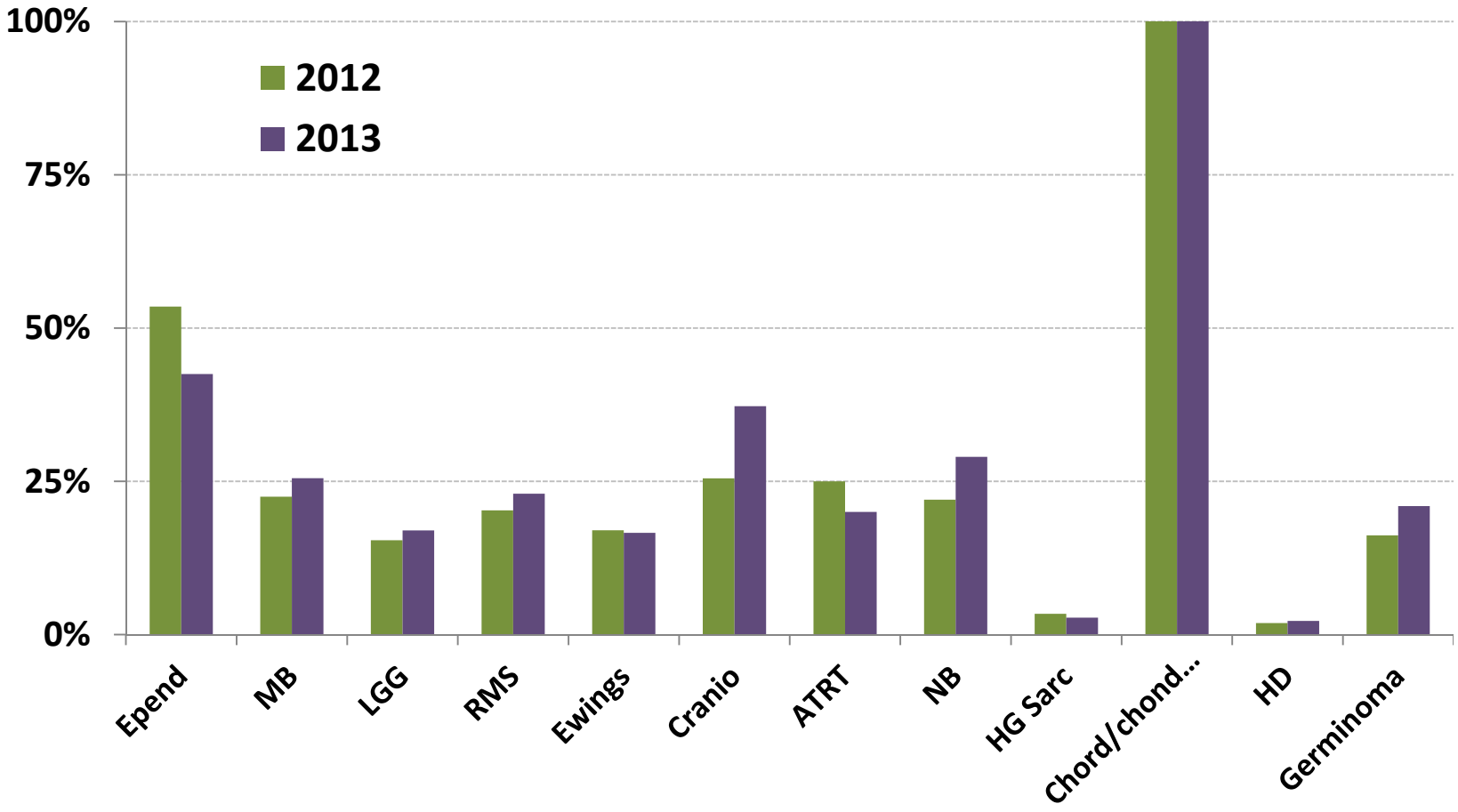
Courtesy of PPF

How can we can improve?



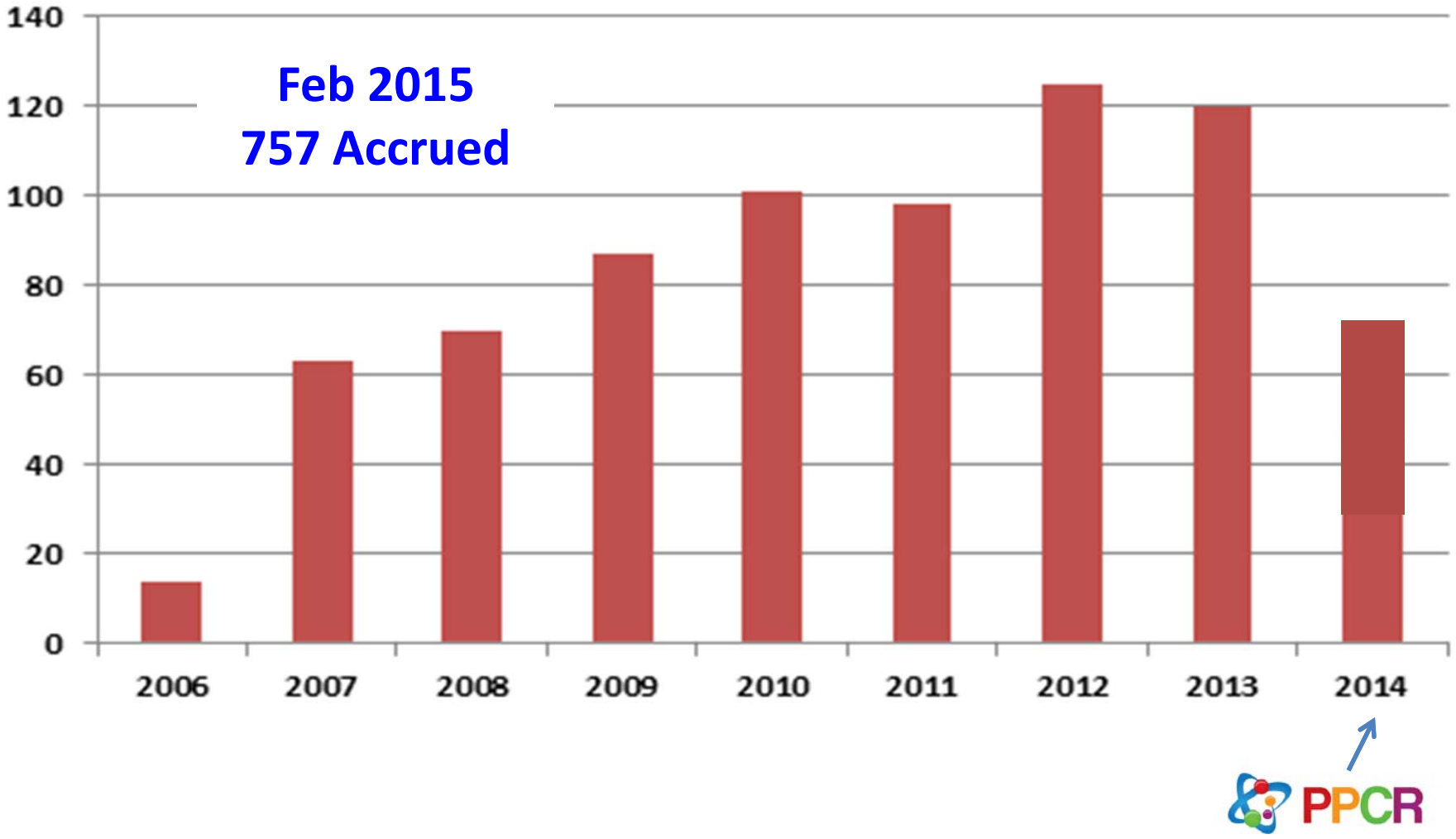
Courtesy of PPF

Estimated % of New Diagnosis in US



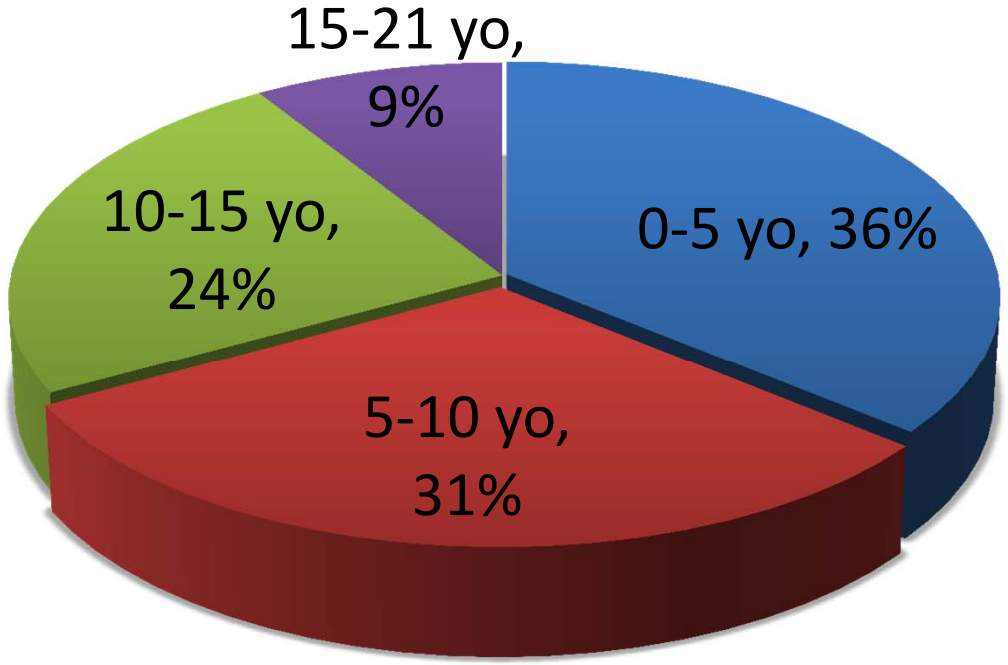
MDA Experience

MDA Pedi Normal Tissue Protocol

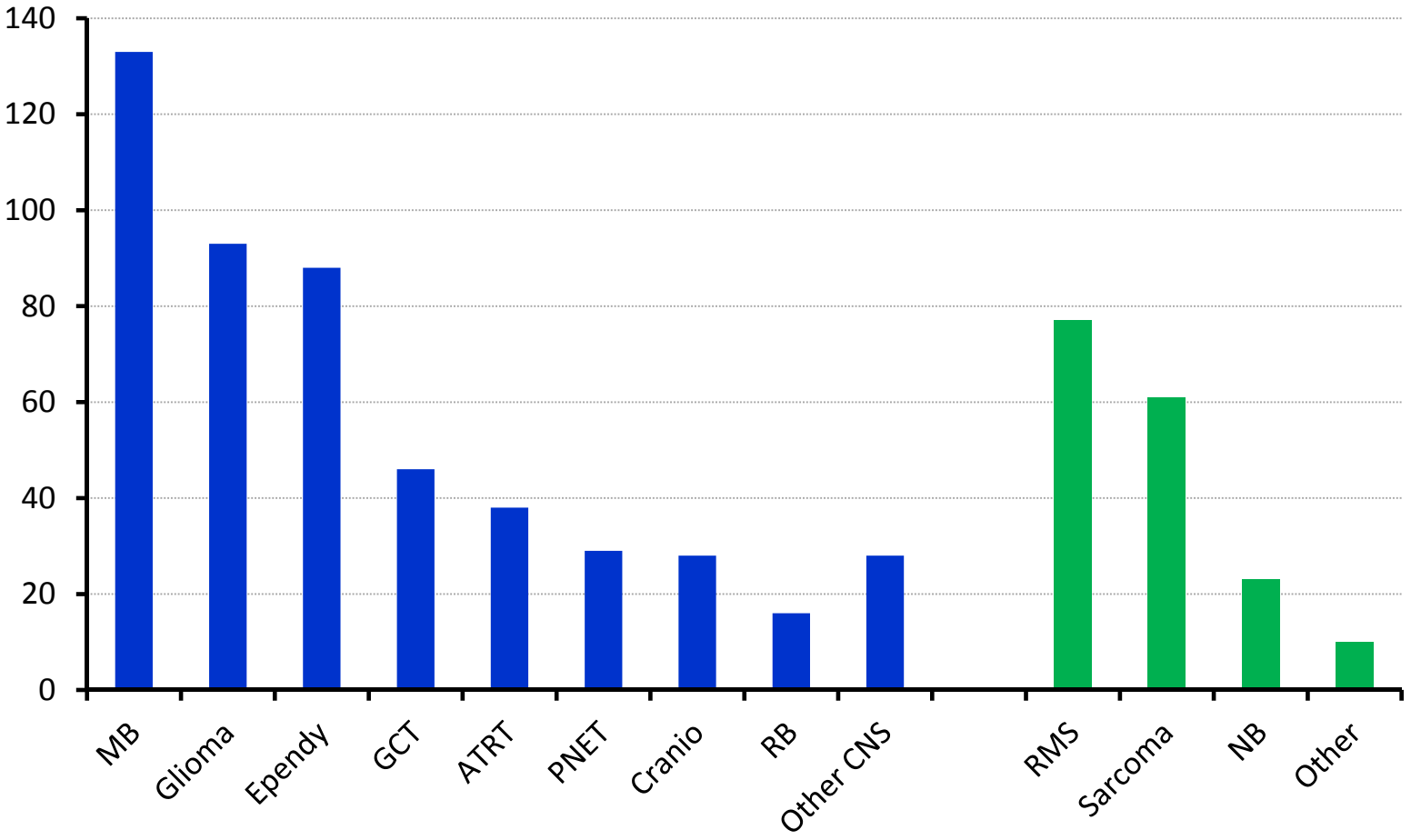


Patient Age

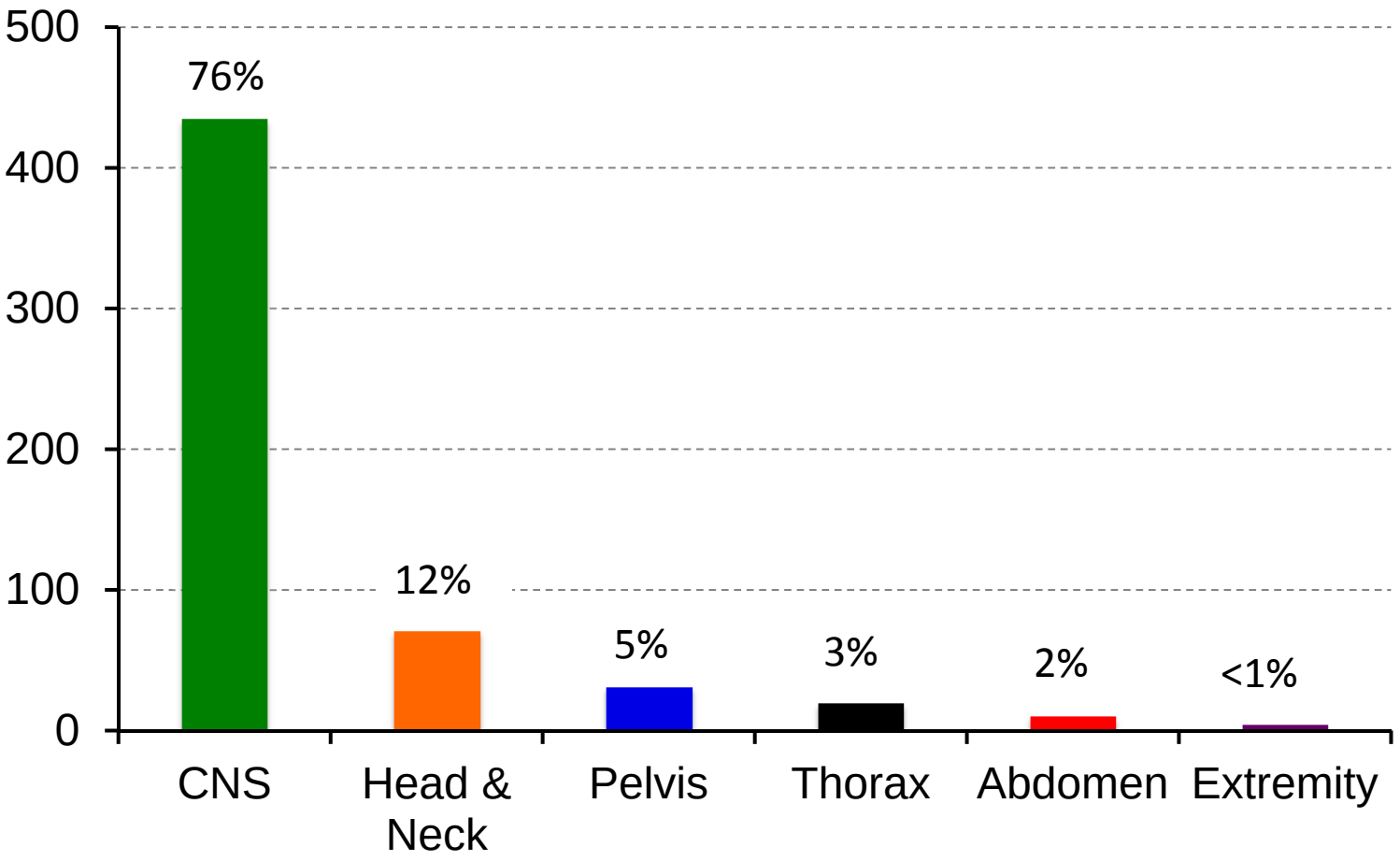
Proton Centers tend to get younger patients



Histology

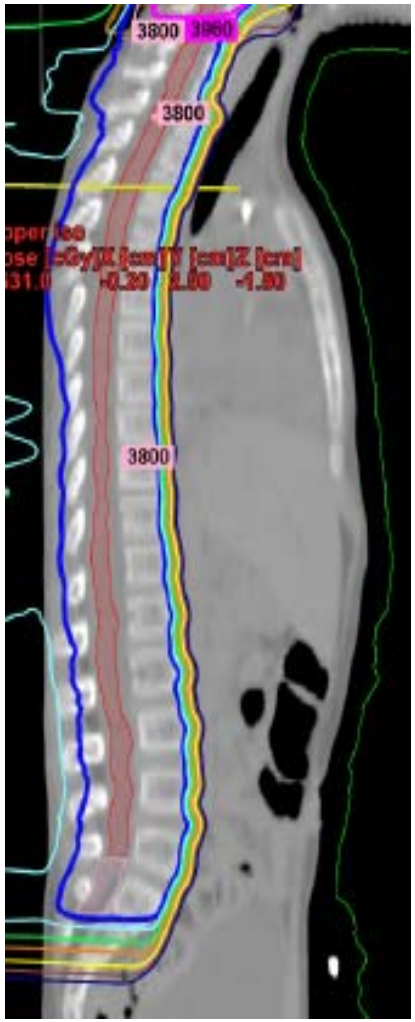

140
120
100
80
60
40
20
0
MB
Glioma
Ependy
GCT
ATRT
PNET
Cranio
RB
Other CNS
RMS
Sarcoma
NB
Other

Pediatric Disease Sites

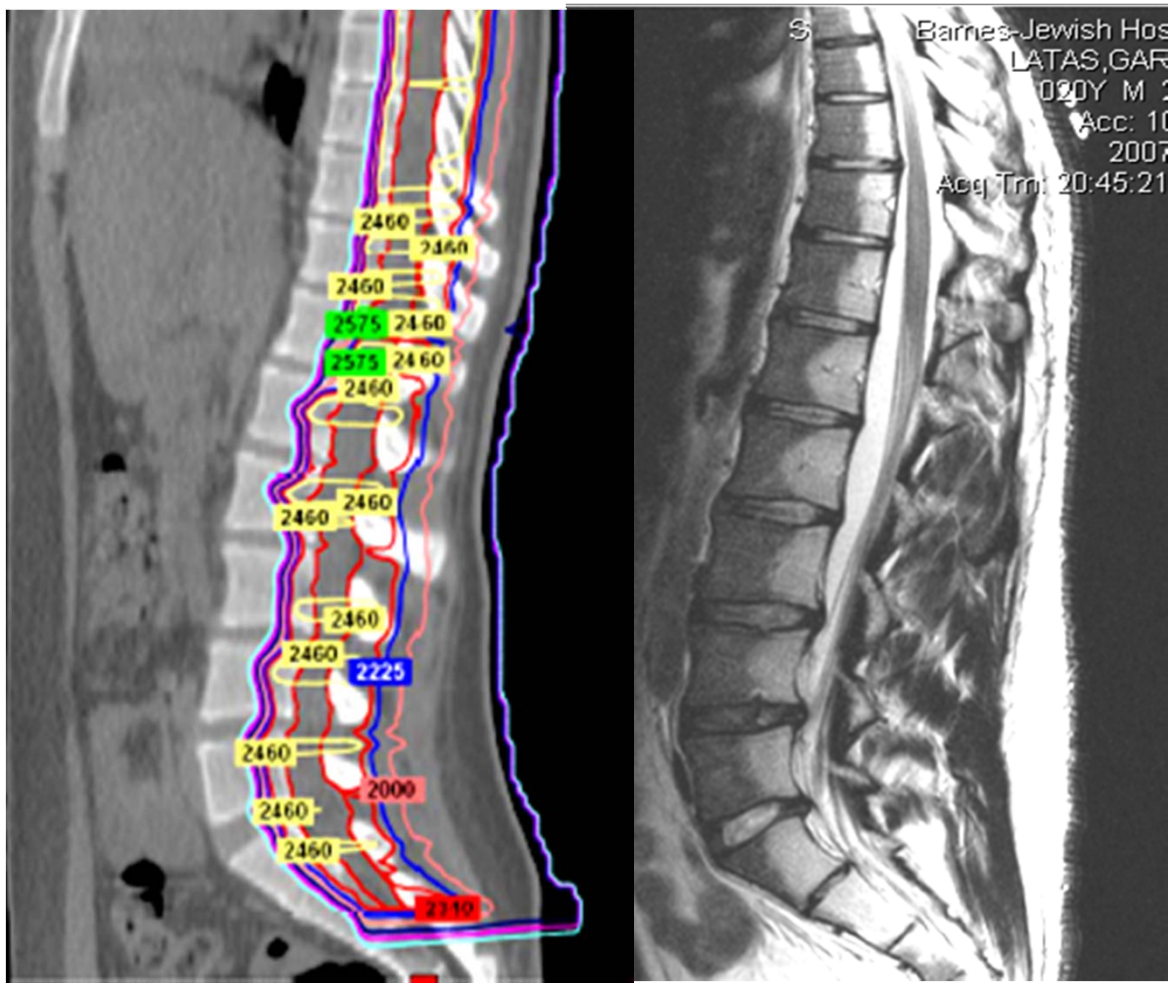


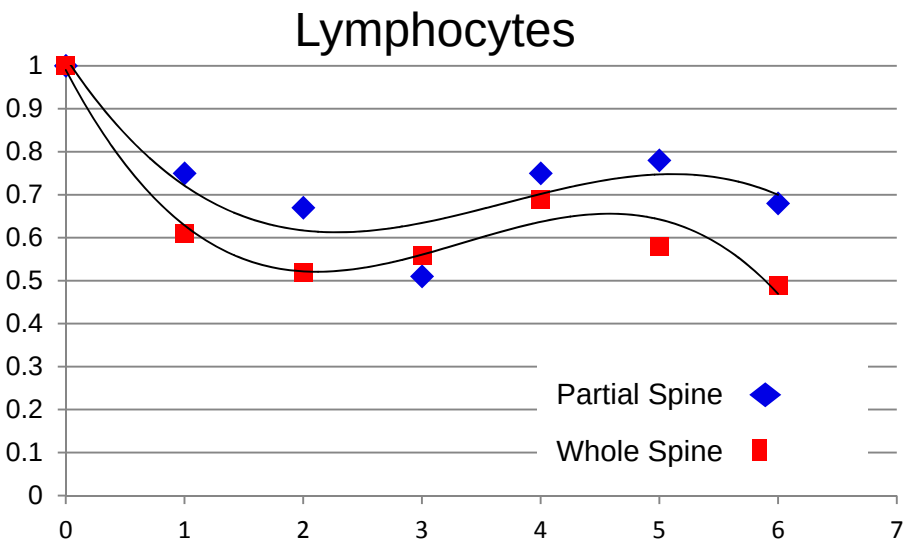
Proton CSI: Bone Marrow Sparing

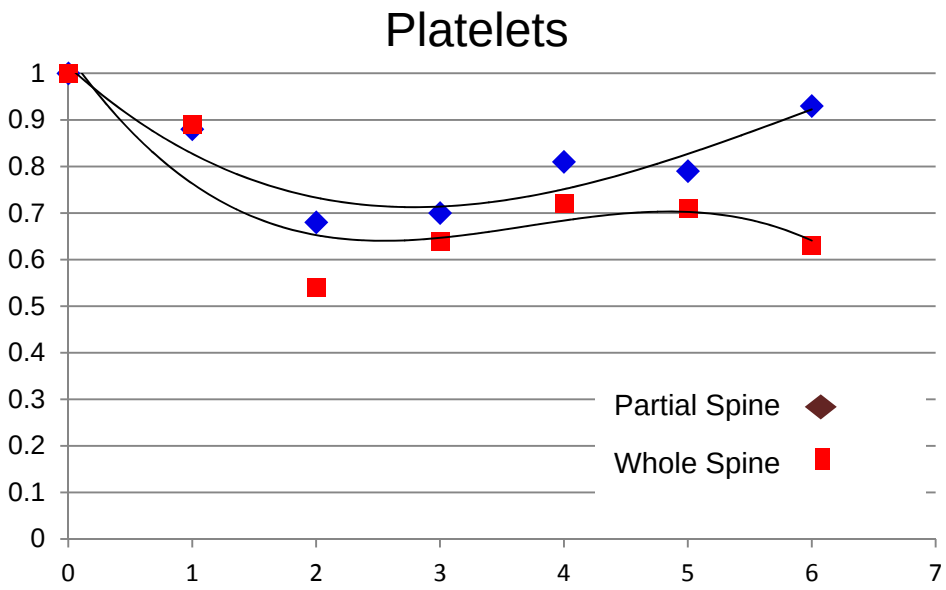
Younger



Older

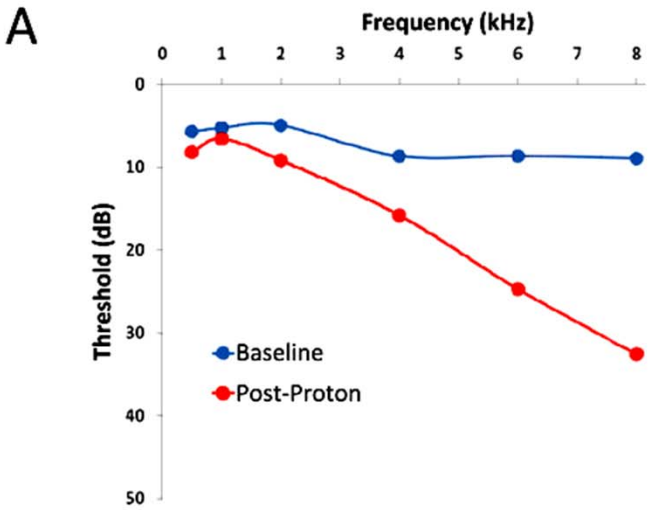


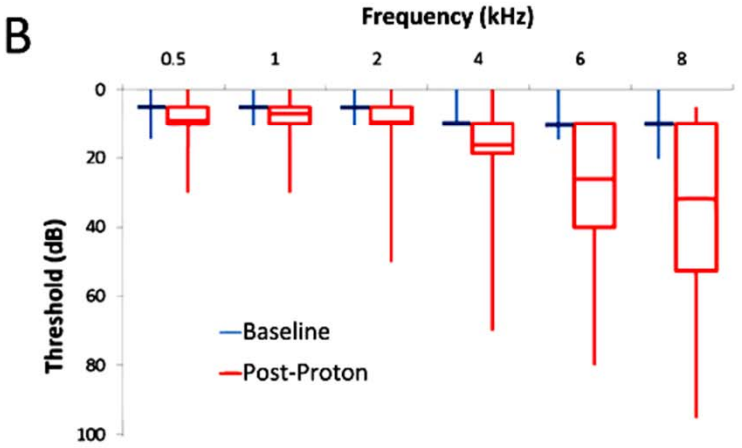




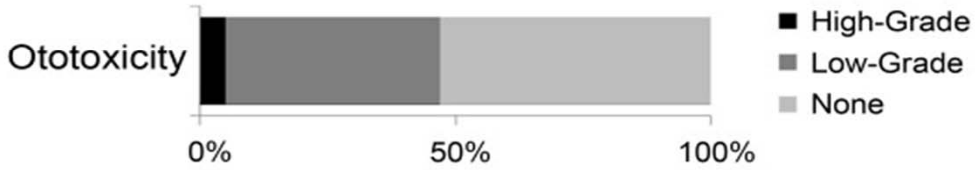
	P-CSI	W-CSI
Median age	16.5	6.5
No chemo	18	18
Chemo pre	27	29
Chemo during	22	25
WBC nadir	67%	50%
WBC wk 5	78%	58%
Platelet nadir	68%	54%
Platelet wk 5	78%	71%

Early Ototoxicity in MB - Proton CSI





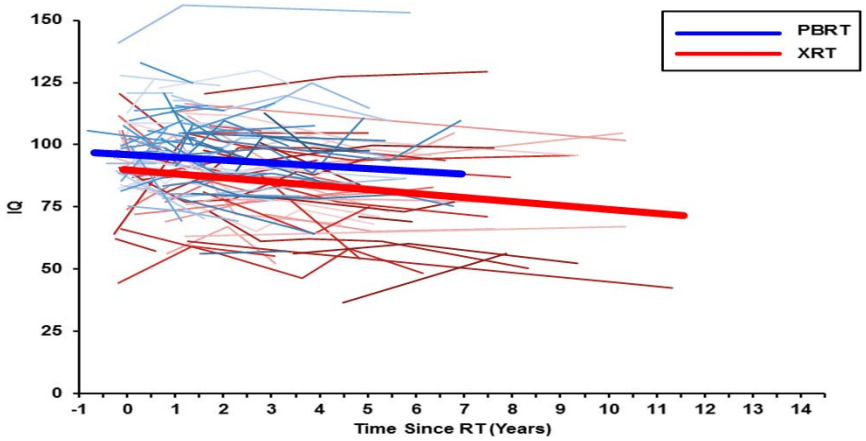
- Rates of high-grade early post-PRT CSI are low
- Need to longer follow up

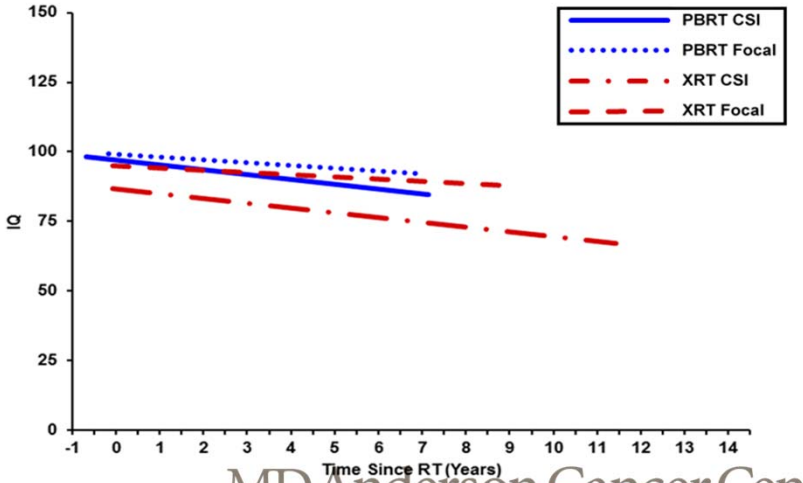


Moeller et al, Radiat Oncol; 6: 58

Early Neurocognitive Results

- Results ofpatients with baseline and follow up IQ scores
- XRT associated with ½ std dev decline/year
- Proton therapy: IQ generally intact





MD Anderson Cancer Center

Collaborations & Future Efforts

- Active in COG protocols
- Development of PBTC protocol for young children with MB
- Ongoing collaboration with MGH
- Protocol development with The Retinoblastoma Center of Houston

Pediatric Proton Ongoing Efforts

- PPCR
  - NIH funded registry through MGH
- Individual institutional outcome measures
- Collaboration with photon institutions
- CPRIT funding for CSI outcomes
- Other efforts

Proton Therapy-Questions

- Neutron Dose
- Uncertainties
- Clinical data so far
- Availability
- Cost

Summary

- Proton therapy is an important modality of the management of pediatric cancer
- Need to plan for pediatric-specific issues
  - Patient size, tumor behaviour, concurrent chemotherapy, sedation needs
- Need to incorporate lessons learned for adult RT efforts
- Work together to collect data and improve outcomes


Thank You