Pediatric Radiation Therapy Planning, Treatment, and Late Effects

Arthur J. Olch, Ph.D., FAAMP
Professor of Radiation Oncology and Pediatrics
USC Keck School of Medicine
Chief of Physics, Children's Hospital Los Angeles
Los Angeles, CA

Chia-Ho Hua, Ph.D.
Associate Member
Radiological Sciences
St. Jude Children's Research Hospital
Memphis, TN

Pediatric Treatment Planning I: Overview of Planning Strategies and Challenges

Arthur J. Olch, Ph.D., FAAMP
Professor of Radiation Oncology and Pediatrics
USC Keck School of Medicine
Chief of Physics, Children's Hospital Los Angeles
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Children's Hospital LOS ANGELES
We Treat Kids Better
USC University of Southern California

Disclosure

No conflict of interest

Mention of certain product names do no constitute an endorsement.

Overview of this Presentation

- Normal tissue tolerance differences between children and adults
- Secondary cancer risk from radiotherapy
- Craniospinal irradiation techniques
- Total Body irradiation techniques
- General treatment planning issues
- Immobilization techniques

CHLA and St. Jude Patient Population

- Treat about 12 (CHLA) - 25 (St. Jude) pts/day
- Sedation every day for < 7 y.o.
- 60% IMRT
- 40-50% Brain/CNS tumors
- Remaining 60% could be to any body site
- Wide range of body size from infant, children, to adolescents (≤21 years old) and weight can approach couch weight limit
- Prescribed doses range from 10Gy to 70Gy depending on disease and site.

Childhood Cancers are Different than Adult Cancers

Childhood Cancer Incidence (2% of all cancers)

- Leukemia (1/3)
- Brain/CNS
- Hodgkin's disease (other lymphoid)
- Non-Hodgkin's Lymphomas
- Bone/Joint
- Connective/soft tissue
- Urinary organs

Adult Cancer Incidence

Male	Female
Prostate	Breast
Lung/Bronchus	Lung/Bronchus
Colon/Rectum	Colon/Rectum
Bladder	Uterus
Lymphomas	Ovary
Oral cavity	Skin Melanoma
Skin Melanoma	Cervix
Leukemia	Leukemia

Childhood (0-14 y.o.) **Solid Cancers** (in order of prevalence)

- Central nervous system (Medulloblastoma most frequent)
- Neuroblastoma (adrenal gland and peripheral nervous system) (<4 y.o.)
- Soft Tissue Sarcomas
- Wilms' Tumor (<4 y.o.)
- Bone tumors (adolescent)
- Germ Cell Tumors (adolescent)
- Retinoblastoma (40% hereditary) (<4 y.o.)
- Hepatoblastoma (<4 y.o.)
- Other (thyroid, melanoma)

Histologies rare to not seen in adults.

Adult cancers are predominantly Carcinomas

Childhood Cancer Survival Rate

- Has steadily increased from the 1960's
- Overall 3 year survival rate = 80%, 5 year = 75%
- Many types with less than 50% 5 yr survival
- Brain Stem Gliomas nearly always fatal
- Treatment Intent nearly always for cure as opposed to palliation.

Dominating Influences to the Planning Process

- Late Effects
- Secondary Malignant Neoplasms

Induction of Second Cancer for Pediatric Patients Treated with RT

- Overall cumulative incidence of SM is 3.5% after 25 years.
- Bone and soft tissue sarcomas are most often seen SM after RT.
- Chemo usually used with RT, both increase risk of SM
- RR of SM after brain tumor irradiation is 3% after 20 years
- RR of SM after Hodgkin's Disease is about 12% after 25 years
- Cum incidence of SM for irradiated hereditary Retinoblastoma is 38% after 50 yrs. Its 21% for non-irradiated patients.
- Solid cancers accounted for 81% of all SM.
- The average latency period is about 15 years
- RR is 3-6 fold higher for children than adults.
- RR is a nearly linear function of dose, up to very high doses.
- 70% of SM occur in the radiation field, 20% adjacent, only 10% distant
- Risk continues to increase over time, 20, 30 years +

Evidence against the increased risk of second malignancy with IMRT

- Multi-beam treatment by itself does not increase integral dose vs. conventional treatments.
- IMRT by itself does not increase integral or peripheral dose vs. conventional treatments.
- IMRT does give 3-4 times higher leakage dose and increases the volume receiving ultra low doses.
- SM **infrequently** occur where head leakage dose dominates, ie. distant from the medium-high dose region.
- SM risk increases with increasing dose.
- Reducing the volume receiving moderate to high doses in trade for increasing the volume receiving <5 Gy should both reduce SM risk and better protect normal structures.

Q1: Which is **TRUE** about the risk of production of second malignancy from radiation therapy:

20%	1. The risk increases with age at time of irradiation
20%	2. Most secondary malignancies occur inside the high dose region
20%	3. Most are secondary leukemias rather than solid tumors
20%	4. The risk plateaus with dose and is small for high doses
20%	5. The risk diminshes after about 15 years

10

The correct answer is:

- Answer: b - Most secondary malignancies occur inside the medium-high dose region
- Ref: Analysis of dose at the site of second tumor formation after radiotherapy to the central nervous system. Int. J. Radiation Oncology Biol. Phys., Vol. 82, No. 1, pp. 90–94, 2012.

Comparison of Critical Structure Dose for Children vs. Adults

Structure	Children	Adult
Whole Brain	18 Gy	35 Gy
Bones	18 Gy	>65 Gy
Pituitary (growth hormone)	20 Gy	none
Ovary/testes (reproduction)	10 Gy	none

Cardiac toxicity may be higher for children, more years for problem to develop than in adults

PENTEC

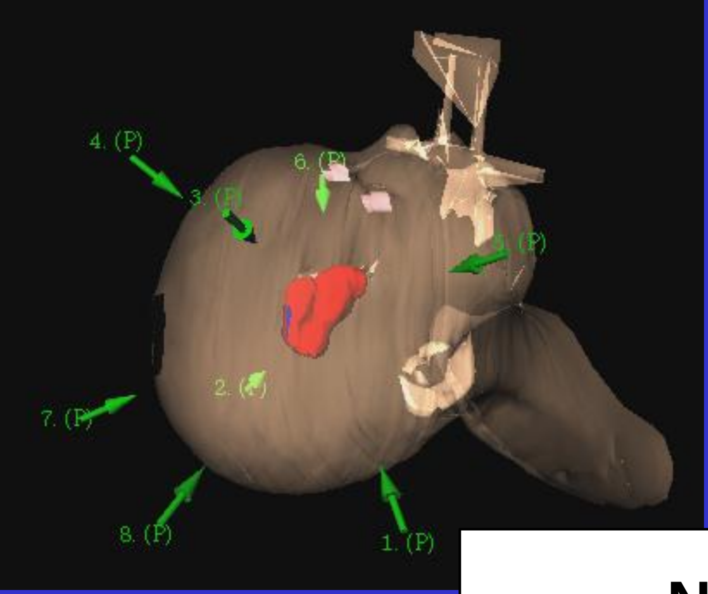
(Pediatric Normal Tissue Effects in the Clinic)

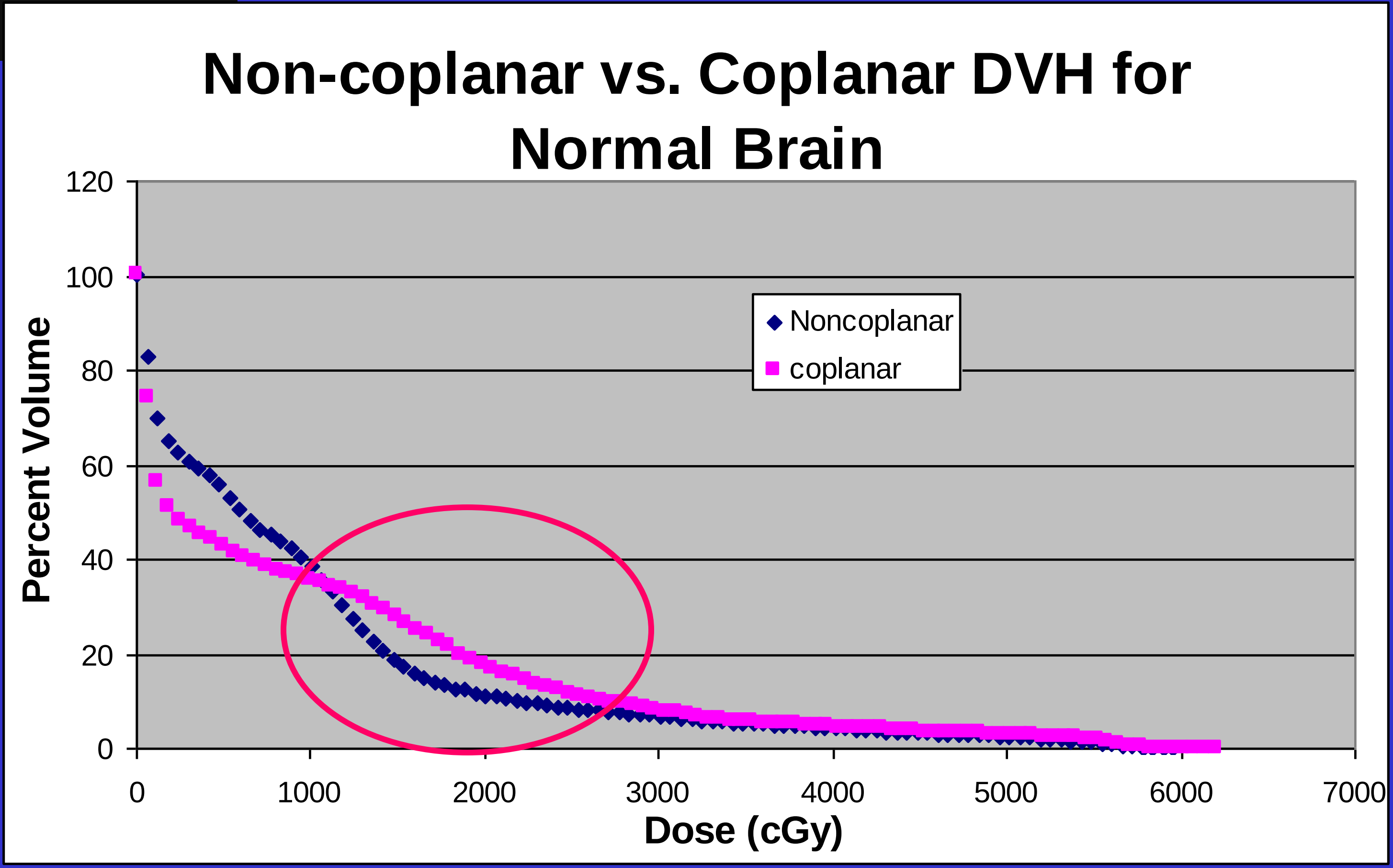
- Pediatric version of QUANTEC
- 18 organs/normal tissues
- Survey the world's literature to define dose-tolerance for each organ
- Challenges include accounting for effects of chemotherapy and developmental status
- Stay Tuned (about 1.5 years from now)

Overview of Planning Issues for Conformal Treatments

- Non-coplanar vs. coplanar beams: spread low dose area around to lessen mid-dose volume
- Immobilization techniques for head and body
- Targets tend to be irregularly shaped and large
- Targets are always surrounded by or near critical structures
- Ratio of safe critical structure dose to tumor dose is usually less than in adults. <30-50% vs. >70%
- Avoid vertex fields that irradiate longitudinally
- Consider out of field/exit dose for testes and ovary

Non-coplanar beams may reduce cognitive deficits for brain targets





Treatment of Medulloblastoma

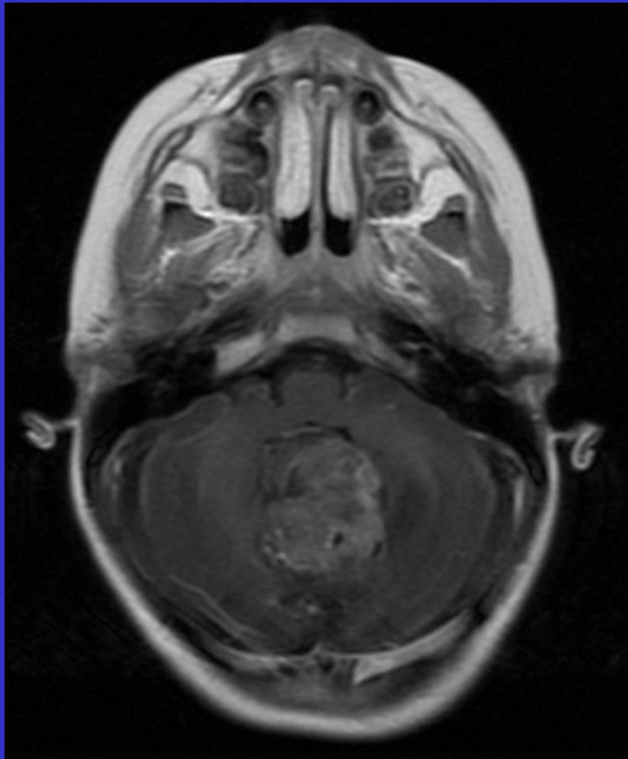
Craniospinal Irradiation Plus Posterior Fossa Boost

7-8 % of intracranial tumors across all ages but…

30% of pediatric brain tumors

¾ of all cases occur in children,

median age 9 y.o.



Treatment of Medulloblastoma

Targets and Critical Structures

Brain (target and OAR)

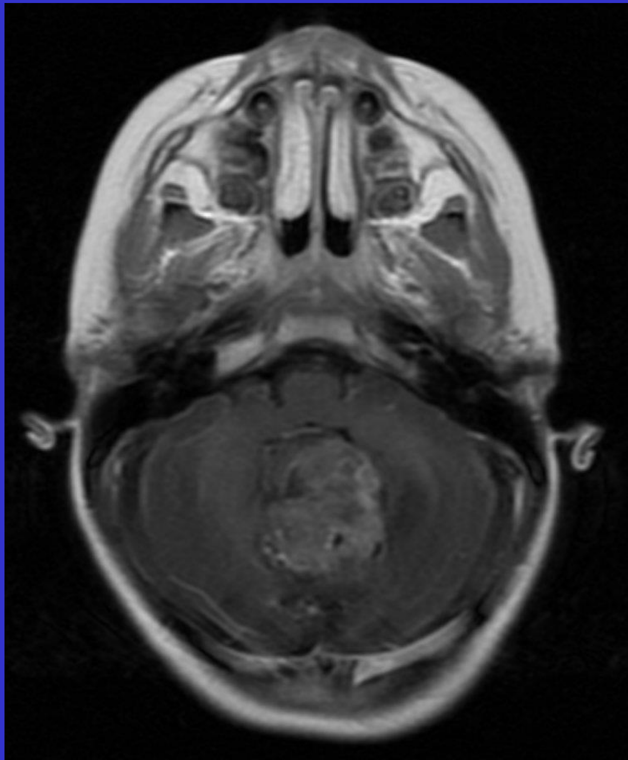
Spinal cord (target and OAR)

Cochlea

Gut, throat, heart (PA spine exit doses)

Lenses

Skin (PA entrance dose)



Craniospinal Axis Treatment

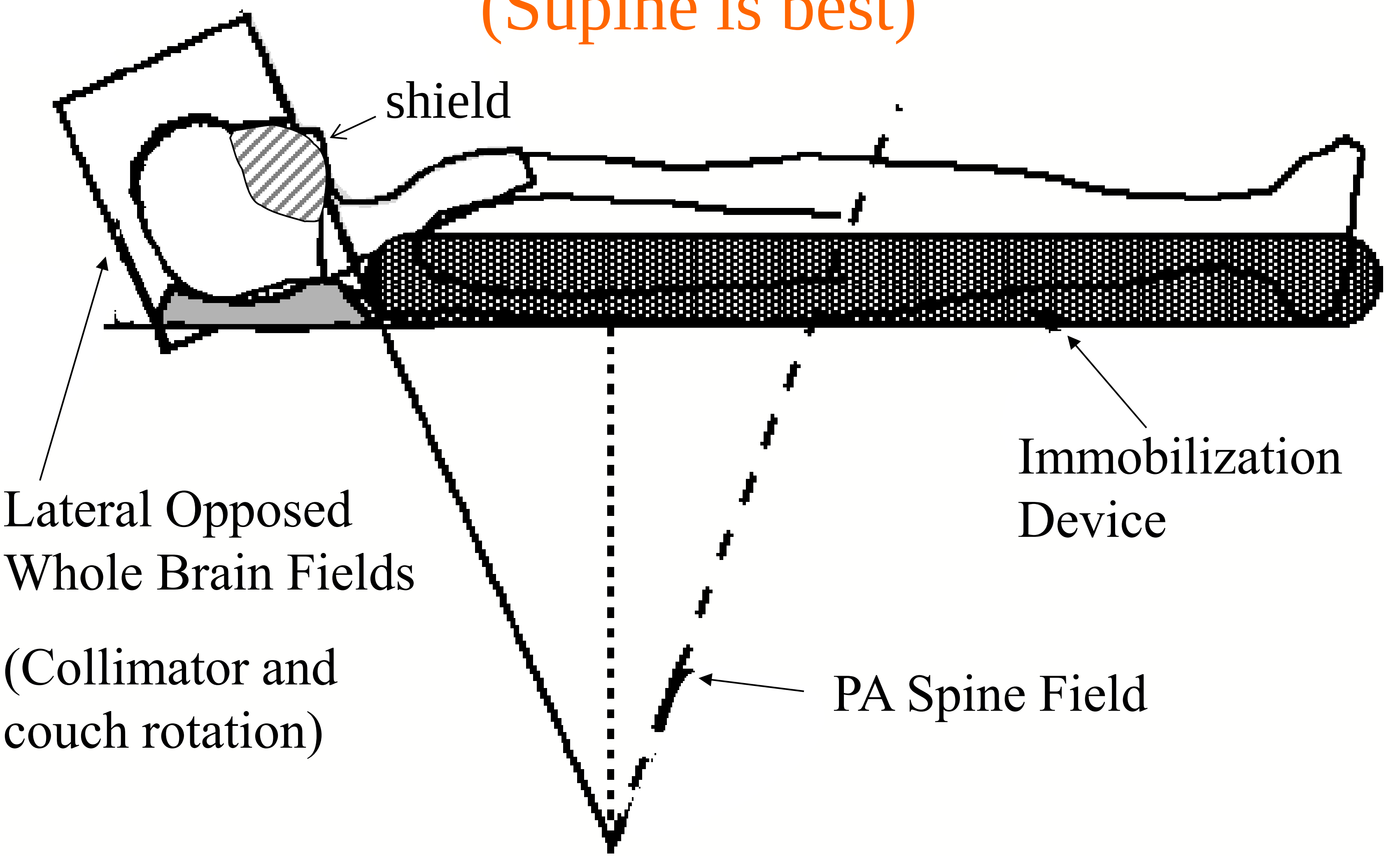
Treat whole spine and brain to either 23.4 Gy (aver. risk) or 36 Gy (high risk) + Boost posterior fossa to total of 54-55.8 Gy

CSI Planning issues:

- Prone vs. Supine
- Spine-brain junction dose (avoid cord overdose), junction level, and shifts
- Extended SSD vs. abutted PA spine fields

Conventional Craniospinal Irradiation Technique

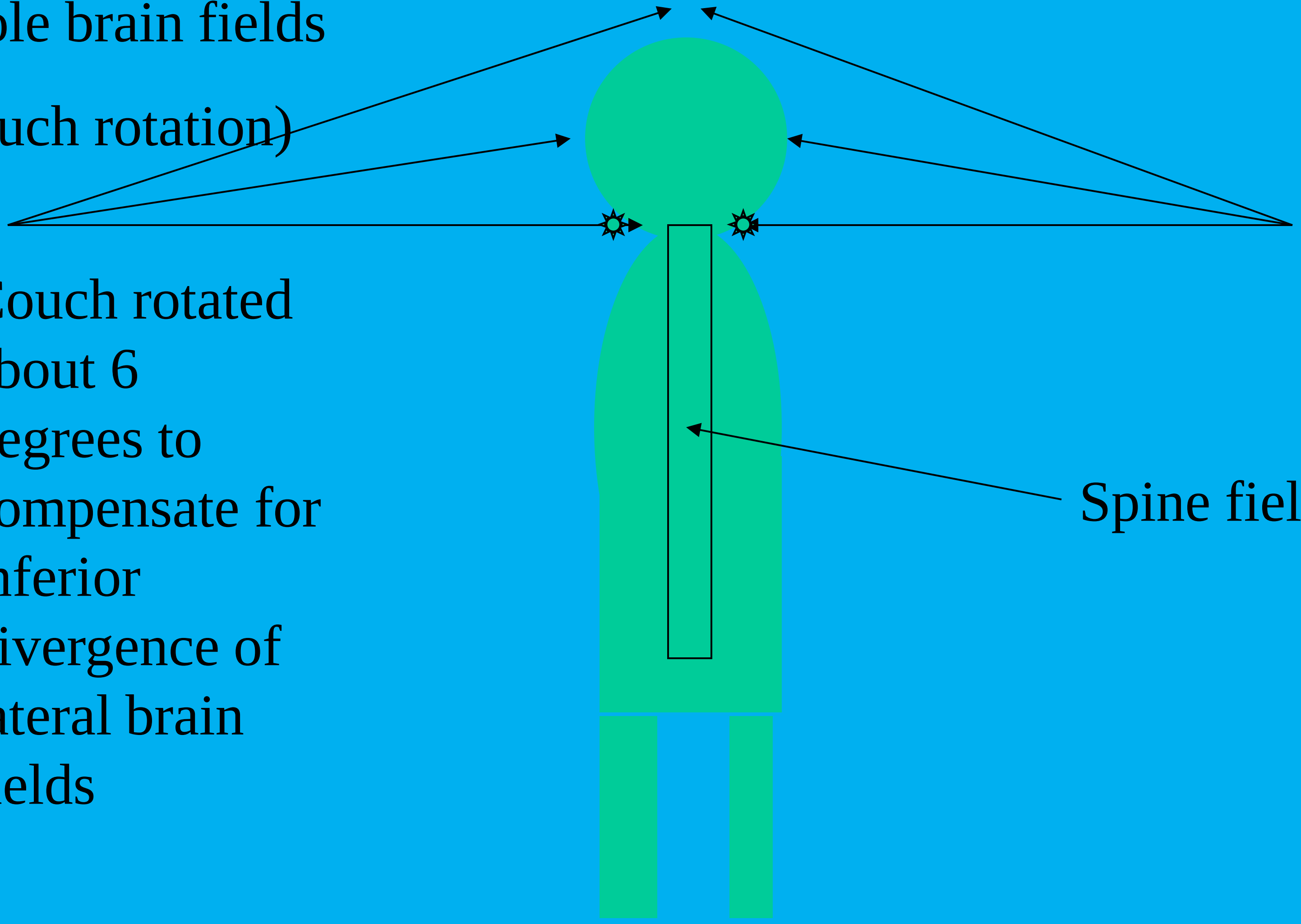
(Supine is best)



Conventional Craniospinal Irradiation Technique

Right and left lateral whole brain fields

(Couch rotation)

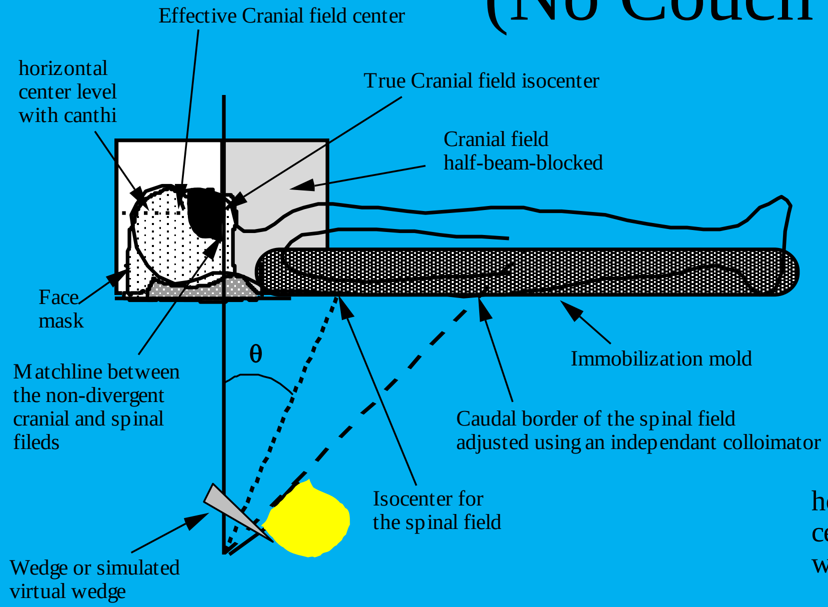


Couch rotated about 6 degrees to compensate for inferior divergence of lateral brain fields

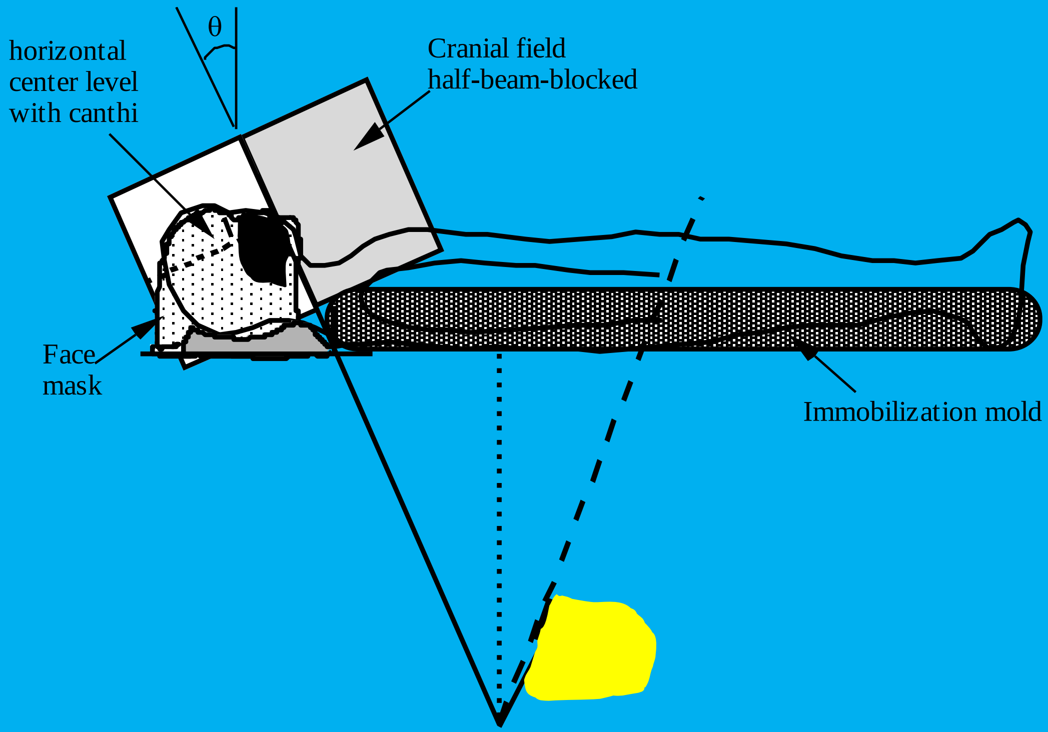
Spine field

Split beam CSI technique

(No Couch Rotation for WB)



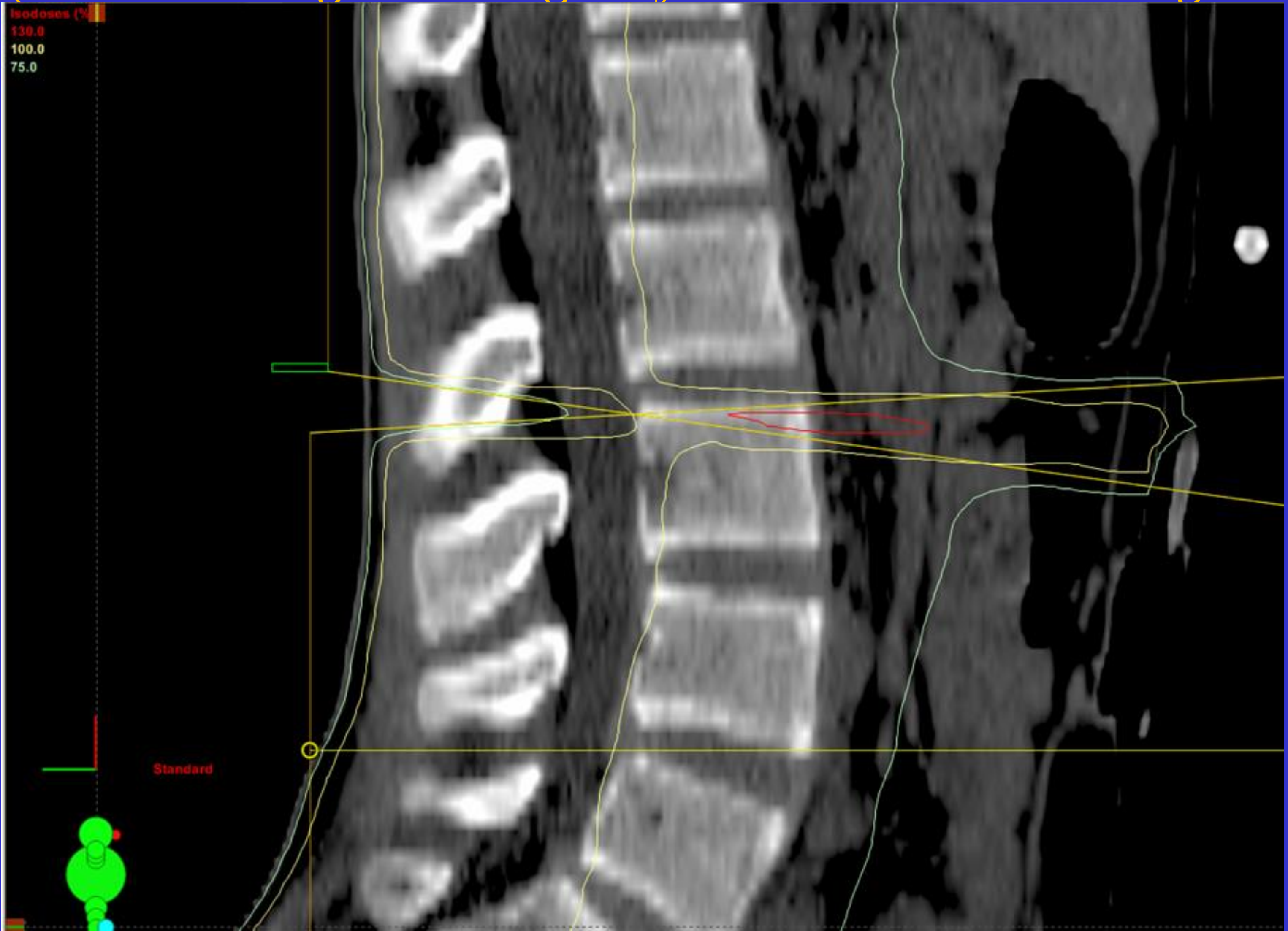
Problem with half-beam block- not long enough for low junction method



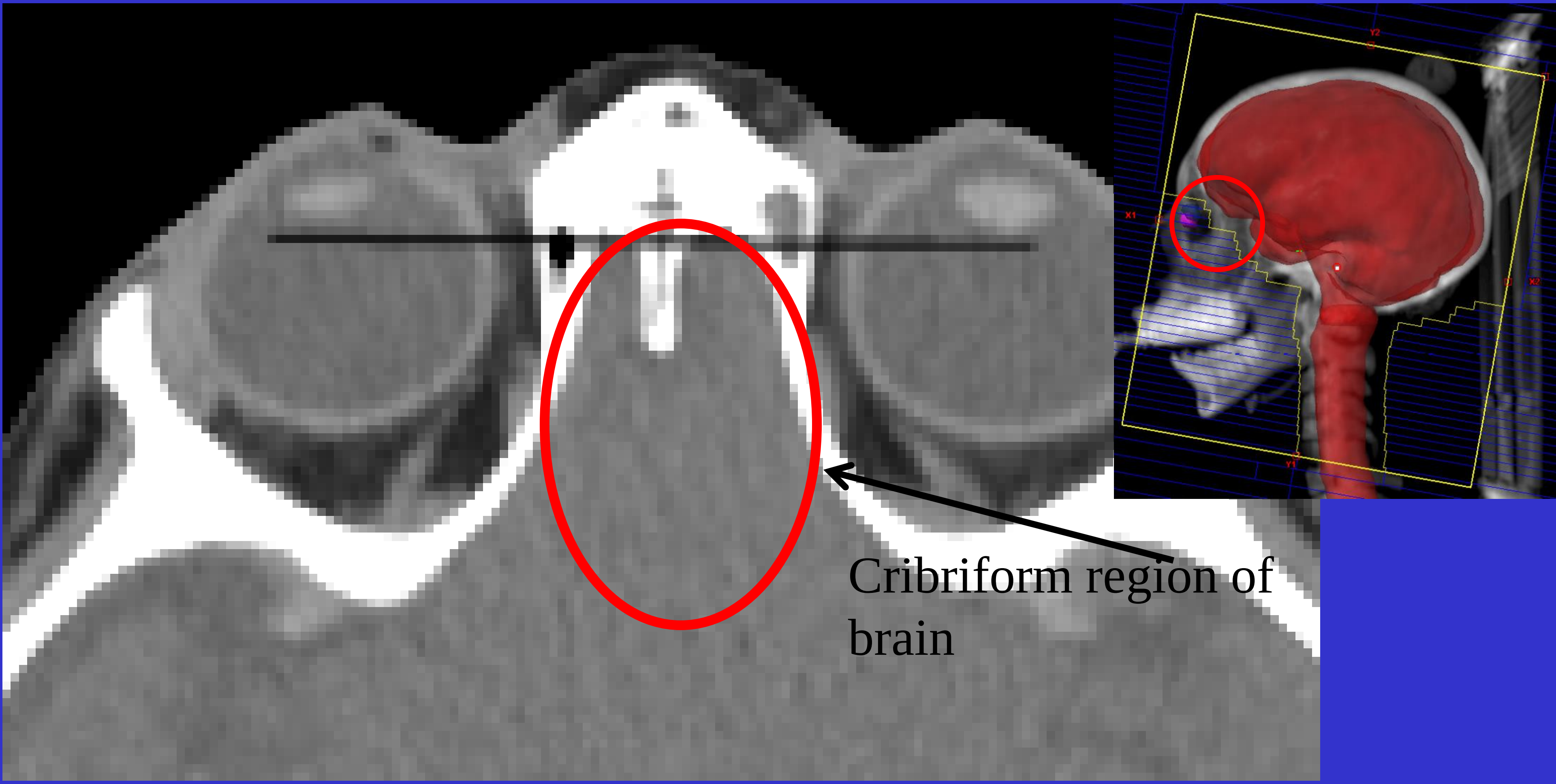
Medical Dosimetry, Vol. 28, No. 1, pp. 35–38, 2003

Need Abutted Spine Fields or Ext SSD for Bigger Kids

(can use 90 deg couch + gantry rotation to avoid divergence)

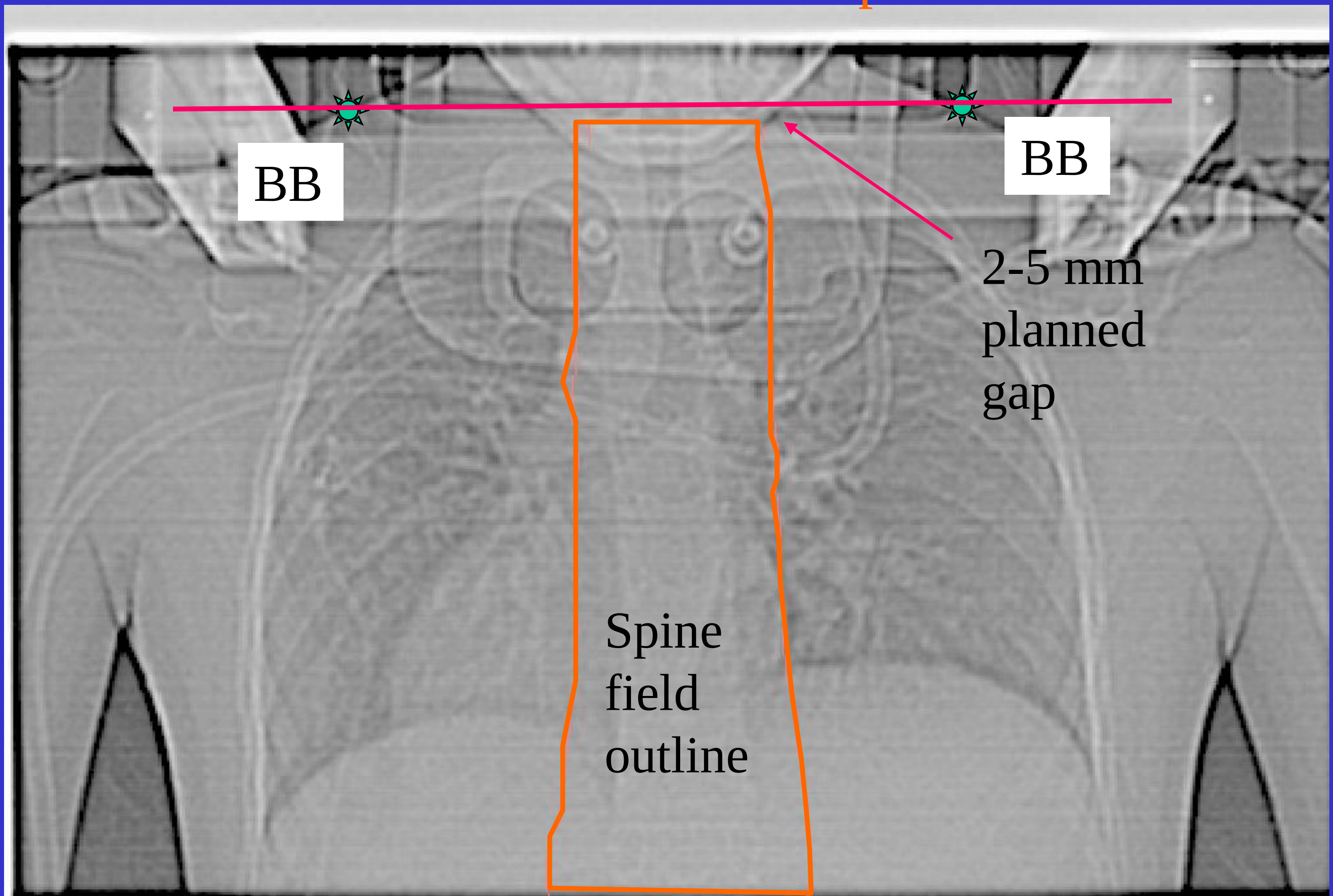


Spare lenses But Don’t Block the Cribriform Plate Region

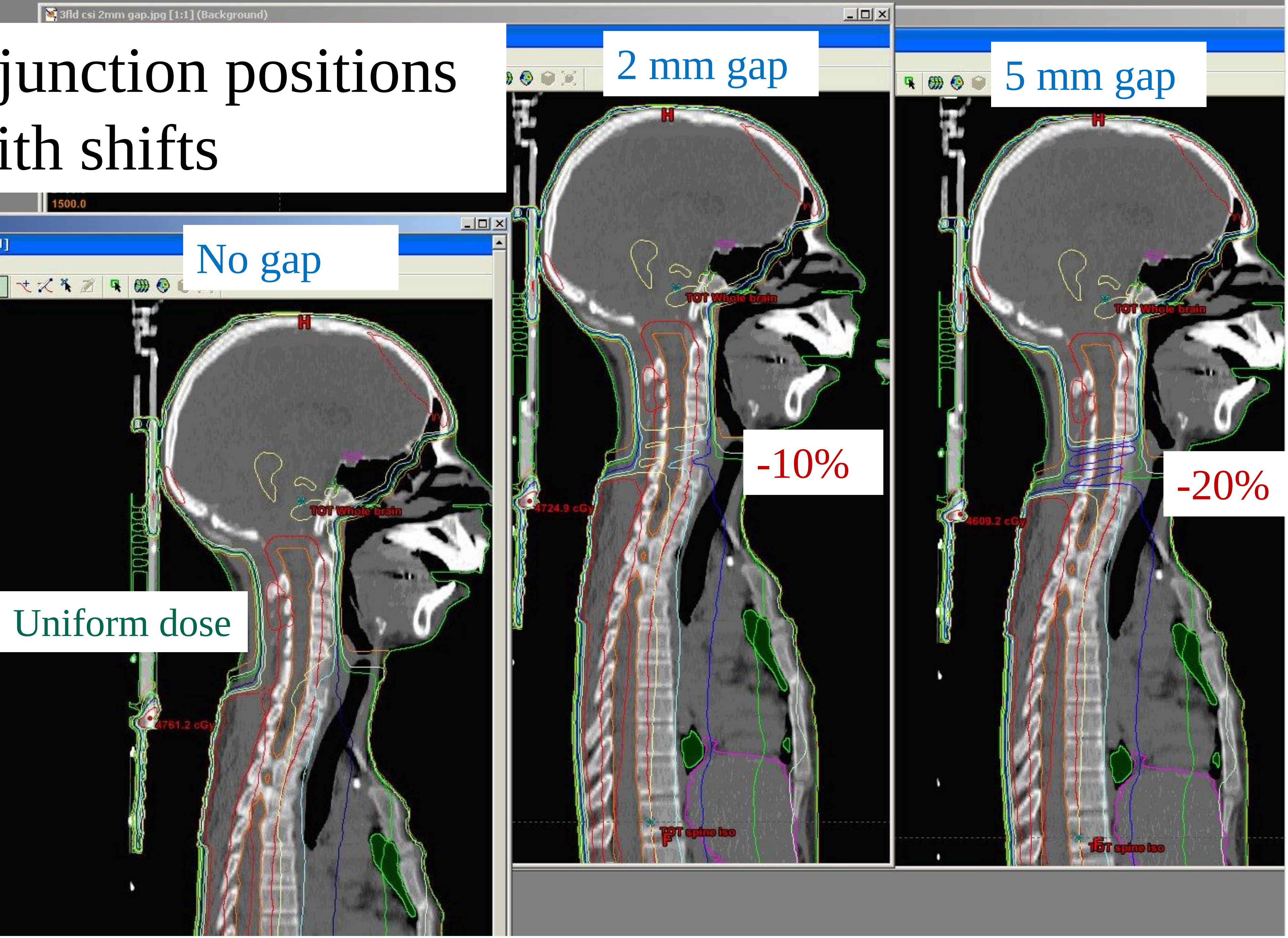


Verification of Brain/Spine Junction for Supine Position

as Seen From PA Spine Field

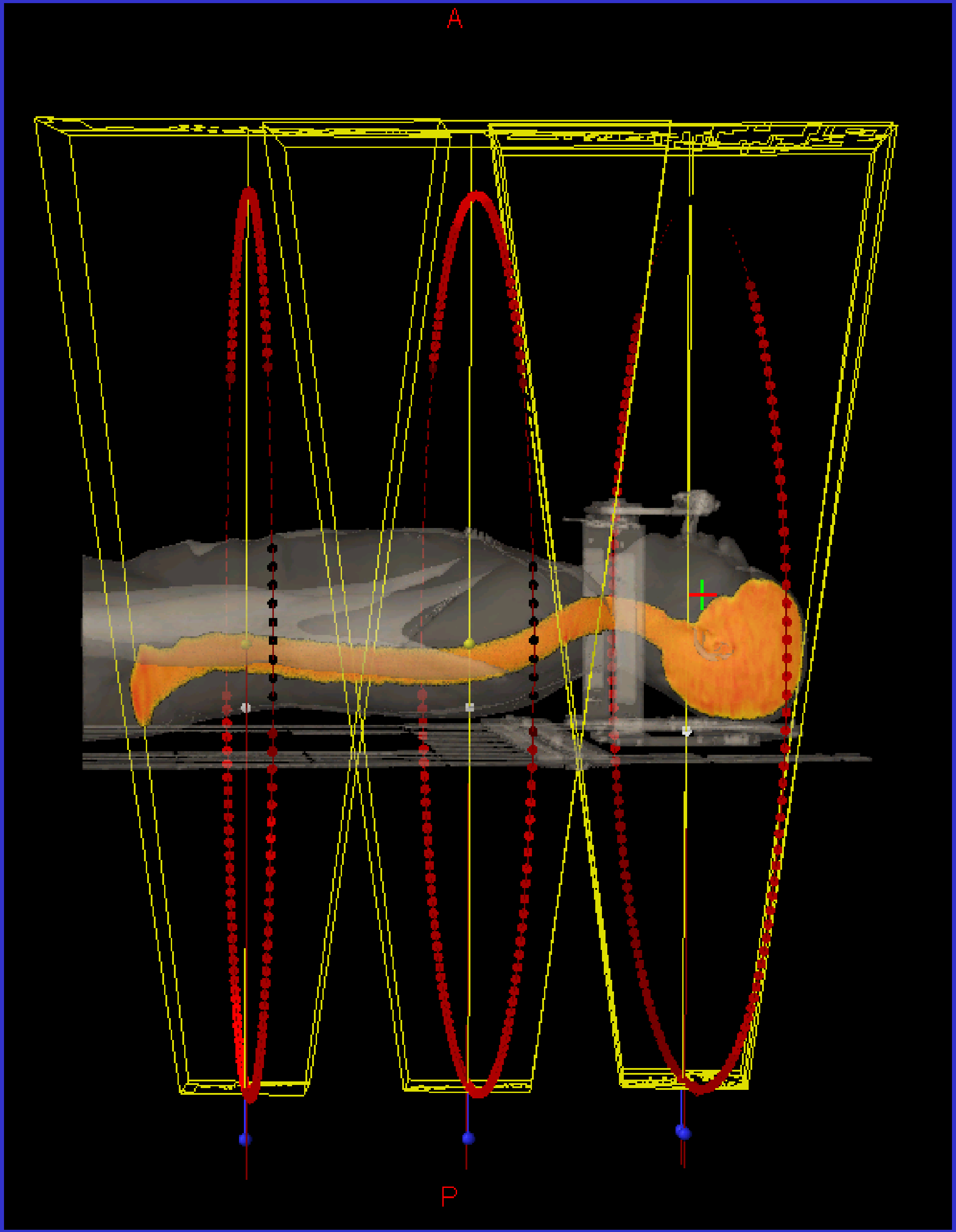


junction positions
ith shifts

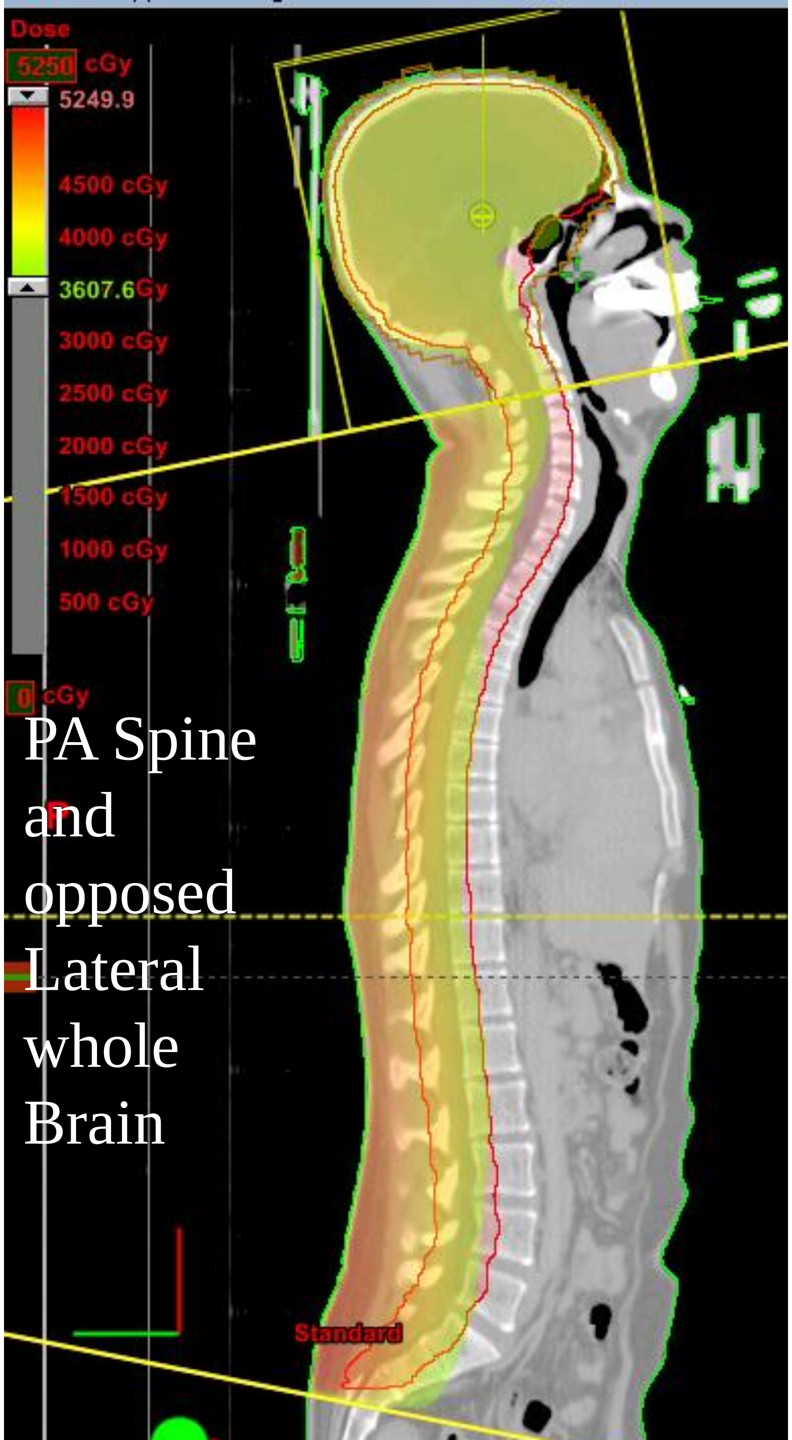


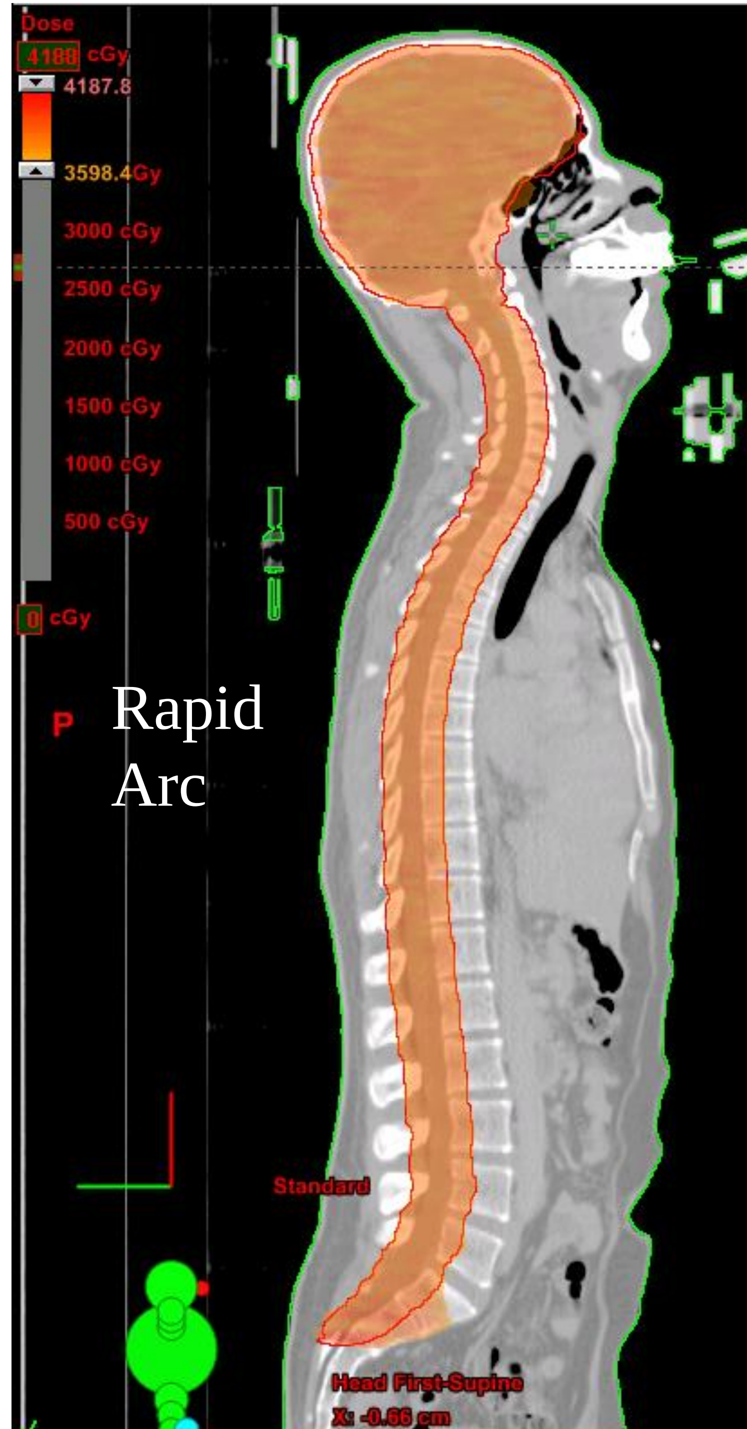
Dosimetry Conventional Opposed Lateral Whole Brain Plus PA Spine

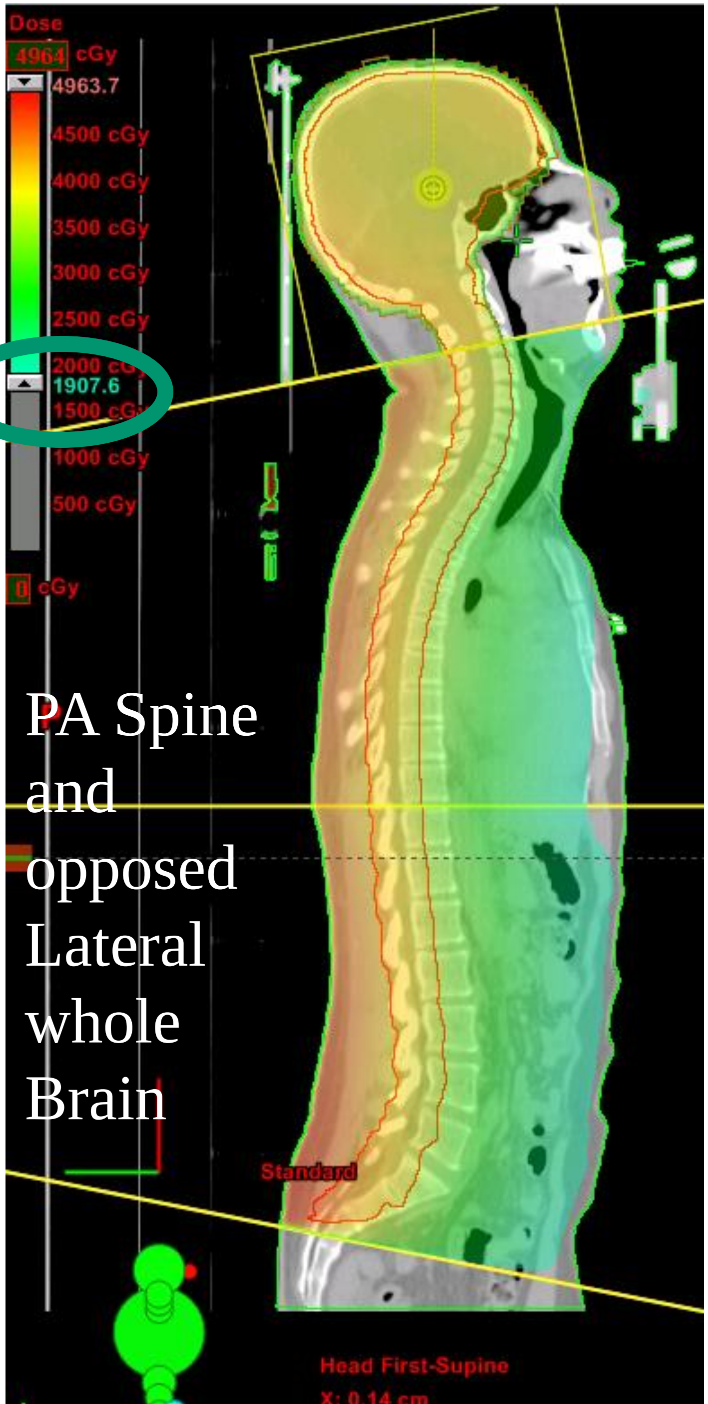
VMAT (Rapid Arc) for Cranial Spinal Irradiation

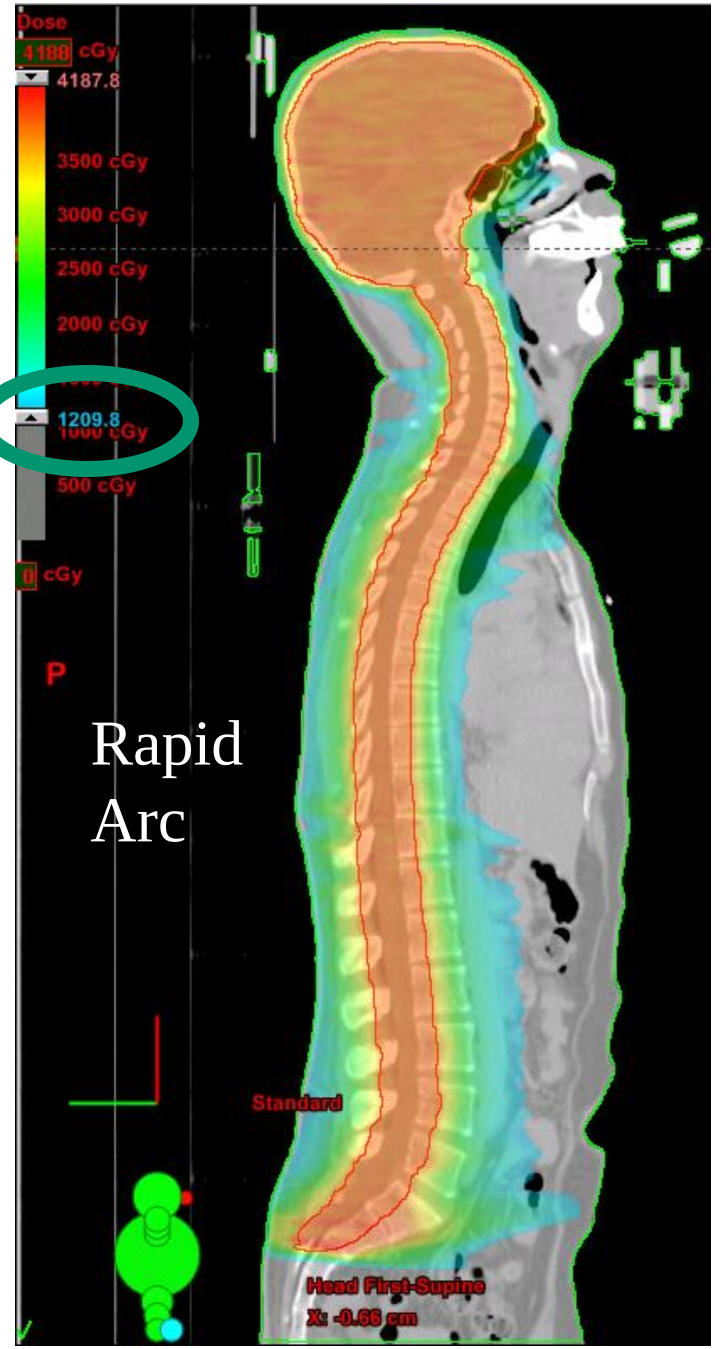


CSI 36 Gy


Dose
5250 cGy
5249.9
4500 cGy
4000 cGy
3607.6Gy
3000 cGy
2500 cGy
2000 cGy
1500 cGy
1000 cGy
500 cGy
0 cGy
PA Spine and opposed Lateral whole Brain
Standard

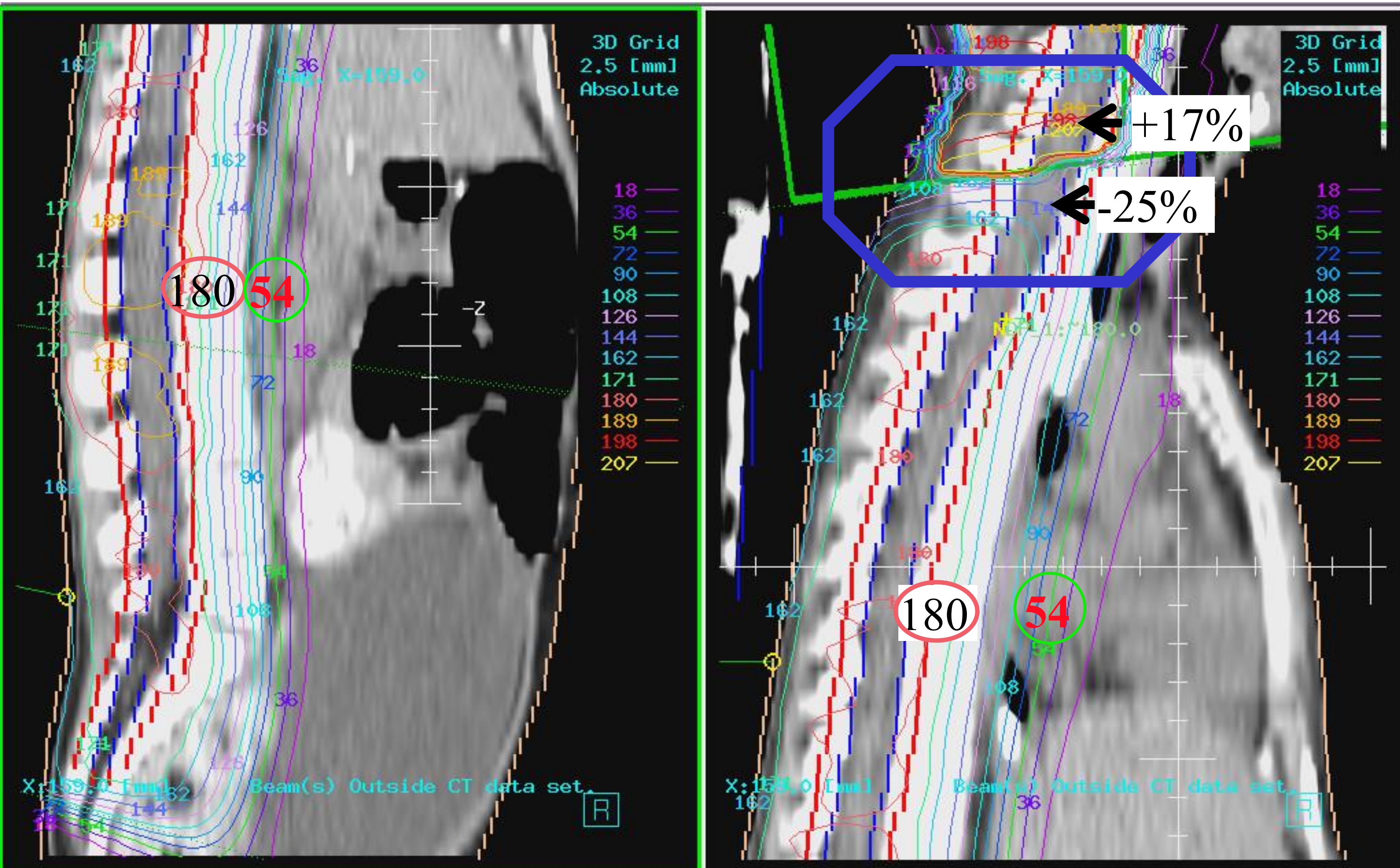

Dose
4188 cGy
4187.8
3598.4Gy
3000 cGy
2500 cGy
2000 cGy
1500 cGy
1000 cGy
500 cGy
0 cGy
P
Rapid Arc
Standard
Head First-Supine
X: -0.66 cm


Dose
4964 cGy
4963.7
4500 cGy
4000 cGy
3500 cGy
3000 cGy
2500 cGy
1907.6
1500 cGy
1000 cGy
500 cGy
0 cGy
PA Spine and opposed Lateral whole Brain
Standard
Head First-Supine
X: 0.14 cm


Dose
4188 cGy
4187.8
3500 cGy
3000 cGy
2500 cGy
2000 cGy
1209.8
1000 cGy
500 cGy
0 cGy
P
Rapid Arc
Standard
Head First-Supine
X: -0.66 cm

16 MeV PA Electron Beam Spine Field

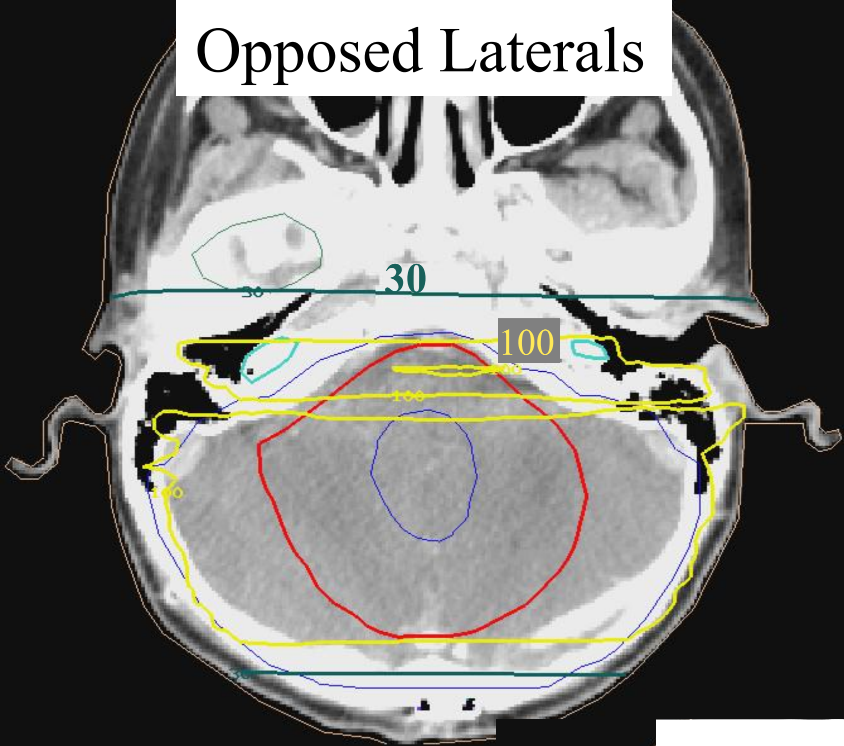
***Requires Patient to be Prone, 2 spine flds ***

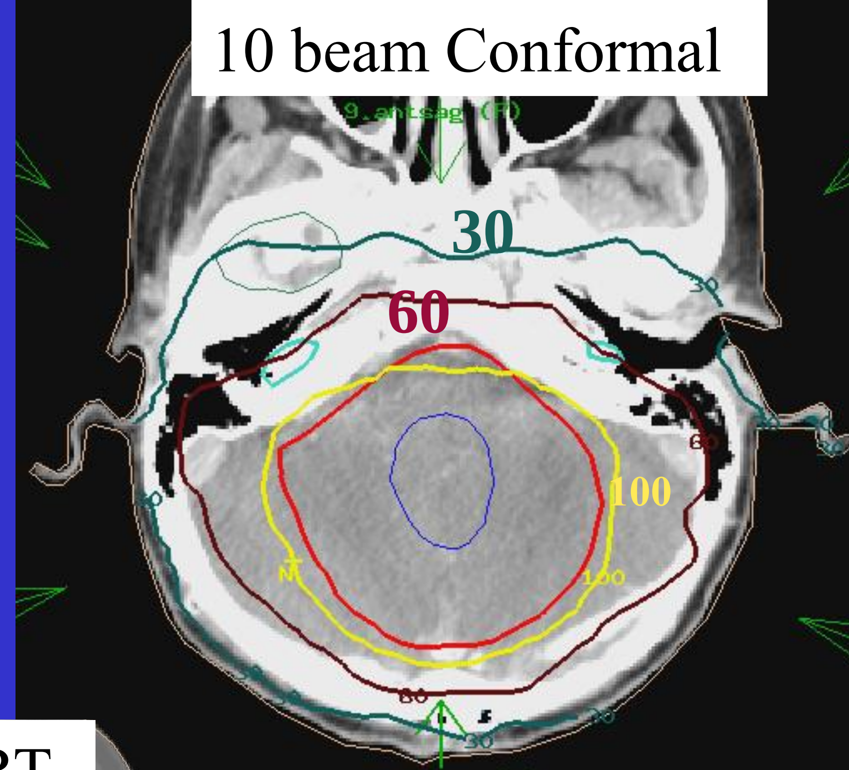


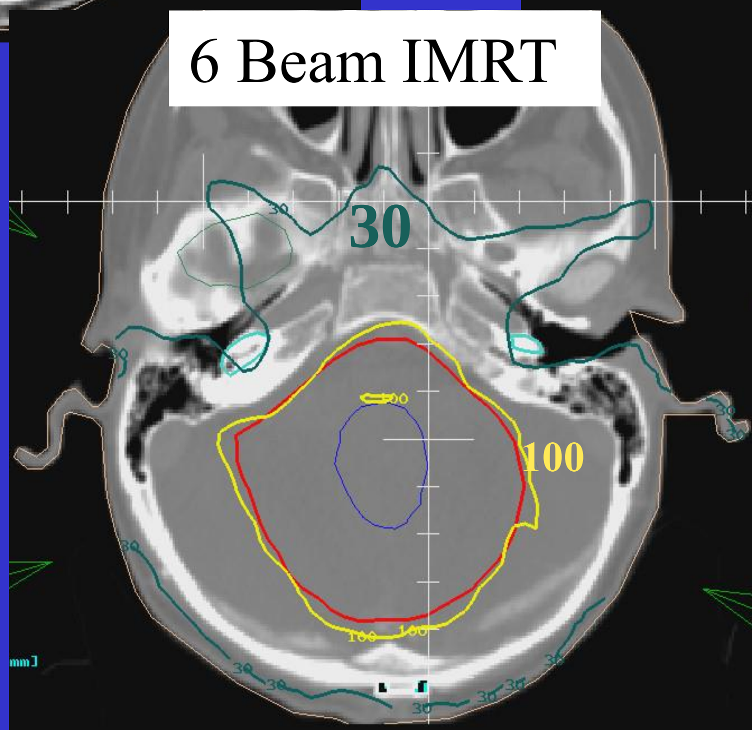
Head to Foot Immobilization

Changing the Boost Treatment for Medulloblastoma

- Reduce severe cognitive and hearing losses associated with this treatment.
- Testing whether reducing the boost volume and dose (for less than 8 y.o.) to just the surgical bed + margin (vs. whole posterior fossa) will change recurrence and morbidity patterns.







Plan comparison for limited volume boost

Q2: Regarding CSI for Medulloblastoma, which is **TRUE**:

20%	1. a common method of treatment is opposed lateral brain fields with couch angles, and a electron field
20%	2. The main concern is protecting the lenses to reduce the risk of catarac
20%	3. a major concern is not overdosing the spinal cord at the junction of brain and spin fields
20%	4. using a 5 mm gap for the junction with three junction shifts produces a very unifo dose across the junction.
20%	5. Prone is preferred over supine because one cannot verify the junction if supine.

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The correct answer is:

- Answer: c – not overdosing the spinal cord

- Ref: The cranial-spinal junction in medulloblastoma: Does it matter? Int. J. Radiation Oncology Biol. Phys., Vol. 44, No. 1, pp. 81–84, 1999.

Treatment of Acute Lymphoblastic Leukemia (A.L.L.)

also A.M.L. and some other diseases

- Most common childhood cancer – 3000 new cases per year.
- Not usually a Radiotherapy disease
- Total Body Radiation (12-13.5 Gy, 1.5-2 Gy BID = lethal dose without bone marrow transplant that follows)

TBI Dosimetric Issues

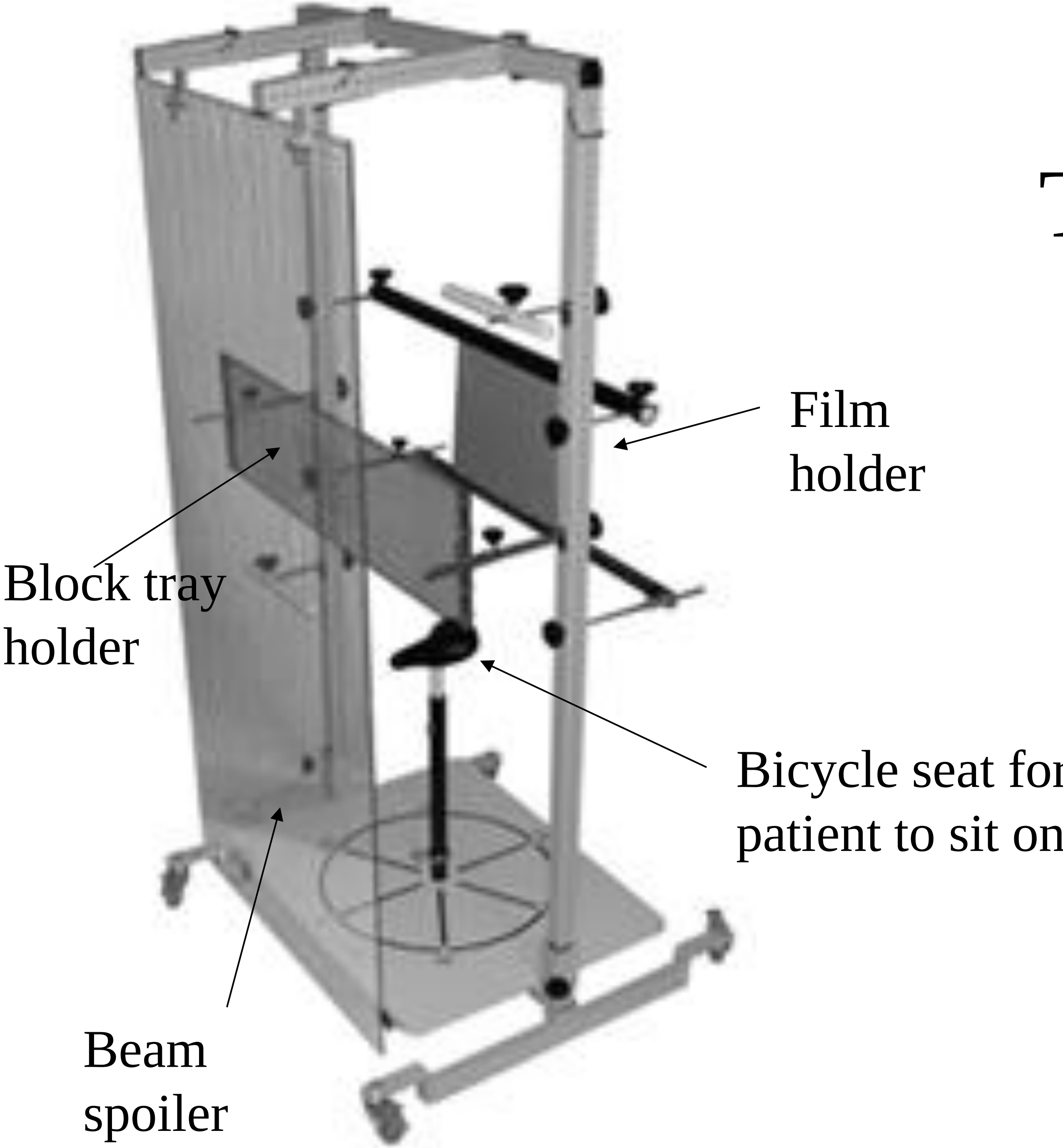
- Treatment method driven by **lung dose**, kidney and brain dose
  - AP/PA
    - **Pros:** Provides better dose homogeneity due to smaller thickness differences across body. lung blocking feasible.
    - **Cons:** Patient required to stand, lung blocks hung on external tray, or lay decubitus.
  - Opposed Lats
    - **Pros:** Patient can lay supine on gurney, lung compensation with arms or external material
    - **Cons:** Larger dose inhomogeneity, more compensation needed. Lung dose much below tumor dose is not feasible.

Other Features

- Beam spoiler typically used to bring full dose to skin surface
- Dose rate kept $\leq$ 10 cGy/min at patient midplane
- Goal is dose uniformity within 10%
- SSD > 3m needed

Total Body Irradiation for Leukemia

TBI stand

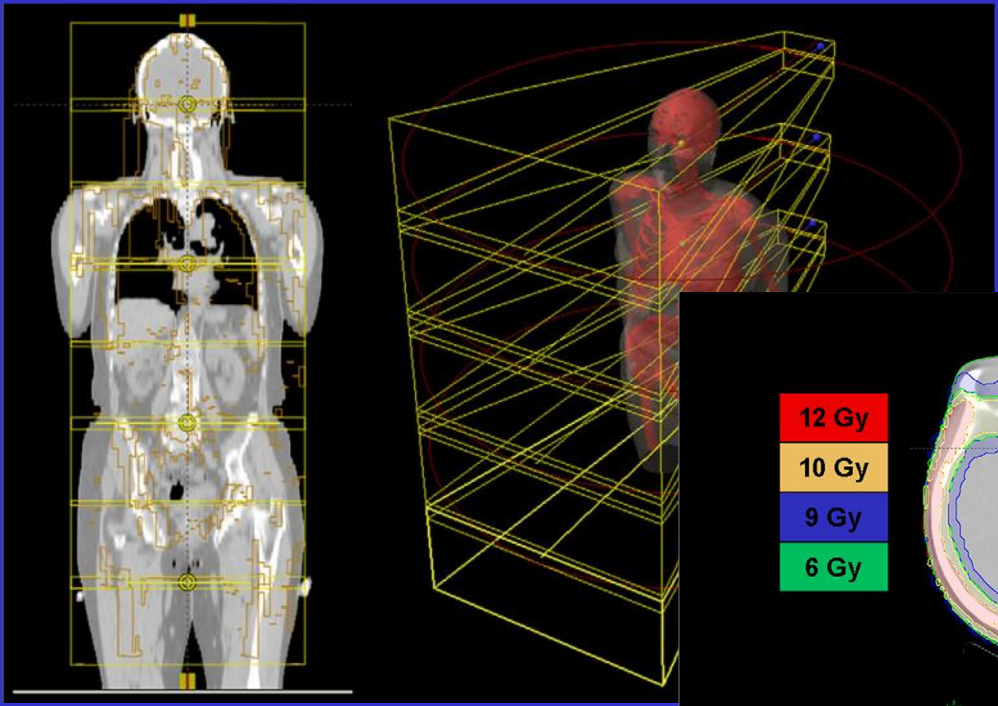


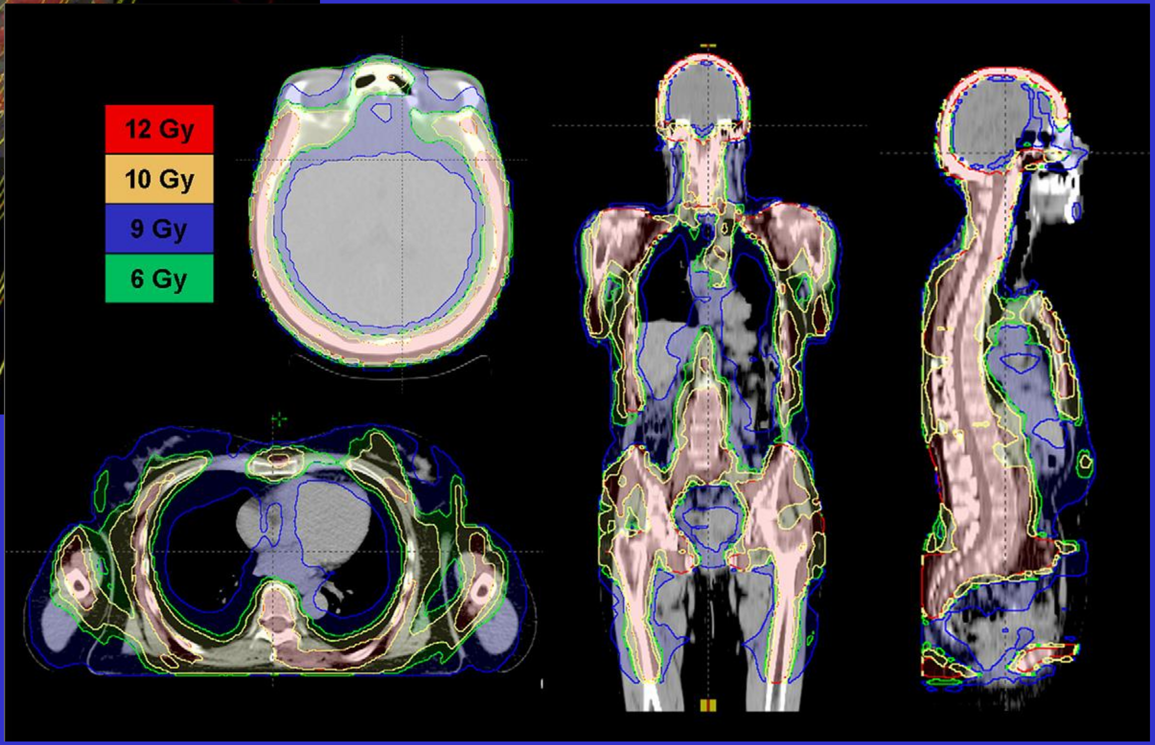
Not practical for children less than about 8 y.o. or for any sedated child

Physics Measurement for Commissioning and Calibration

- Setup a phantom system which simulates patient and treatment geometry
- Measure central axis PDD and OPFs, & output. 30x30x30 cm calibration phantom suitable, make corrections for **smaller** irradiated area for patient treatment
- Measure off axis ratios-across diagonal of 40x40 field, function of depth. Note differential beam hardening.
- In-vivo dosimetry system, TLD, OSLD, diodes, Mosfets, to verify patient dose.
  - Entrance and exit dose used to calculate midline dose
  - See AAPM reports #17 and #87

Total Marrow Irradiation with VMAT





Folgliata, IntJRadOncBiolPhys 2011

Q3: Acute Lymphoblastic Leukemia (ALL) is infrequently treated by radiation therapy but when it is, which is **NOT** a key consideration for total body irradiation:

20%	1. APPA vs Opposed Laterals
20%	2. Methods to homogenize the dose
20%	3. Patient position reproducibility
20%	4. Minimizing extremity dose
20%	5. Minimizing lung dose

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The correct answer is:

- Answer: d - Extremity dose

- Ref: AAPM report 17: The physical aspects of Total and half body photon irradiation, 1986

Summary

- Children get different cancers than adults.
- Treating children with radiotherapy is more challenging than adults.
- One must be aware of the different tolerance doses and increased risk for SM
- Medulloblastoma (CSI) and TBI (ALL) are common complex treatments.
- Most other cases are complex as well.
- Many children will be on a clinical trial requiring physics support.

- And now, Dr. Hua