Total body Irradiation (TBI) and Craniospinal Irradiation (CSI)

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Overview

- **TBI**
  - Purpose of TBI
  - Current practice
  - Toxicities with current practice
  - COG recommendations and Initiatives
  - A little bit about TMI –pros and cons
- **CSI**
  - Purpose of CSI
  - Current practice
  - Issue with current practice
  - A little bit about VMAT CSI –pros and cons

Total Body Irradiation

- A conditioning regimen for patients with acute myeloid leukemia (AML) and acute lymphoid leukemia (ALL) undergoing hematopoietic stem cell transplant (HCT).
- Purpose :

  (i) Myeloablation –elimination of clonogenic malignant cells

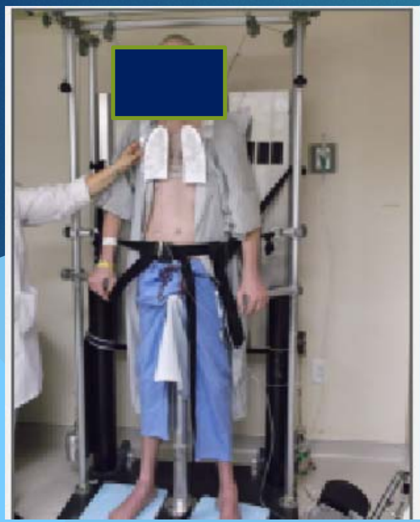
  (ii) immuno-supression

Typical fractionation

- **High dose –myeloablation/immunosupression**
  - **12 Gy (2 Gy per fraction BID)**
  - **12-13.5 Gy (1.5 Gy per fraction BID)**
  - **12-13.2 Gy (1.2 Gy per fraction 3x daily)**
  - **12 Gy (3 Gy per fraction, daily)**
- **Low dose –immunosuppression**
  - **2 Gy single fraction**

TBI treatment positions

AP/PA-standing/floor, decubitis



Lateral

Toxicity with current TBI - acute

- Most common acute toxic effect - radiation induced interstitial pneumonitis
  - Single large fraction (8- 10 Gy) – 50% incidence – fatal in 50% of these cases.
  - Fractionation – 25% incidence
- Other acute effects- parotitis, dry mouth and mucocitis, nausea and vomiting, diarrhea, fatigue, decreased appetite, erythema, esophagitis and alopecia.

Wong JYC, Filippi AR, Dabaja BS, Yahalom J, Specht L. Total Body Irradiation: Guidelines from the International Lymphoma Radiation Oncology Group (ILROG). Int J Radiat Oncol Biol Phys. 2018 Jul 1;101(3):521-529.

Toxicity with current TBI – late effect

- Long term toxicity resulting from irradiation of entire organ
  - Cataracts – 30-40% (with fractionated high dose TBI)
  - Gonadal failure
  - Thyroid and kidney dysfunction
  - Multiple endocrine disorder - children are at higher risk
  - Survivors of TBI – development of cardiometabolic traits, secondary cancers (3-7 % in 15 years).
  - **Age of receipt of TBI (<30 year), incidence of secondary cancer 67% higher that patients who received chemo alone –Han C – 2017 .**
  - Another study (Socie, 2000) of second cancers identified that age < 5 years was the most important risk factor for the development of secondary cancer.

- Wong JYC, Filippi AR, Dabaja BS, Yahalom J, Specht L. Total Body Irradiation: Guidelines from the International Lymphoma Radiation Oncology Group (ILROG). Int J Radiat Oncol Biol Phys. 2018 Jul 1;101(3):521-529.
- Han C, Wong J, Schultheiss T. Comparison of radiation-induced secondary cancer occurrence rates for major organs between total body irradiation and total marrow irradiation (abstract 3413). Int J Radiat Oncol Biol Phys 2017;99(Suppl 2):E594
- Socie ´ G, Curtis RE, Deeg HJ, et al. New malignant diseases after allogeneic marrow transplantation for childhood acute leukemia. J Clin Oncol 2000;18:348-357

Can we reduce toxicity?

COG initiative – examine relationship between lung radiation dose in TBI and survival

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Clinical Investigation

Higher Reported Lung Dose Received During Total Body Irradiation for Allogeneic Hematopoietic Stem Cell Transplantation in Children With Acute Lymphoblastic Leukemia Is Associated With Inferior Survival: A Report from the Children's Oncology Group

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Conclusions of above study

- Variability in TBI technique resulted in uncertainty with reported lung dose.
- Variability in reporting lung dose
- Patients treated with lung dose <8 Gy had better outcome.

Need to address variability, especially in reporting of doses.

Formation of COG TBI physics workgroup – mid 2018

Goal:

- **Review current techniques and dose reporting**
- **Provide guidelines on methods of TBI and dose reporting**

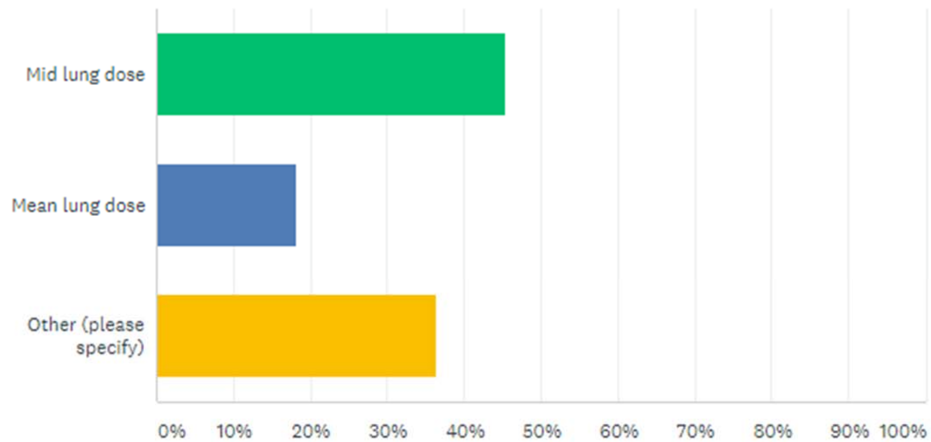
Preliminary result of survey – a glimpse of 10 institutions (TBI group members)

- Children's Hospital Los Angeles
- City of Hope Medical Center
- Cleveland clinic
- Huntsman Cancer institute, University of Utah
- Memorial Sloan Kettering Cancer Center
- Northwestern memorial hospital
- Oregon Health & Science University, Portland,OR
- Princess Margaret Cancer Center
- Stanford Medical Center
- St. Jude Children's Research Hospital

Variability in lung dose specification

How is the lung dose specified?

Answered: 11 Skipped: 2

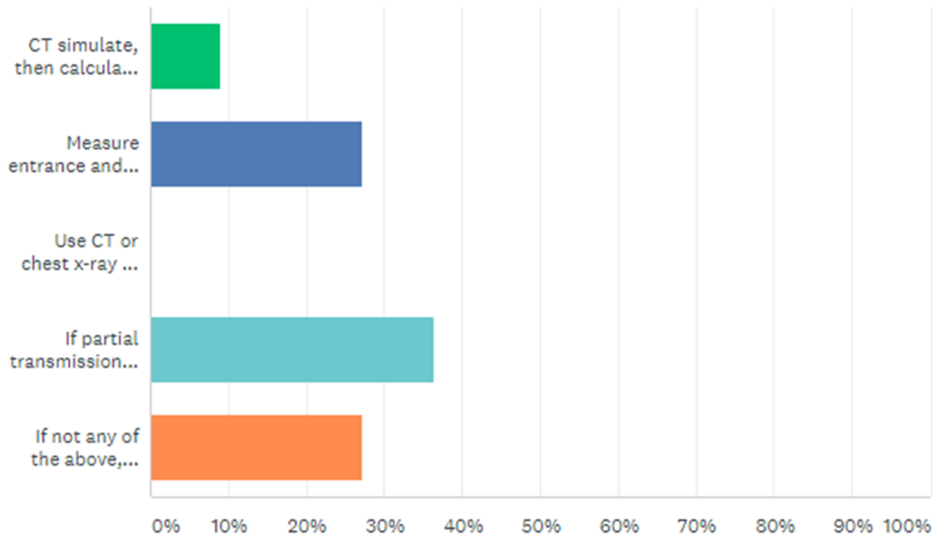


ANSWER CHOICES		RESPONSES	
Mid lung dose		45.45%	5
Mean lung dose		18.18%	2
Other (please specify)	Responses	36.36%	4

Variability in lung dose determination

How is the lung dose most commonly determined?

Answered: 11 Skipped: 2



ANSWER CHOICES	RESPONSES	
CT simulate, then calculate mid and/or mean lung doses	9.09%	1
Measure entrance and exit dose, then average with or without correction factor to get mid lung dose	27.27%	3
Use CT or chest x-ray to correct depth to midline for lung density to obtain mid lung dose	0.00%	0
If partial transmission is used, multiply percent transmission and prescribed dose (with or without other correction factors) to obtain mid lung dose	36.36%	4
If not any of the above, describe your method of calculating mid lung dose Responses	27.27%	3

Total Marrow Irradiation – a method to reduce toxicity?

- Benefits of Total marrow Irradiation
  - Normal tissue sparing
  - Lung dose 50% of conventional dose
  - Patient on couch – no fall risk

Fig. 2. RapidArc volumetric arc therapy total marrow irradiation isodose distributions in colorwash: (a) head and neck axial, (b) chest axial, (c) sagittal, and (d) coronal view. Dose range shown from 6 (blue) to 12 Gy (red).

Aydogan B, Yeginer M, Kavak GO, Fan J, Radosevich JA, Gwe-Ya K.
Int J Radiat Oncol Biol Phys. 2011 Oct 1;81(2):592-9. doi: 10.1016/j.ijrobp.2010.11.035. Epub 2011 Feb 23.

Current practices of VMAT TMI

Prescription	1.5 - 2.0 Gy per fraction/ BID
	12-15Gy total dose
Target volume	a. skeletal bones or
	b. skeletal bone, up to mid thigh major lymph nodes + spleen or
	c. whole body spare lung/kidney
Simulation	8 -10 mm axial scan
	total scan length limited to abt 160 cm, may need to flip pt to treat lower extremities.
	consider breathing motion -ribs, spleen, kidney
	immobilization device - whole body
Treatment planning	Contour ptv
	8 segments, 8-12 isocenters
	significantly more intensive than conventional TBI
QA	IMRT QA
Delivery	10-15mins beam on time
	Set up +verification 1 -2 hrs
	in vivo dose verification

Craniospinal irradiation

Craniospinal Irradiation

- Main reason for treatment : Medulloblastoma

  (most common brain lesion in children) 70-80 % affect children under 16 [1].

  - Tx : resection surgery followed by CSI irradiation, nearly 70% survival rates.

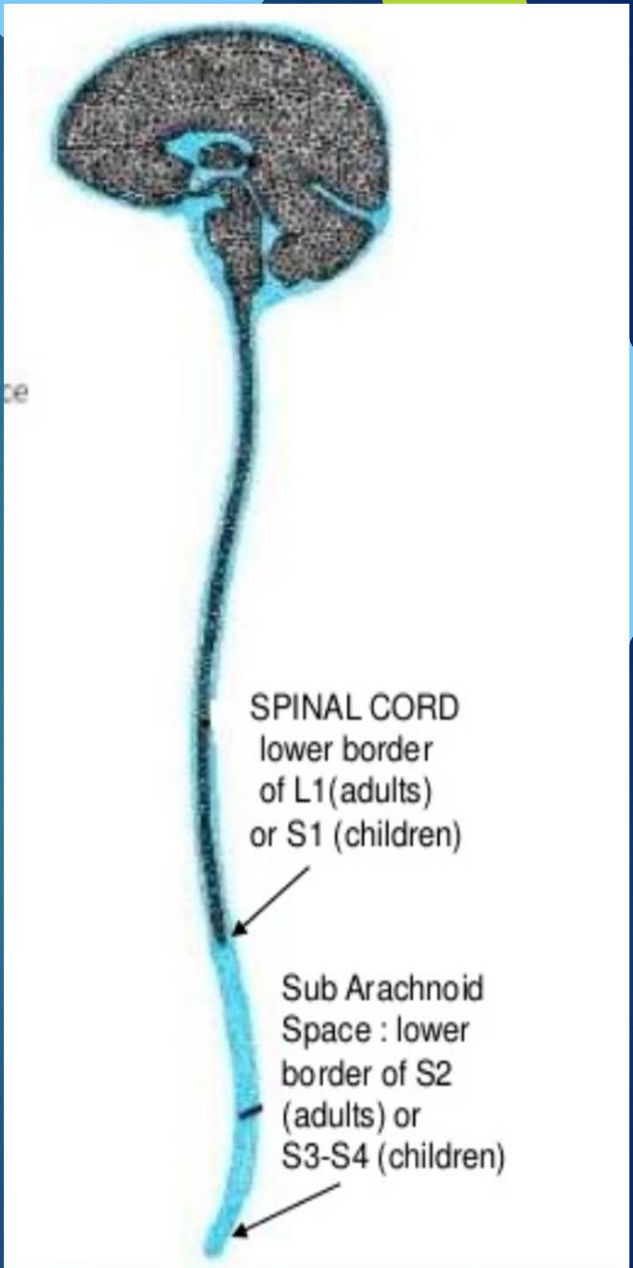
- Other reasons for CSI-

  - Anaplastic Ependynoma, Pineoblastoma, Germinoma, Supratentorial PNE

1 Taillandier L, Blonski M, Carrie C, et al. Les médulloblastomes: revue générale [Medulloblastomas: review]. *Rev Neurol*. 2011;167(5):431–448

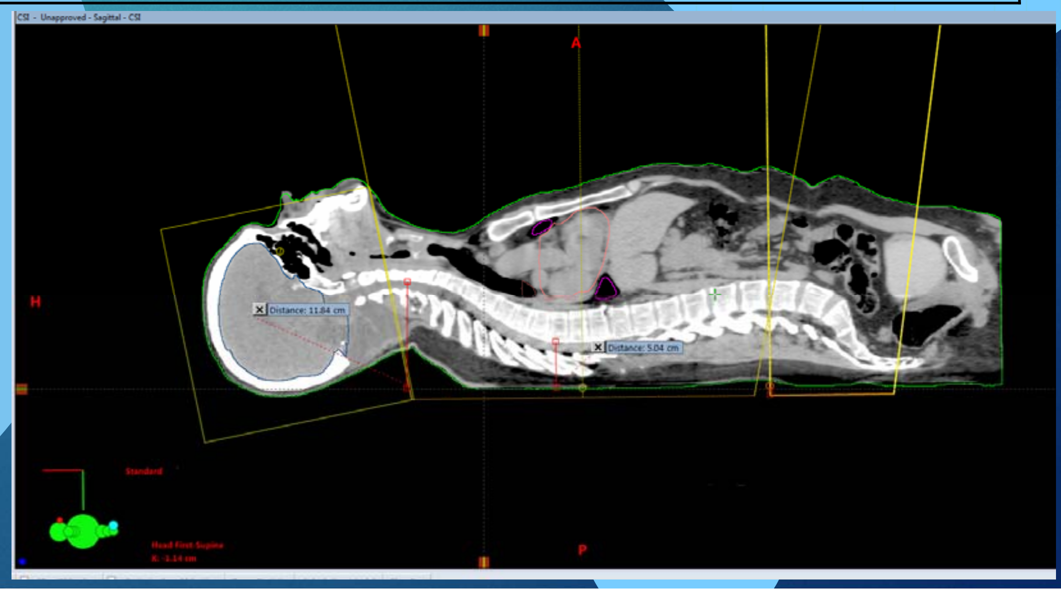
Goal

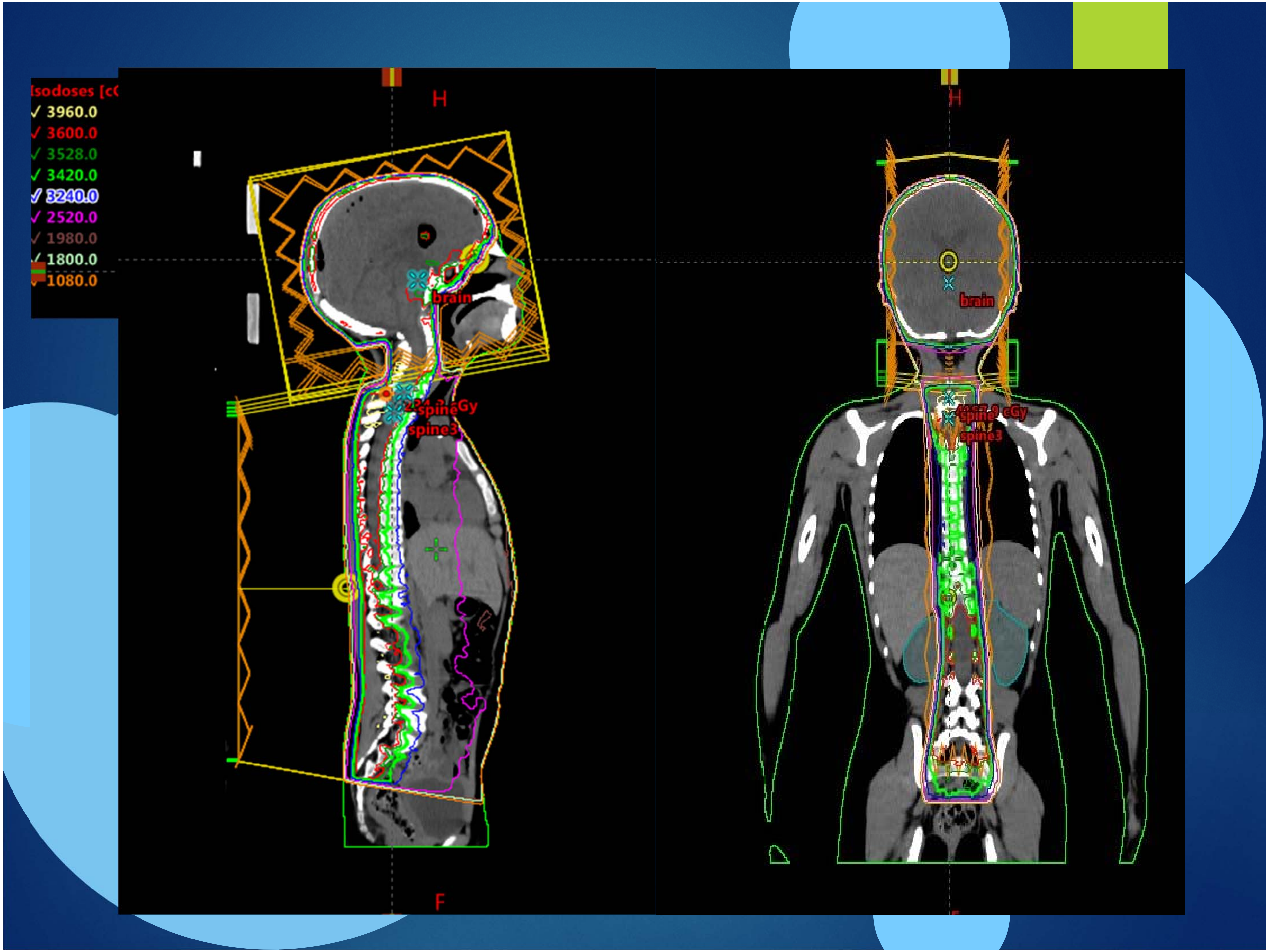
- To treat the entire CNS sub Arachnoid space, which encompasses the cranial vault and spinal canal (S3-4) children.
- Treatment is complicated because of the length of treatment area



Conventional treatment

Prescription	36 Gy (1.80 Gy x 20) to whole brain and spine Post fossa bst : to 54 Gy
Simulation	Extended neck (avoid spine field exiting through maxilla) Supine/prone (under anesthesia?) Scan whole spine
Planning	Lateral cranial fields and one or more spine fields. Match Cranio-spinal Junction (collimator rotation/couch kick) Feather junction every 5 fractions
Treatment delivery	Position, verity and treat. (20 -30 min slot)

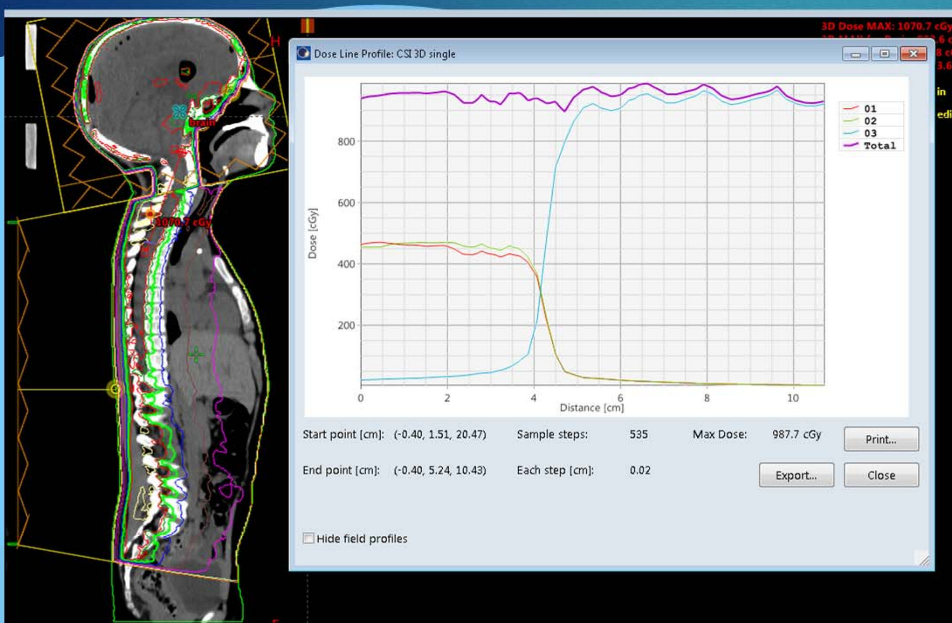


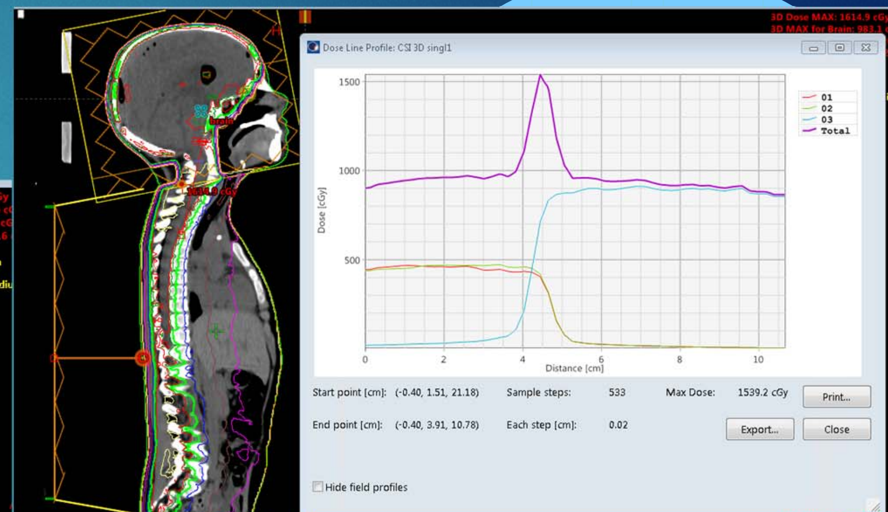

Isodoses [c
3960.0
3600.0
3528.0
3420.0
3240.0
2520.0
1980.0
1800.0
1080.0
H
brain
spine
spine3
F
H
brain
spine
cGy
spine3

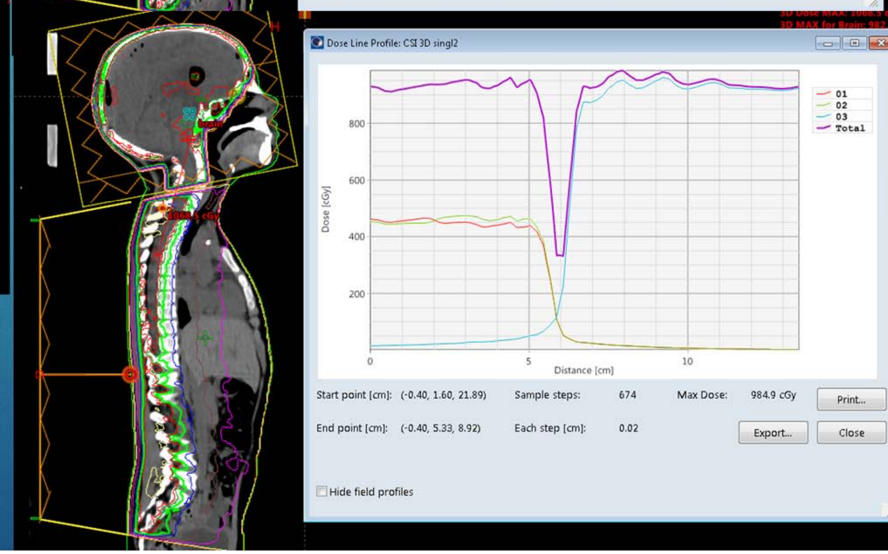
Cons in current practice

- Clinical - complications –
  - declined cognition
  - retarded growth
  - endocrine dysfunction,
  - hearing disability
  - cataract formation
  - secondary malignancy
- Technical – occurrence of hot and cold spots.
  - Can be reduced by feathering junction

Junction dose with conventional CSI







Question?

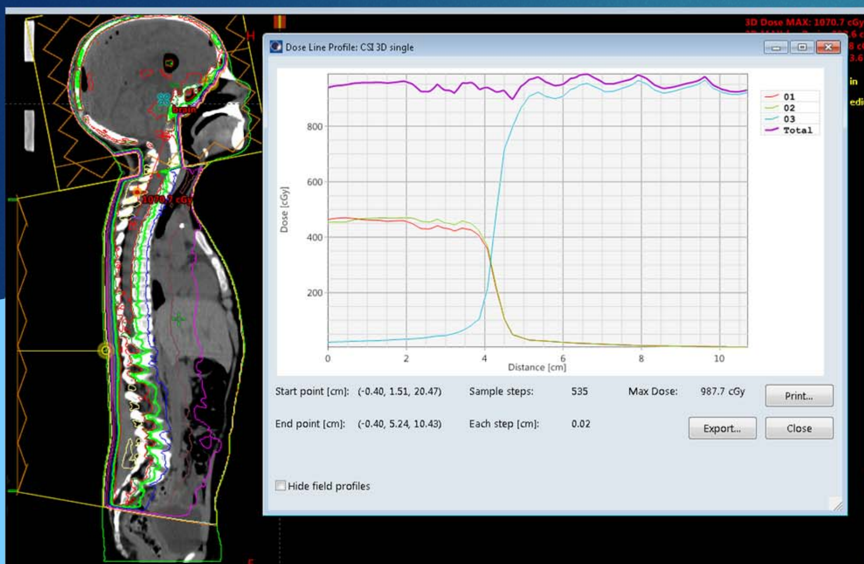
- Can we reduce complications?
- Do we have the technology/resources to do so?

Intensity modulated CSI (photons)

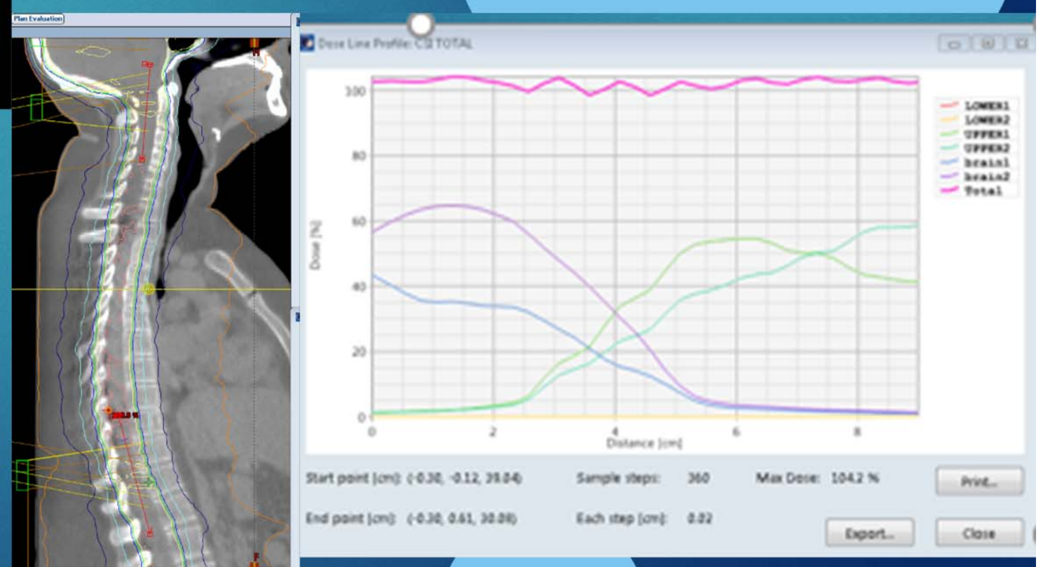
- Reduce clinical complication
  - A method to carve out doses to reduce organ at risk doses –
- Reduce technical complexity.
  - No need to match junctions with couch and collimator rotations
  - No need for feathering
  - Junction doses – more forgiving – less likely to produce hot or cold spots

Junction dose gradient

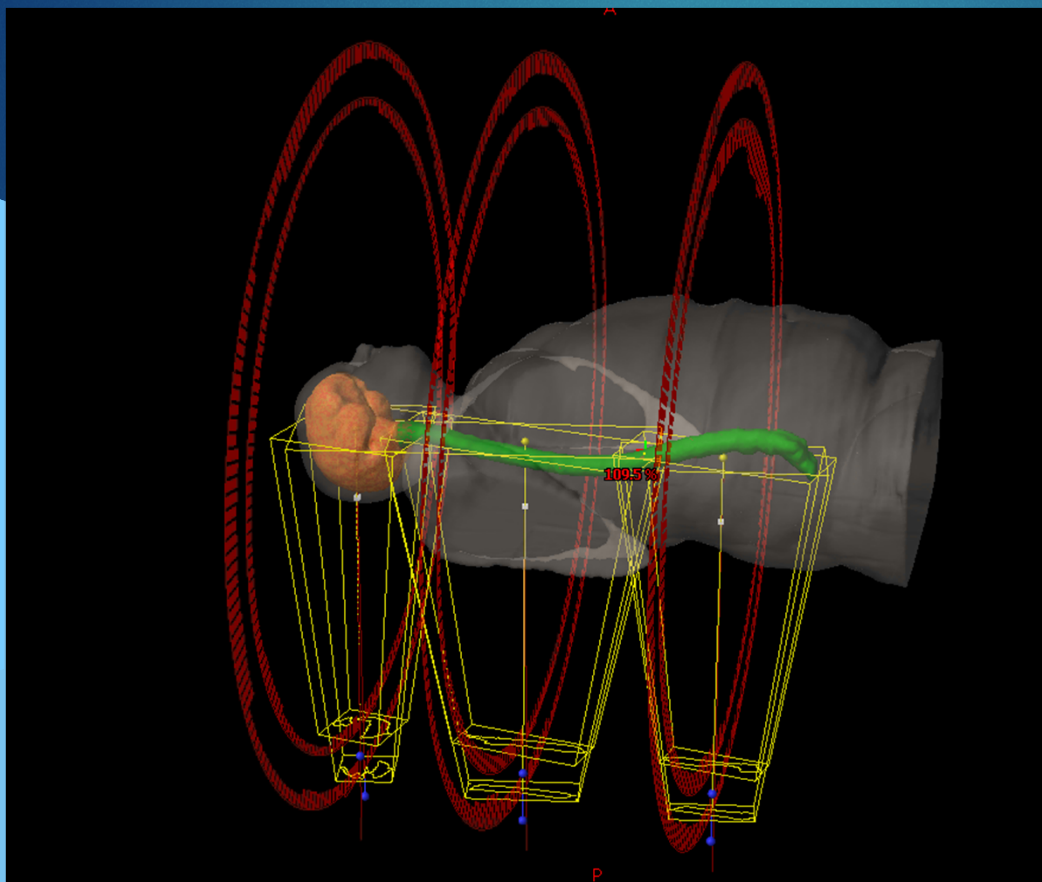
Conventional CSI

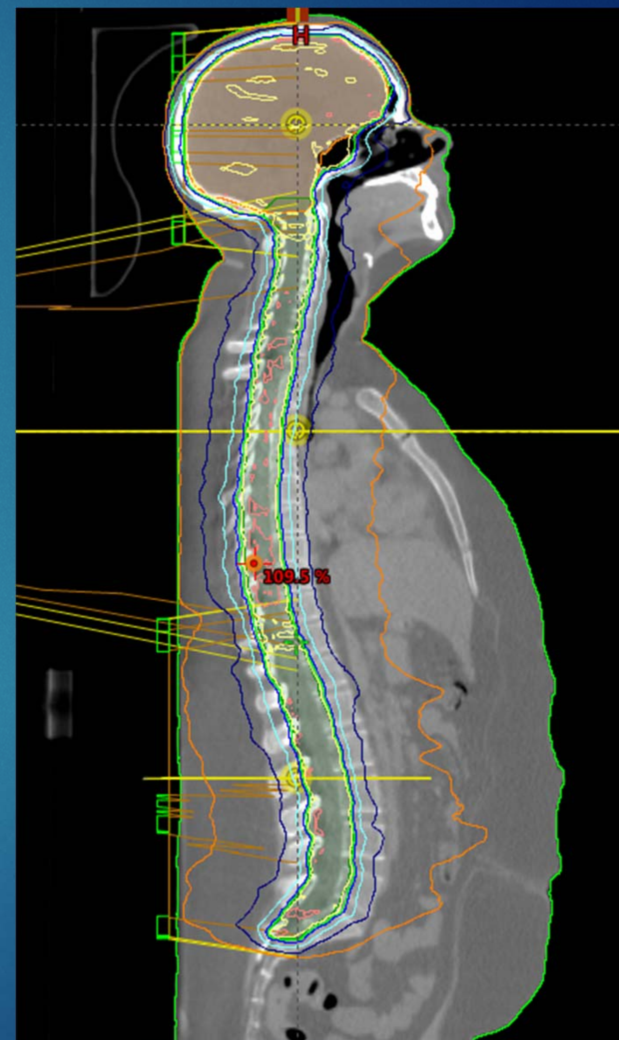


VMAT CSI



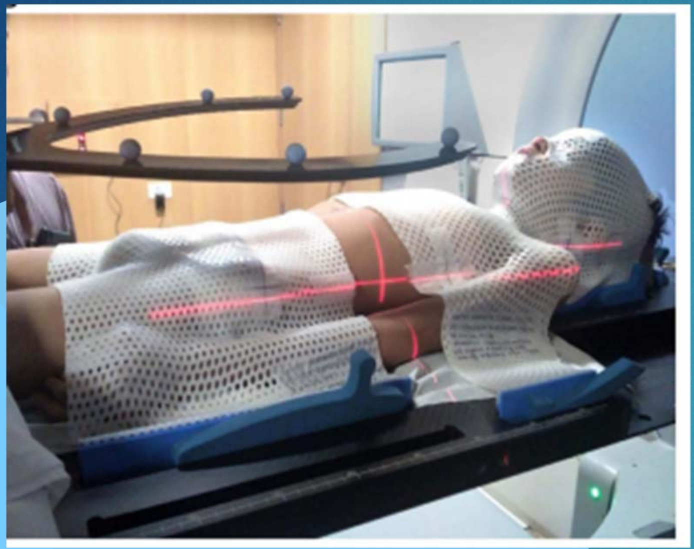
VMAT CSI plan





To address prior to embarking on IMRT CSI

- Simulation – Immobilization



- PTV Margin
  - Brain 3- 5 mm
  - Spine 5 – 10 mm

Dose goals

- Expect – more contouring

Structure:	Dose Goal:		
PTV_total	90% to 95%		
PTV_Spine	90% to 95%		
PTV_Brain	95% to 95%		
Eye_L	Dmax <	32 Gy	
Eye_R	Dmax <	32 Gy	
Lens_L	Dmax <	7 Gy	
Lens_R	Dmax <	7 Gy	
Optics+5mm	Dmax <	50 Gy	
Optics+3mm	Dmax <	50 Gy	
Chiasm	D50% <	54 Gy	
	D10% <	56 Gy	
Brainstem	Dmax <	95 Gy	
Hypothalamus	Mean dose <	41 Gy	Lower if achievable
Pituitary	Mean dose <	41 Gy	Lower if achievable
Cochlea	Mean dose <	45 Gy	Lower if achievable
Parotid_L	Mean	< 15Gy	
Parotid_R	Mean	< 15Gy	
OralCavity	V10 Gy <	20%	
OralCavity	V5 Gy <	50%	
Larynx	Mean	V15	
Thyroid	Mean dose <	15 Gy	
Total Lung	V10 Gy <	30%	
Total Lung	V5 Gy <	50%	
Heart	V7 Gy <	50%	Lower if achievable
Esophagus	Dmax <	37 Gy	
Liver	V10 Gy <	30%	
Kidney_L	V5 Gy <	25%	
Kidney_R	V5 Gy <	25%	
Breast Buds	Dmean <	2 Gy	
Testis	Dmean <	1.5 Gy	

- Pediatrics : attention to dose homogeneity to vertebrae

Protons

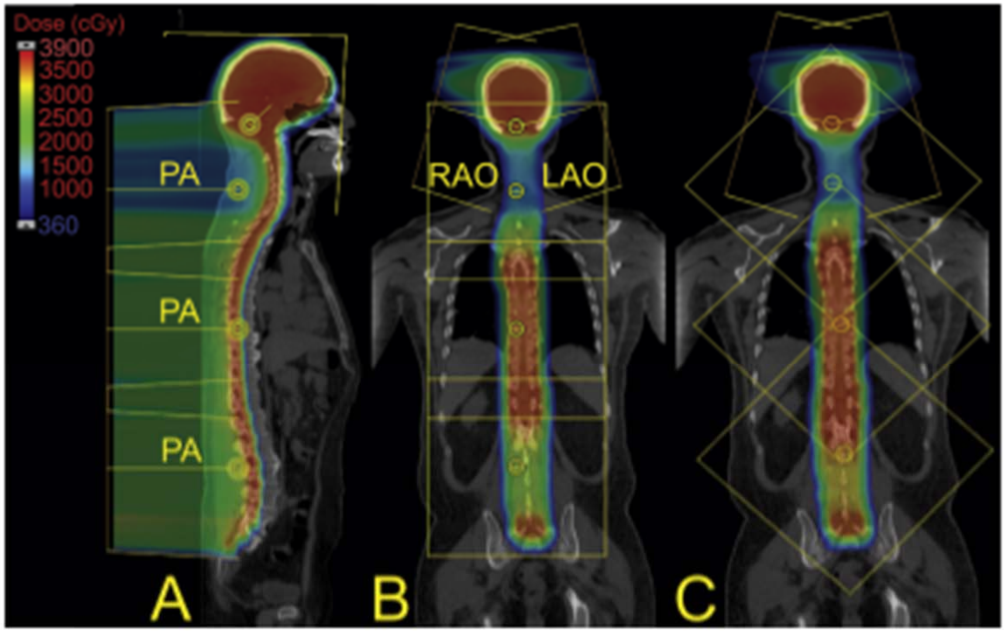


Fig. 1. (A) Sagittal view demonstrating placement of PA beams along the patient's spine. (B) Coronal view demonstrating placement and orientation of spine and cranial treatment fields. (C) Coronal view demonstrating PA beams with 45° couch rotation. LAO = left anterior oblique; PA = posterior-anterior; RAO = right anterior oblique.

- **Stoker JB**, Grant J, Zhu XR, Pidikiti R, Mahajan A, Grosshans DR.Int J Radiat Oncol Biol Phys. 2014 Nov 1;90(3):637-44. doi: 10.1016/j.ijrobp.2014.07.003. Epub 2014 Sep 3.

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- COG TBI physics team members

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Thank you!