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MEDULLOBLASTOMA - CONTEMPORARY MANAGEMENT AND RADIATION THERAPY PLANNING

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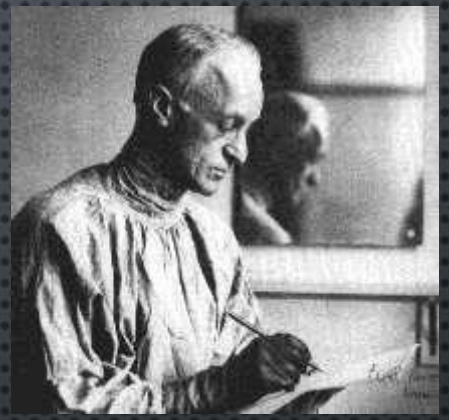
HISTORY

- *First described by Harvey Cushing and Percival Bailey*
- *At that time this tumor was described variously – sarcoma, neuroblastoma and neurocytoma.*
- *Initially described as "spongioblastoma cerebelli" - a soft, suckable tumor usually arising in the vermis of cerebellum*
- *In 1925, changed name to medulloblastoma – from "medulloblast" - a hypothetical multipotent cell*

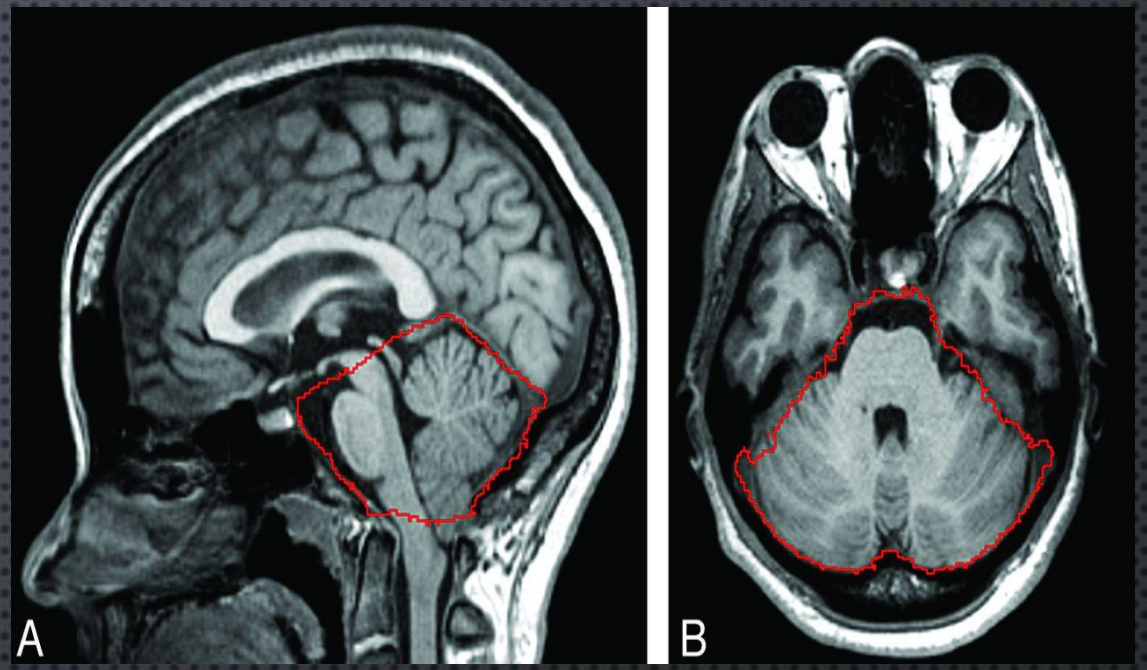


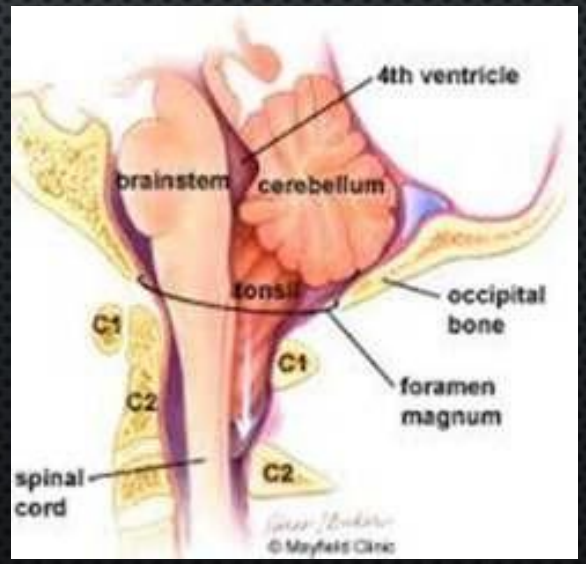
Harvey Cushing

Percival Bailey

POSTERIOR FOSSA TUMOURS

- Cerebellar Astrocytomas- mostly Pilocytic
- Brainstem Gliomas
- Embryonal tumors- Medulloblastoma (40%) & Atypical Teratoid/Rhabdoid Tumor(AT-RT)
- Ependymoma
- Choroid Plexus Tumors
- Rosette-forming glioneuronal tumors of IV ventricle





MEDULLOBLASTOMA

- 20-25% of brain tumors in children.
- Most common malignant brain tumour in children
- Median age:6 years (range 3-10 years); 20% at < 3years.
- Arises from either external granular layer / ventricular zone of cerebellum.
- CNS dissemination– 10%-40%
- Extra-cranial dissemination –lymph nodes, bone, bone marrow, lungs.
- Overall Survival-40-90%

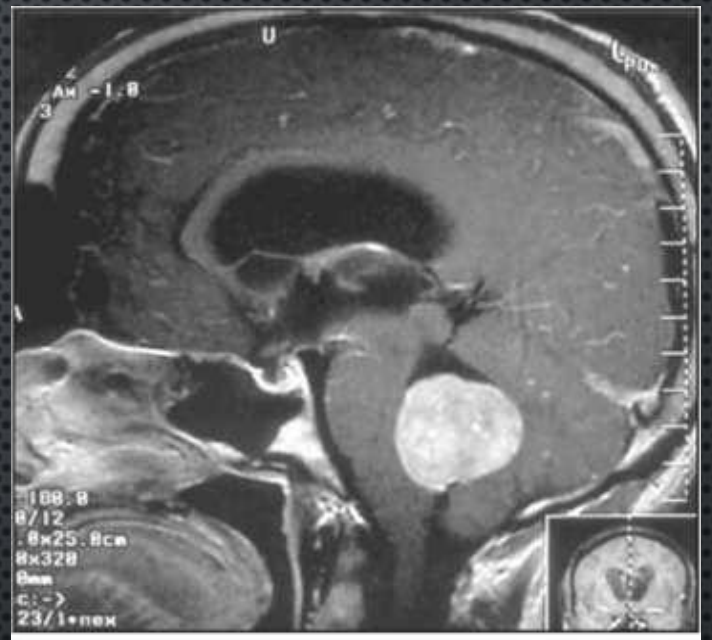


Fig 5. Sagittal T1 weighted MRI after contrast injection showing a midline cerebellar mass with posterior compression of the brain stem.

Etiology

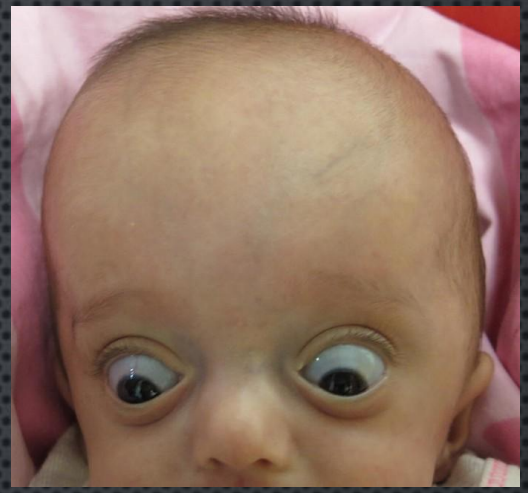
- Majority are sporadic
- Familial Cancer Syndromes (*< 7%*): Turcot's (*APC gene -WNT*), Gorlin's (*PTCH-SHH*), Li-Fraumani's (*TP53*), Rubinstein-Taybi syndromes, Fanconi's anemia.
- Loss of chromosome 17p occurs in 50%
- Inactivation of *HIC*-1 tumor suppressor gene by hypermethylation
- *Myc* amplification
- Over-expression of ErbB2
- Previous irradiation

DIAGNOSIS - CLINICAL

- 80-90% - obstructive hydrocephalus at presentation

  Headache & vomiting, papilloedema (60-80%),

  6th N palsy, large heads in infants – 'setting sun' sign
- Truncal unsteadiness-50%
- Head tilt, neck stiffness, nystagmus
- Psychomotor delays, lethargy, feeding difficulty, weight loss, loss of developmental milestones
- Acute coma – Hydrocephalus/haemorrhage



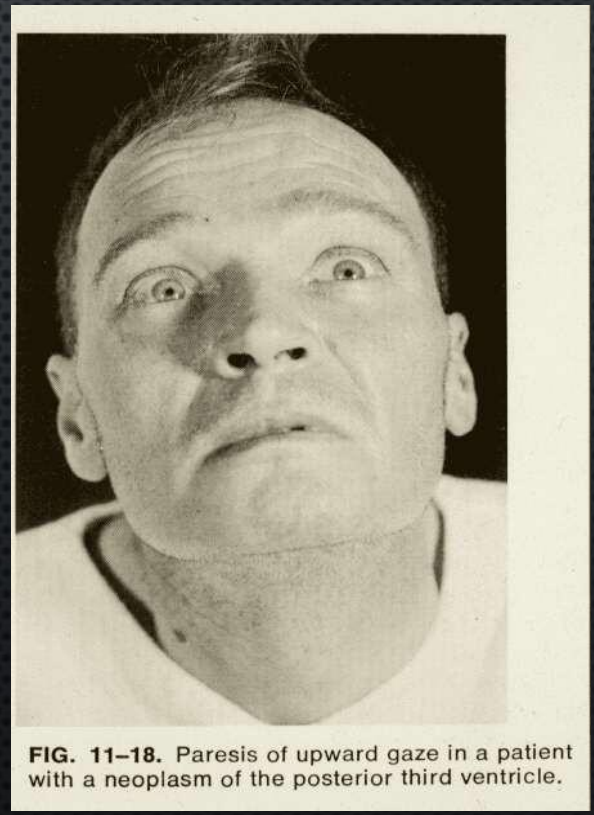
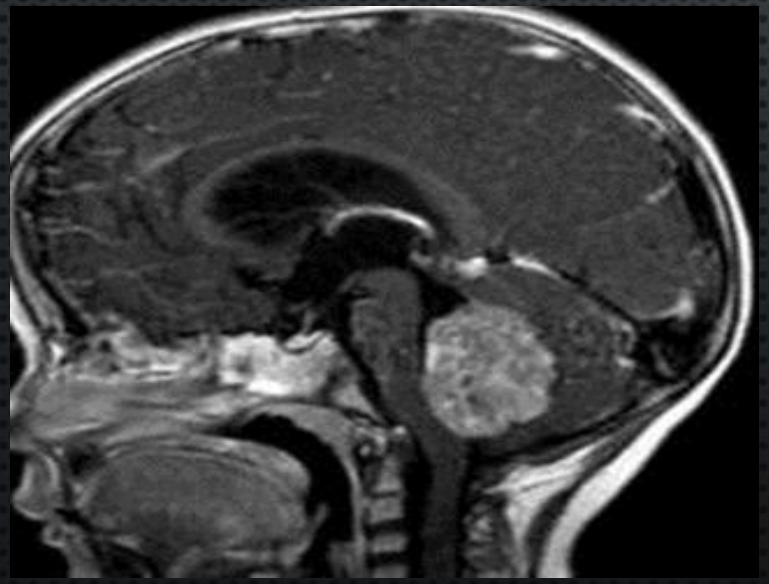


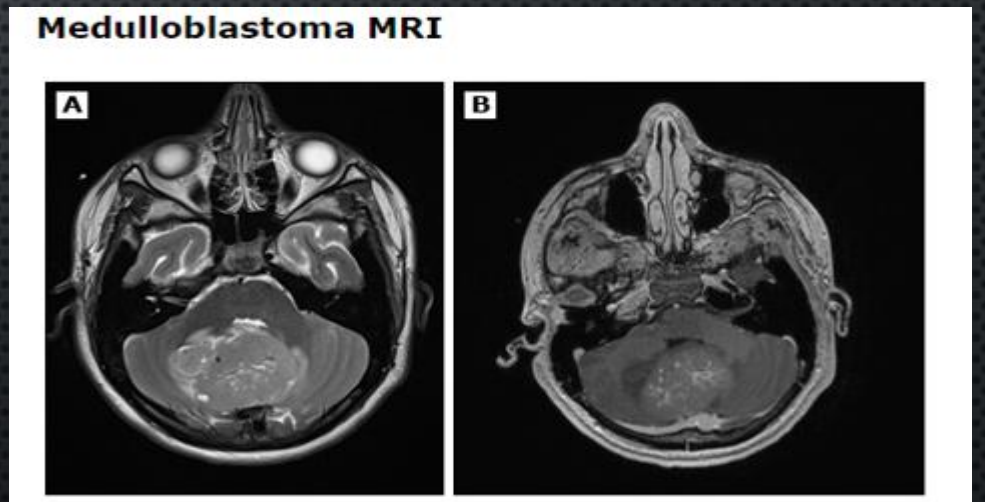
FIG. 11–18. Paresis of upward gaze in a patient with a neoplasm of the posterior third ventricle.

DIAGNOSIS - RADIOLOGY

Response Assessment in Pediatric Neuro-Oncology committee RAPNO

- CT/MRI brain: homogenously enhancing solid masses arising in the cerebellar vermis and projecting into the IV ventricle.
- Restricted diffusion due to increased cellularity.
- *DD*:
- AT/RT & Ependymoma
- MRI Spine : enhancing nodules over leptomeninges (10-30%)

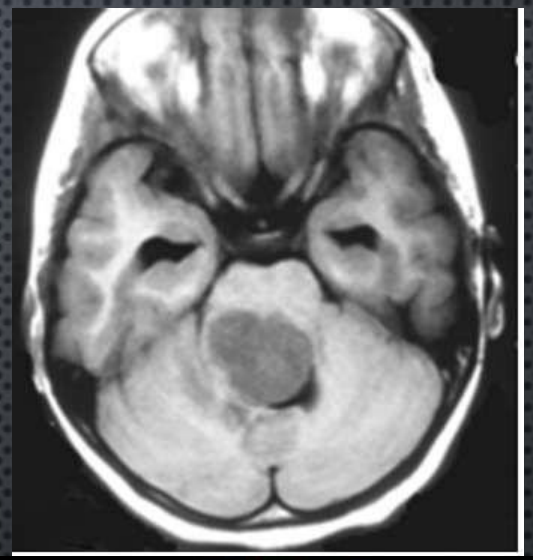




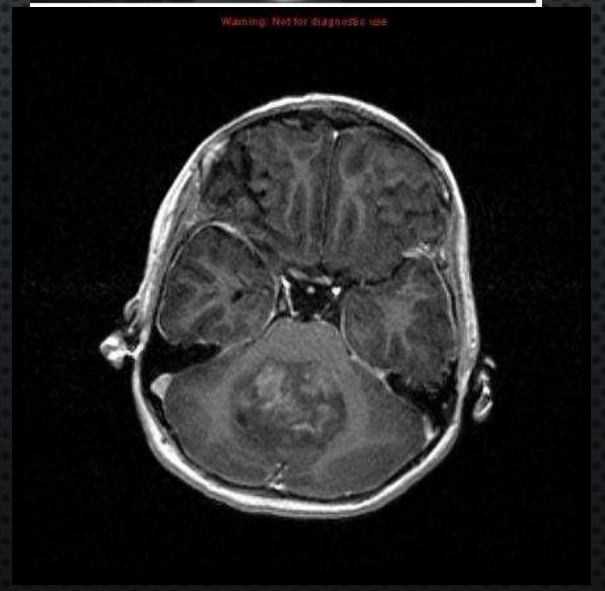
10-year-old child with a newly diagnosed medulloblastoma heralded by new-onset headaches, emesis, and tiredness. Axial T2-weighted MRI (A) demonstrates a large hyperintense mass in the fourth ventricle with associated swelling. Axial T1-weighted MRI with contrast (B) demonstrates heterogeneous enhancement within the mass.

DIAGNOSIS - RADIOLOGY

- Iso- to- hypointense relative to white matter (T1 images)



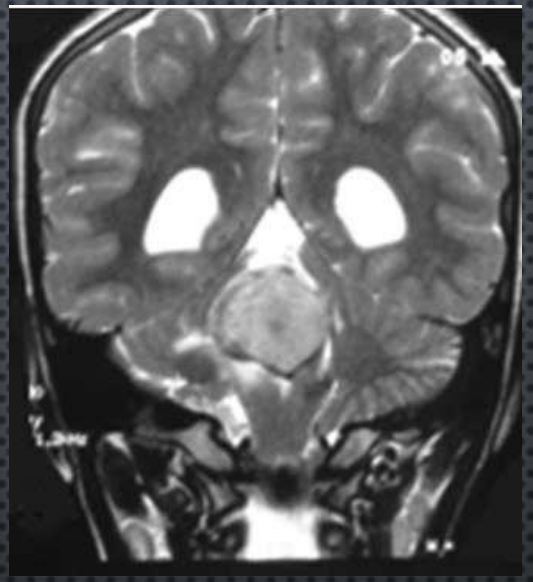
- Enhance following contrast (90%)
- Heterogeneous enhancement.
- Vasogenic edema +

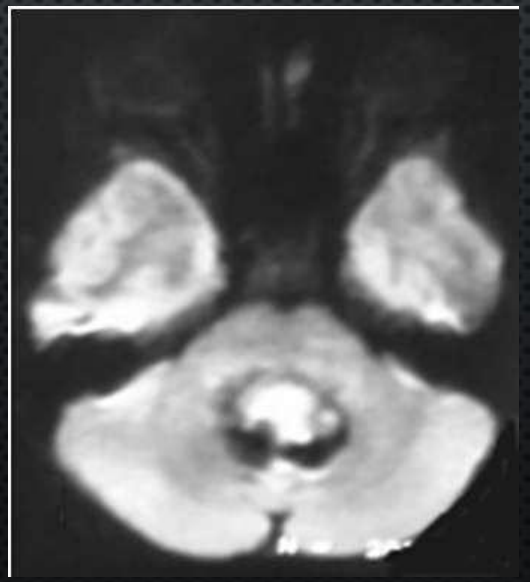


DIAGNOSIS - RADIOLOGY

T2-weighted images :

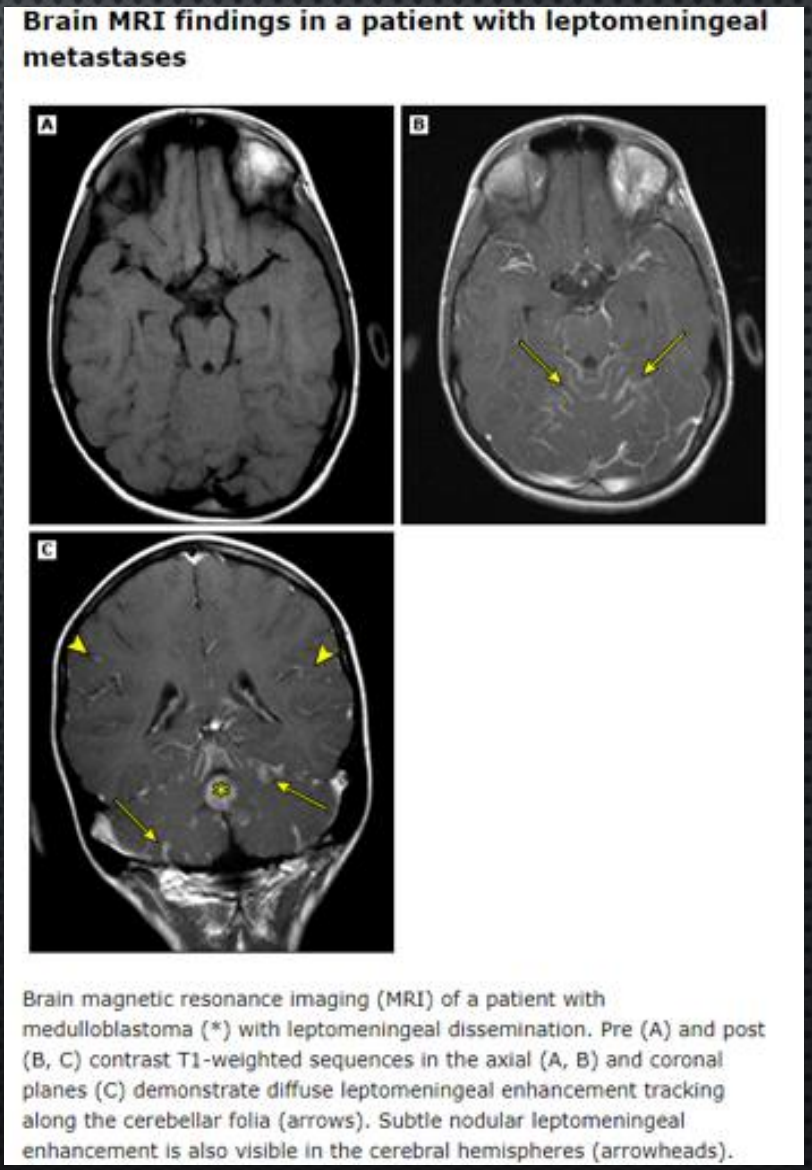
- densely cellular component of the tumor being hypointense
- the less cellular areas being iso- to hyperintense
- Intra-tumoral or peri-tumoral cysts, if any, appear hyperintense,
- calcification generally exhibits a low signal on T2-weighted sequences





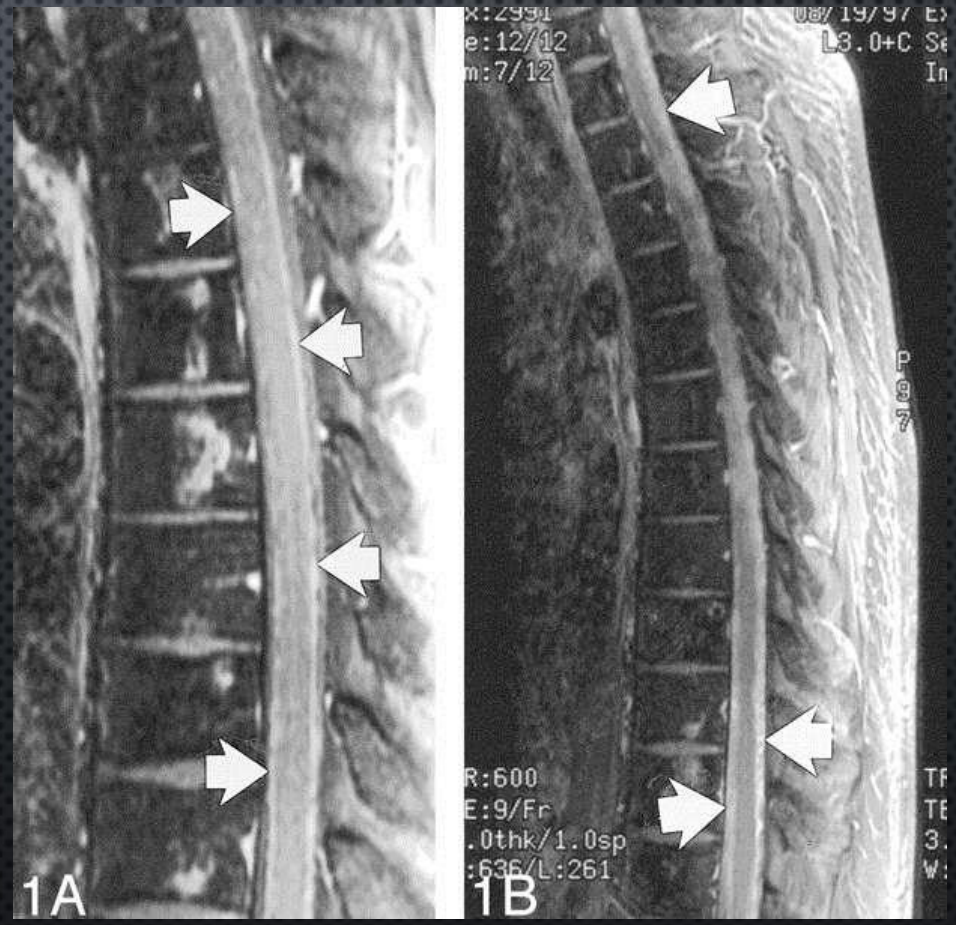
DIFFUSION WEIGHTED IMAGES

- densely packed cells within the tumor,
- restriction of diffusion : low apparent diffusion coefficient (ADC) values



DIAGNOSIS – RADIOLOGY : MRI SPINE

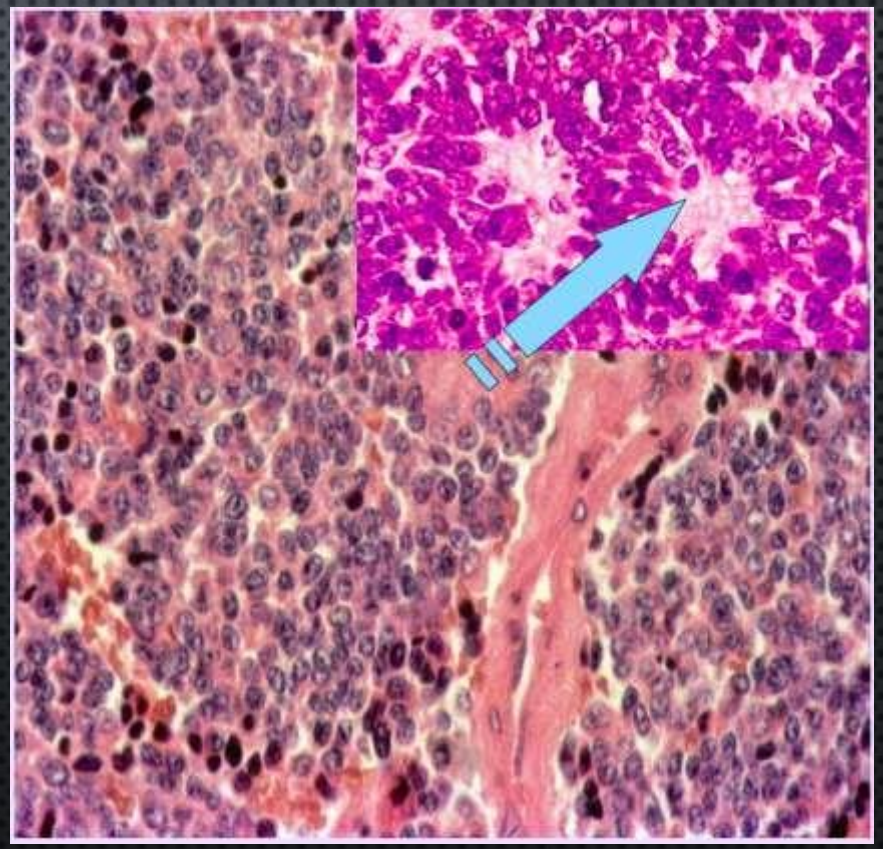
- Most metastases are found along the posterior margin of the spinal cord -
- CSF flow from cisterna magna to posterior margin of spinal cord
- **Sagittal fat-suppressed post-contrast MRI** of the spine is strongly recommended in the pre-operative setting as a screening tool to rule out any leptomeningeal metastases.



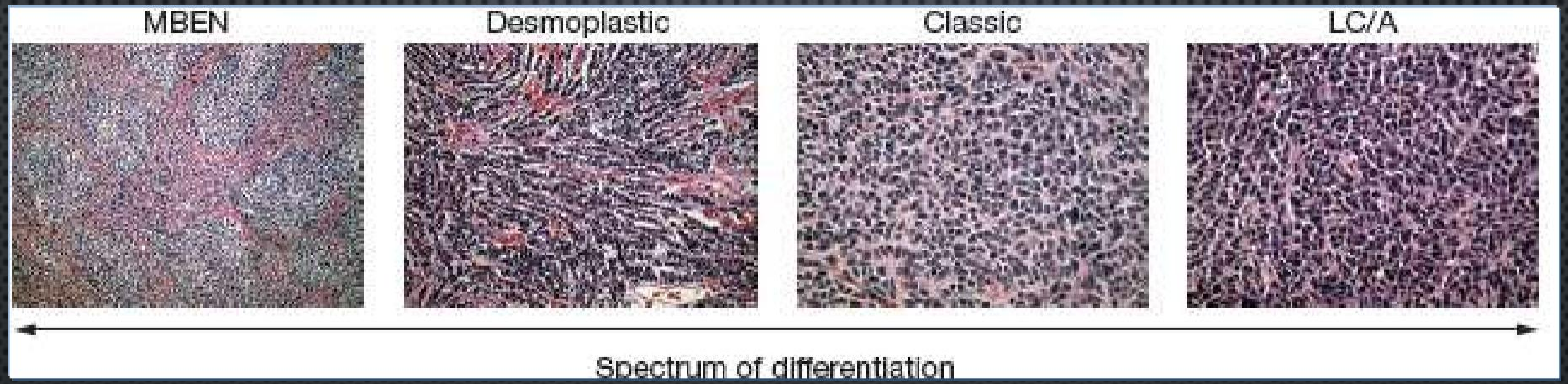
RAPNO guidelines for medulloblastoma

HISTOPATHOLOGY

- Small round blue cell tumor
- Cell Of Origin:fetal remnant cells in the external granular layers of the cerebellum
- Most common embryonal tumor of the CNS (others include PNETs, ATRT)
- Molecularly distinct from PNETs 40% have Homer-Wright rosettes Most stain + for neuron-specific enolase, synaptophysin, and nestin



HISTOLOGICAL VARIANTS WHO -2007



- 3%
- Infants
- Good prognosis

- 7%
- Adults
- Better prognosis

- 70-80%
- Poor prognosis

- 10-22%
- Aggressive
- Early CSF dissemination
- anaplasia
- Worst
- prognosis

MOLECULAR SUB GROUPING

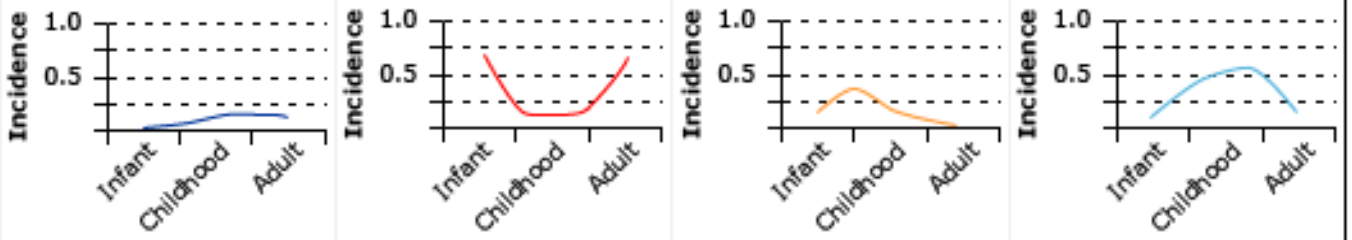
For a better prognostication and refined risk-stratification.

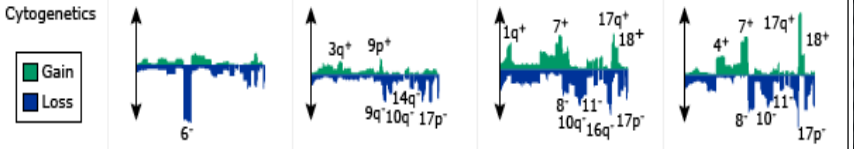
- **Wingless related integration site type (WNT) activated**
- **Sonic Hedgehog (SHH) activated**
- **Group 3**
- **Group 4**

- These four molecular sub-groups have different
  - developmental origins
  - phenotypes
  - transcription and genetic profiles,
  - diverse biological behaviour
  - markedly variable prognosis and clinical outcomes

Acta Neuropathol (2012) 123:465–472

CLINICAL AND GENOMIC FEATURES OF MEDULLOBLASTOMA GROUPS

	WNT (~10%)	SHH (~30%)	Group 3 (~25%)	Group 4 (~35%)
Clinical features				
Sex ratio (M/F)	~1/1	~1.5/1	~2/1	~3/1
Age distribution				
Histology	Classic; very rare LCA	Classic >demoplastic/ nodular >LCA >MBEN	Classic >LCA	Classic; rarely LCA
Metastasis at diagnosis	~5-10%	~15-20%	~40-45%	~35-40%
Overall survival (5 years)	~95%	~75%	~50%	~75%
Proposed cell of origin	Lower rhombic lip progenitor cells	CGNPs of the EGL and cochlear nucleus; neural stem cells of the SVZ	Prominin 1$^+$, lineage$^-$ neural stem cells; CGNPs of the EGL	Unknown

Genomic features				
Cytogenetics				
Driver genes¶	▪ *CTNNB1* (90.6%) ▪ *DDX3X* (50%) ▪ *SMARCA4* (26.3%) ▪ *MLL2* (12.5%) ▪ *TP53* (12.5%)	▪ *PTCH1* (28%) ▪ *TP53* (13.6%) ▪ *MLL2* (12.9%) ▪ *DDX3X* (11.7%) ▪ *MYCN* (8.2%) ▪ *BCOR* (8%) ▪ *LDB1* (6.9%) ▪ *TCF4* (5.5%) ▪ *GLI2* (5.2%)	▪ *MYC* (16.7%) ▪ *PVT1* (11.9%) ▪ *SMARCA4* (10.5%) ▪ *OTX2* (7.7%) ▪ *CTDNEP1* (4.6%) ▪ *LRP1B* (4.6%) ▪ *MLL2* (4%)	▪ *KDM6A* (13%) ▪ *SNCAIP* (10.4%) ▪ *MYCN* (6.3%) ▪ *MLL3* (5.3%) ▪ *CDK6* (4.7%) ▪ *ZMYM3* (3.7%)
Expression signature	WNT signalling	SHH signalling	MYC signature Retinal signature	Neuronal signature

WNT: Wingless-related integration site; SHH: sonic hedgehog; LCA: large cell and anaplastic; MBEN: medulloblastoma with extensive nodularity; CGNPs: cerebellar granule neuron precursors; EGL: external granule cell layer; SVZ: subventricular zone; *CTNNB1*: β-catenin; *DDX3X*: DEAD-box helicase 3 X-linked; *SMARCA4*: SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 4; *MLL*: mixed lineage leukemia; *TP53*: tumor protein p53; *PTCH1*: patched 1; *BCOR*: BCL6 co-repressor; *LDB1*: LIM domain binding 1; *TCF4*: transcription factor 4; *GLI2*: GLI family zinc finger 2; *OTX2*: orthodenticle homeobox 2; *CTDNEP1*: CTD nuclear envelope phosphatase 1; *LRP1B*: low density lipoprotein receptor-related protein 1B; *KDM6A*: lysine-specific demethylase 6A; *SNCAIP*: α-synuclein interacting protein; *CDK6*: cyclin-dependent kinase 6; *ZMYM3*: zinc finger MYM-type containing 3; SCNA: somatic copy number aberration.

Molecular Subgroups of Medulloblastoma

CONSENSUS	WNT	SHH	Group 3	Group 4
Cho (2010)	C6	C3	C1/C5	C2/C4
Northcott (2010)	WNT	SHH	Group C	Group D
Kool (2008)	A	B	E	C/D
Thompson (2006)	B	C', D	E, A	A, C

DEMOGRAPHICS

Age Group: infant, child, adult

Gender: ♀ ♂

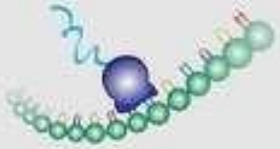
CLINICAL FEATURES

	WNT	SHH	Group 3	Group 4
Histology	classic, rarely LCA	desmoplastic/nodular, classic, LCA	classic, LCA	classic, LCA
Metastasis	rarely M+	uncommonly M+	very frequently M+	frequently M+
Prognosis	very good	infants good, others intermediate	poor	intermediate

GENETICS

	WNT	SHH	Group 3	Group 4
	6-	3q+, 9q-, 10q-	7+, 1q+, 17q+, 18q+, 11p-, 5q-, 10q-, 16q-, 8-	7+, 17q+, 18q+, 11p-, X-, 8-
	CTNNB1 mutation	*PTCH1/SMO/SUFU* mutation *GLI2* amplification *MYCN* amplification	i17q *MYC* amplification	i17q *CDK6* amplification *MYCN* amplification

GENE EXPRESSION



WNT	SHH	Group 3	Group 4
WNT signaling	SHH signaling	Photoreceptor/GABAergic	Neuronal/Glutamatergic
MYC +	*MYCN* +	*MYC* +++	minimal *MYC* / *MYCN*

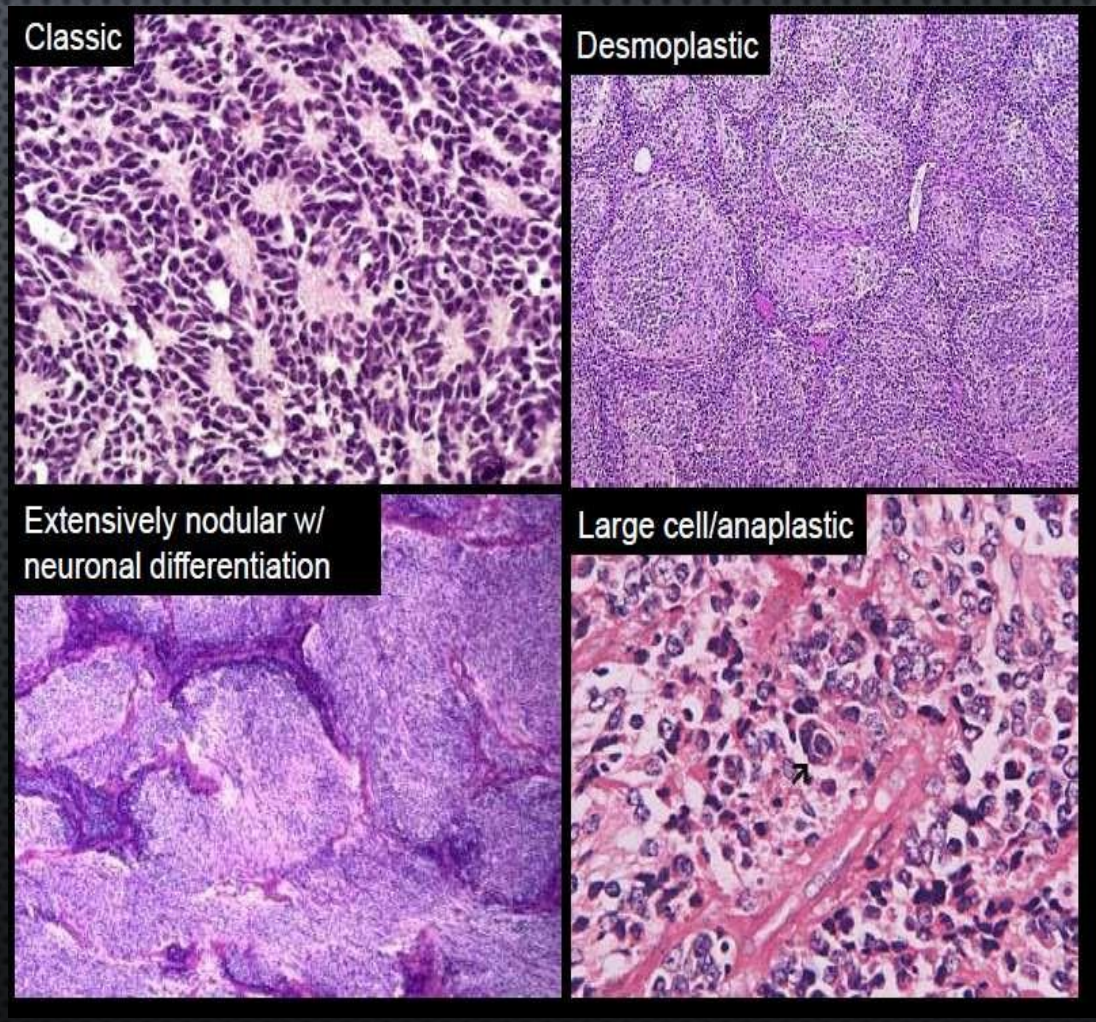
WHO 2021 CLASSIFICATION

Embryonal tumours

Medulloblastoma, genetically defined
- 1 Medulloblastoma, WNT-activated
- 2 Medulloblastoma, SHH-activated and TP53-mutant
- 3 Medulloblastoma, SHH-activated and TP53-wildtype
- 4 Medulloblastoma, non-WNT/non-SHH
  - *Medulloblastoma, group 3*
  - *Medulloblastoma, group 4*

Medulloblastoma, histologically defined
- 1 Medulloblastoma, classic
- 2 Medulloblastoma, desmoplastic/nodular
- 3 Medulloblastoma with extensive nodularity
- 4 Medulloblastoma, large cell/anaplastic

Medulloblastoma, NOS



STAGING- CLINICAL PATHOLOGICAL STAGING (MODIFIED CHANG)

Box 1 Chang staging system.

The T stage does not demonstrate prognostic significance. The extent of disease progression summarized in the M stage remains a highly prognostic factor. Permission obtained from Lippincott Williams and Wilkins © Halperin EC *et al.* (2005) *Pediatric Radiation Oncology*.[4]

Tumor stage	Description
T1	Tumor is less than 3 cm in diameter and is limited to the midline position in the vermis, the roof of the fourth ventricle and less frequently cerebellar hemispheres
T2	Tumor more than 3 cm in diameter, further invading one adjacent structure or partially filling the fourth ventricle
T3a	Tumor invading two adjacent structures or completely filling the fourth ventricle with extension into the aqueduct or Sylvius, foramen of Magendie or foramen of Luschka, thus producing marked internal hydrocephalus
T3b	Tumor arising from the floor of the fourth ventricle or brain-stem cell and filling the fourth ventricle
T4	Tumor further spreading through the aqueduct of Sylvius to involve the third ventricle or midbrain, or tumor extending to the upper cervical cord
Metastasis stage	**Description**
M0	No evidence of gross subarachnoid or hematogenous metastasis
M1	Microscopic tumor cells found in cerebrospinal fluid
M2	Gross nodule seedlings demonstrated in the cerebellar, cerebral subarachnoid space or in the third or lateral ventricles
M3	Gross nodule seedlings in the spinal subarachnoid space
M4	Extraneuroaxial metastasis

M STAGING

- M_0—no dissemination.
- M_1—CSF-positive cytology only.
- M_2—gross nodular seeding in cerebellar-cerebral subarachnoid space and/or lateral or third ventricle.
- M_3—gross nodular seeding in spinal subarachnoid space.
- M_4—extraneural metastasis.

- Postoperative degree of residual disease is designated as:
- *Gross-total /near-total resection*- non-measurable residual disease.
- *Subtotal resection*- measurable residual disease (< /≥1.5cm^2)
- *Biopsy* - only a sample of tumor tissue is removed.

- No evidence of residual tumor at surgery and negative postoperative imaging :Gross total resection
- > 90% : Total or near total
- 51 - 90% : Subtotal resection
- 11 - 50% : Partial resection
- < 10% : Biopsy

STAGING – RISK STRATIFICATION

Average/Standard	High
> 3years	< 3years
<1.5cm^2 residue after surgery	>1.5cm^2 residue after surgery
M_0	M_{1-4}
Classic/Desmoplastic type	Large cell/anaplastic type
Complete staging done	Incomplete staging

RISK STRATIFICATION – MOLECULAR

Table 6: Consensus risk-stratification in the molecular era for medulloblastoma

Risk category	WNT	SHH	Group 3	Group 4	Others
Low Risk (expected survival >90%)	<16 years				
Standard Risk (expected survival 75-90%)		TP53 wild type No MYC amplification Non-metastatic	All of the following No MYC amplification Non-metastatic	All of the following Non-metastatic Chr 11 loss	
High Risk (expected survival 50-75%)		One or both MYC amplification Metastatic		All of the following Non-metastatic No Chr 11 loss	
Very High Risk (expected survival <50%)		TP53 mutation (metastatic or non-metastatic)	Metastatic	Metastatic	
Unknown	Metastatic		Non-metastatic with MYC amplification; anaplasia; isochromosome 17q	Anaplasia	Melanotic medulloblastoma Medullomyoblastoma Indeterminate between groups 3/4

RISK GROUP BASED ON AGE OF CHILD

Risk groups for children aged 3–5 years old and over.

	Molecular features	Histology	Residual disease	Metastatic disease
Low-risk	WNT subgroup (under 16 years old) *TP53* wildtype *MYC/N* non-amplified	Classic, Desmoplastic / nodular	< 1.5 cm^2	M0
Standard-risk	*TP53* wildtype *MYC/N* non-amplified (except Group 4 *MYCN* amplified)	Classic, Desmoplastic / nodular	Any	M0
	WNT subgroup (any age and not low-risk)	Classic, Desmoplastic / nodular	Any	M+ if under 16 M0 if over 16
	non-WNT subgroup No biological high-risk features	Classic, Desmoplastic / nodular	≥ 1.5 cm^2	M0
High-risk	*TP53* mutant and / or *MYCN* amplified (except Group 4 *MYCN* amplified)	Any	Any	Any
	Any non-WNT and WNT > 16 years	Any	Any	M+
	MYC amplified Any	Any Large-cell / anaplastic	Any Any	Any Any

Risk groups for children aged < 3–5 years.

	Molecular features	Histology	Residual disease	Metastatic disease
Low-risk	SHH-*TP53* wildtype *MYC/N* non-amplified	DN/MBEN	Any	M0
Standard-risk	not high-risk non-WNT	Classic	Any	M0
	SHH-*TP53* wild-type *MYC/N* non-amplified	DN/MBEN	Any	M+
High-risk	*TP53* mutant and/or *MYC/N* amplified	Any	Any	Any
	non-SHH, non-WNT	Classic	Any	M+
	Any	Large-cell / anaplastic	Any	Any

Medulloblastoma therapy: Consensus treatment recommendations from SIOP-Europe and the European Reference Network S. Bailey *EJC Paediatric Oncology, Volume 5,2025,*

General principles for management- ICT,edema

Management of ICT and edema

- Surgery
- CSF Diversion (ETV)
- Glucocorticoids(**Steroid of choice** : dexamethasone 0.5- 1mg/kg IV (max = 10mg)

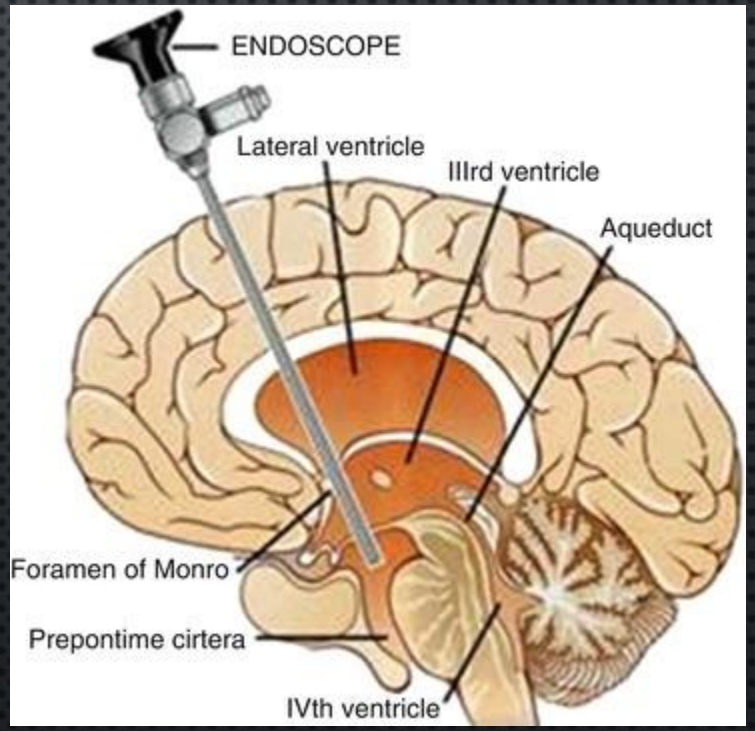
Severe cases, dexamethasone treatment begins with a **10 mg intravenous loading dose**, followed by a **maintenance dose of 8–16 mg daily in divided doses,**

Mild symptoms, **2–4 mg daily** suffices without a loading dose

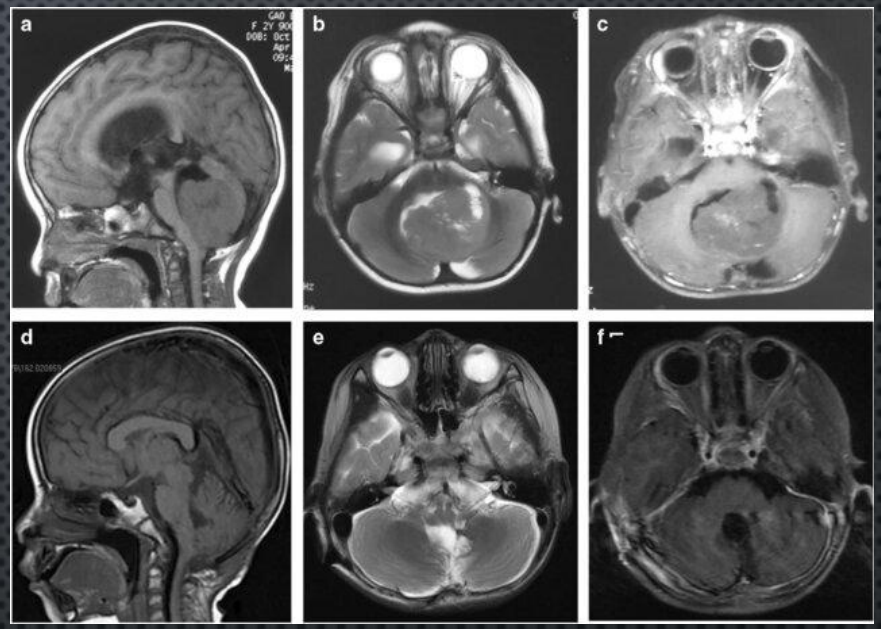
General principles for management-CSF diversion

CSF diversion:

- Controlled External Ventricular drain(EVD) /Endoscopic Third Ventriculostomy (ETV) for relief of hydrocephalus *(if immediate surgery is not possible).*
  - VP shunt -*no longer recommended*
- Post-op persistent obstructive hydrocephalus-ETV/VPS



GENERAL PRINCIPLES FOR MANAGEMENT-EXTENT OF SURGERY



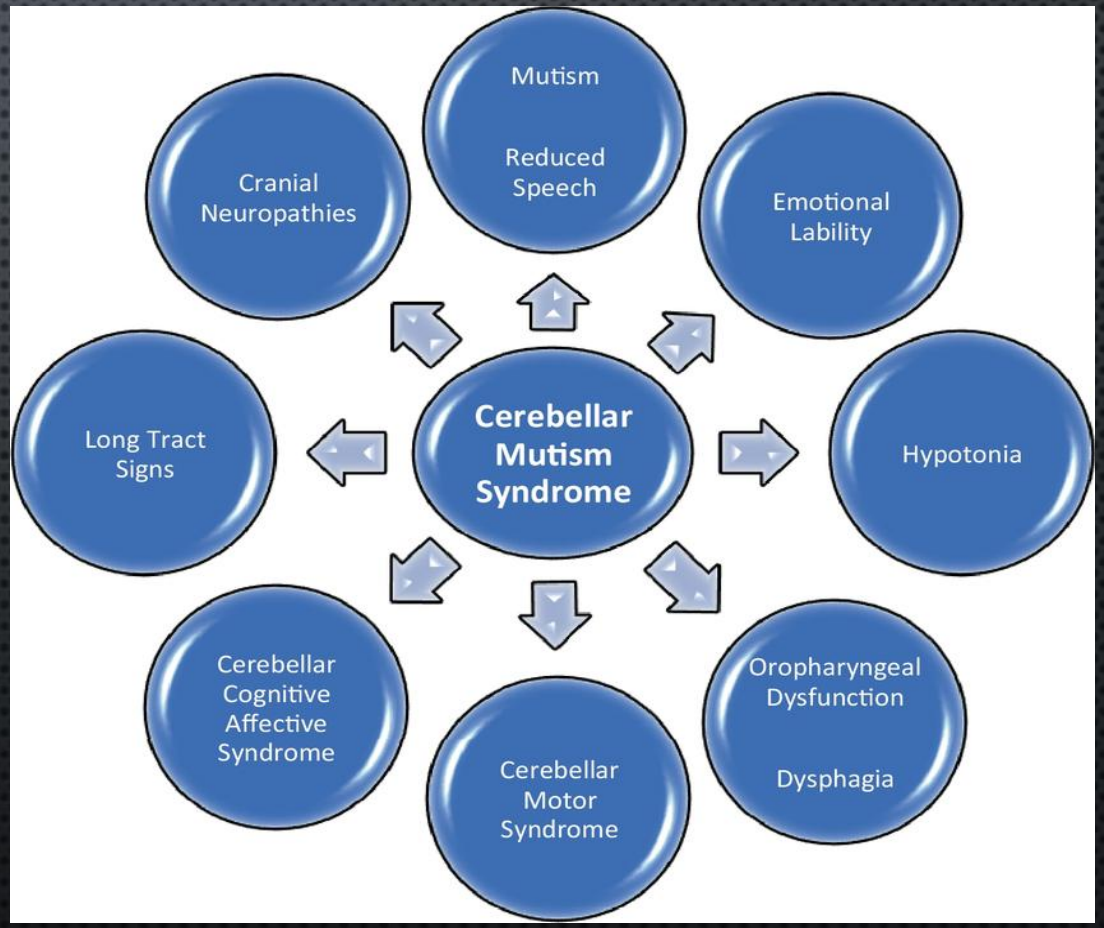
Maximal safe resection

- **Standard of care** : Safe Total / Near-Total resection
  ↑*outcome*
  for non-disseminated stage.
- Small residuum acceptable *if there is risk of serious morbidity*
  (tumor adherent to brainstem)
- Second look surgery- *appropriate for large residuum*.

- No evidence of residual tumor at surgery and negative postoperative imaging :Gross total resection
- > 90% : Total or near total
- 51 - 90% : Subtotal resection
- 11 - 50% : Partial resection
- < 10% : Biopsy

GENERAL PRINCIPLES FOR MANAGEMENT- SURGICAL COMPLICATIONS

- **Cerebellar mutism syndrome**(10%-30%)
  - Posterior fossa syndrome
  - Within 48 hrs
  - Mutism + dysarthria + apraxia
  - Behavioural changes
  - Mechanism- controversial(dentate nucleus)
- Meningitis
- Cervical spine instability
- Cranial nerve palsies
- Anaesthetic complications

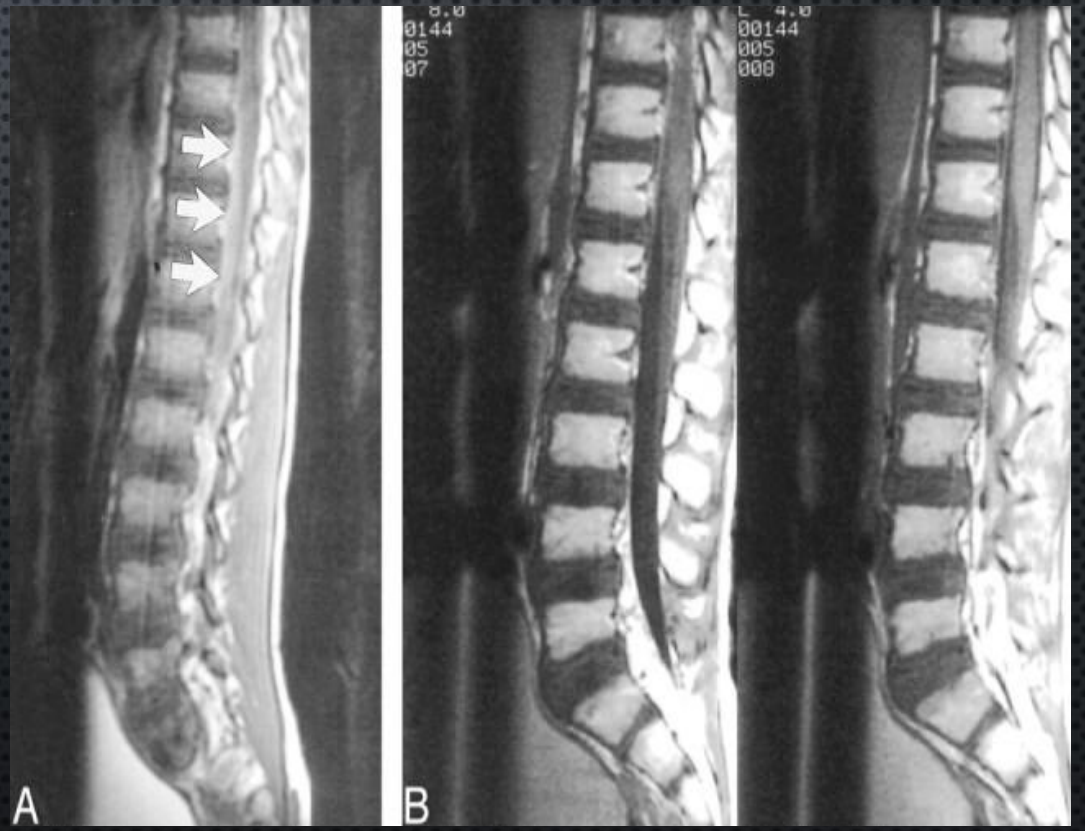


GENERAL PRINCIPLES FOR MANAGEMENT- POST OPERATIVE SPINE MRI IMAGING

- To identify extent of resection & quantify residual disease

- Timing - 2options
  - **Within 24-48 hours post surgery**
    or
  - **2-3 weeks post surgery** (not later than 4 weeks) - to allow resolution of post-op changes (blood products & surgical debris)

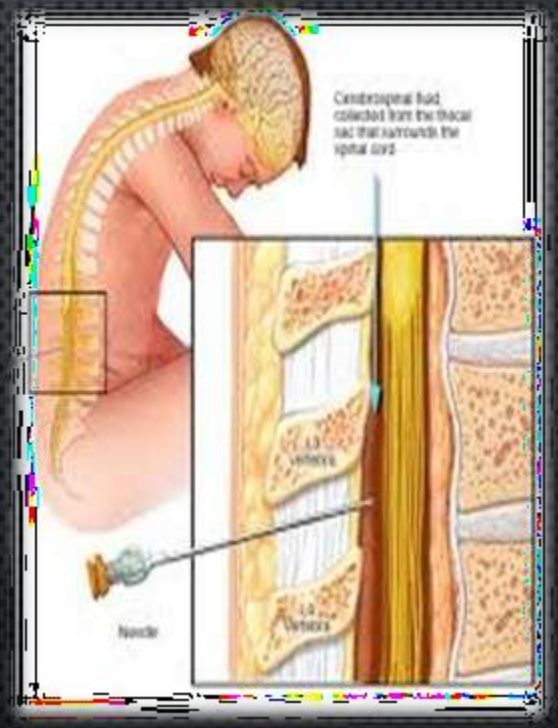
- **Spinal screening** if not done prior
  - 2-3 weeks post surgery - erroneous interpretation of post op enhancement of leptomenegis



MR images of a 7-year-old boy, obtained 3 days (A) and 17 days (B) after surgery.

GENERAL PRINCIPLES FOR MANAGEMENT- POST OPERATIVE CSF CYTOLOGY

- A part of the **post-operative staging work up**
- To be performed (14days or more) **2-3 weeks post-op** to avoid false positivity
- CSF via ventricular tap at the time of surgery is not considered appropriate for neuraxial staging



TREATMENT OF MEDULLOBLASTOMA

Newly diagnosed patients	Treatment
Children > 3 years Average-risk	Surgery + Adjuvant therapy (radiation and chemotherapy)
Children > 3 years High-risk	Surgery + Adjuvant therapy (radiation and chemotherapy)
Children ≤3 years	Surgery + Adjuvant Chemotherapy +/- radiation after completing 3 years

CHEMOTHERAPY

ADJUVANT CHEMOTHERAPY

Indication for CT :

1. *As Adjuvant with Surgery in child <3 yrs to delay/avoid RT.*
2. *In Recurrent /Progressive disease .*
3. *In patients with Extra cranial mets .*
4. *High risk Pt. to improve cure rates*
5. *In avg. risk group to* ***allow reduced RT dose.***

Non-disseminated, totally resected, desmoplastic tumors in children < 3 years showed long-term survival with chemotherapy alone(5Yr EFS :77-90% and OS: 85-100%).

INTEGRATION OF CHEMOTHERAPY

- Delay in starting RT results in inferior outcome: Halperin
- Prolongation of RT duration negatively impacts upon survival: Del Charco & SIOP PNET 3
- Pre RT CT inferior to post RT CT: CCG 921 and HIT 91
- Pre RT CT does not improve survival compared to RT alone: SIOP II & SIOP PNET 3
- Pre RT CT followed by reduced dose CSI inferior: SIOP II

GENERAL PRINCIPLES: ADJUVANT CHEMOTHERAPY

- **Timing of adjuvant CT after radiation**
  - Ideal: 3weeks
  - Preferably: within 4 weeks
  - Definitely: not beyond 6 weeks

- Every cycle to be given after **sufficient myelo-recovery**
  - ANC > 1000
  - Platelet > 1lakh
  - RFTT, LFT, s. electrolytes

- **Baseline auditory assessment** is mandatory
  - PTA

CHEMOTHERAPY

Table 3 Detailed Chemotherapy Strategies for Medulloblastoma by Risk Group and Protocol in Europe and North America

Patient group	Objective	Chemotherapy regimen (examples by protocol)	Region/protocol
Young children (< 3–5 yrs)	Delay or avoid craniospinal RT	Cisplatin, Vincristine, Cyclophosphamide	COG, SIOP PNET 4, HIT 2000
Average-risk children	Reduce recurrence and RT exposure	Cisplatin + Etoposide + Carboplatin; Cisplatin, Lomustine, Vincristine	COG ACNS0331, HIT 2000
High-risk children	Maximize therapeutic efficacy	Multi-agent (e.g., Methotrexate-based, Cyclophosphamide/Vincristine)	COG ACNS0332, SIOP PNET 5

Regimens vary by trial (e.g., SIOP, HIT, COG) and molecular subgroup; refer to specific protocols for detailed dosing and schedules

CHILDREN'S ONCOLOGY GROUP

AVERAGE RISK MEDULLOBLASTOMA ACNS0331 CHEMOTHERAPY DETAILS

Surgery			Chemoradiotherapy								Maintenance								
	31 Days		Radiation Therapy (XRT)							4 wks									
		Cycle									1	2	3	4	5	6	7	8	9
		Week	0	1	2	3	4	5	6		11	17	23	27	33	39	43	49	55
		Day	1	8	15	22	29	36	43										
				Chemotherapy							Maintenance Chemotherapy								
				V	V	V	V	V	V		A	A	B	A	A	B	A	A	B

Maintenance

Cycle A (42 Days)

Cisplatin (75 mg/m^2) IV over 6 hours on Day 1

Lomustine (CCNU) (75 mg/m^2) orally on Day 1

Vincristine (1.5 mg/m^2, maximum dose 2.0 mg) IV push or infusion Days 1, 8, and 15

Cycle B (28 Days)

Cyclophosphamide (1000 mg/m^2) IV over 1 hour on Days 1 and 2

Vincristine (1.5 mg/m^2, maximum dose 2.0 mg) IV push or infusion on Days 1 and 8

MESNA (360mg/m^2/dose) IV infusion over 15-30 minutes starting 15 minutes prior to or at the same time as cyclophosphamide and repeated at 4 and 8 hours.

Cumulative cisplatin dose 450 mg/m2

INFANT MEDULLOBLASTOMA- CHEMOTHERAPY

- 1. **CONVENTIONAL SYSTEMIC CHEMOTHERAPY ALONE** EG: UKCCSG
- 2. **CHEMOTHERAPY +/- FOCAL RT** EG: COG P 9934
- 3. **INTRAVENTRICULAR CHEMOTHERAPY** (MTX) EG: HIT P
- 4. **HIGH DOSE CHEMOTHERAPY + AUTOLOGOUS STEM CELL RESCUE** EG HEAD START TRIAL

GOLD STD IN INFANT MB (DESMOPLASTIC/NODULAR/MBEN)- CONVENTIONAL CHEMOTHERAPY + EITHER AUTOLOGOUS STEM CELL RESCUE OR INTRAVENTRICULAR CHEMOTHERAPY (MTX)

MEDULLOBLASTOMA: IF NOT SUB GROUPED: TREATMENT OVERVIEW (CHILDREN ~3+)

- **Standard risk**: children with M0 disease and GTR or less than 1.5 cm^2 of residual disease, classic or desmoplastic histology.
  - Standard therapy: CSI to 23.4 Gy with PF/IF boost to 54 Gy +/- weekly vincristine (vcr) followed by chemotherapy. (usually cisplatin, vcr, cyclophosphamide or CCNU)
  - 5 year EFS/OS = 81%, 86% (Packer, 2006, *JCO*, 24:4204)
- **High-risk**: M+ disease or STR with >1.5 cm^2 of residual in primary site.
  - Standard therapy: CSI to 36 Gy with PF(IF) boost to 54 Gy, usually with concurrent CT (vcr and/or carboplatin) and followed by cisplatin based regimen.
  - 5 year EFS = 60-70%

RADIATION THERAPY

GENERAL GUIDELINES FOR RADIOTHERAPY

- Children must be referred 7-10days post surgery
- Adjuvant RT MUST begin at earliest- Preferably within 4 weeks but not more than 6 weeks post op
- Overall treatment time should preferably be within 50days, and definitely not more than 8weeks
- Hematological toxicity - start with or switch over to boost phase

- Anti-emetic prophylaxis – ondansetron 0.2mg/kg 45-60minutes prior to RT
- Weekly blood counts; avoid GCSF until absolute necessity

RADIOTHERAPY RATIONALE

- Tumor radiosensitivity
- Poor surgical outcome
- PF RT (focal)
- PF +SC RT

  leptomeningial relapses
- CSI

  supratentorial relapses

Landberg et al reviewed serial treatment results (10 year survival) at Sweden:

VOLUME	5YR OS
PF	5%
PF+SC	25%
CSI	53%

Craniospinal radiation is the corner stone in treatment of medulloblastoma

CEREBELLAR MEDULLOBLASTOMA:
TREATMENT BY IRRADIATION OF THE WHOLE CENTRAL NERVOUS SYSTEM

by

Edith Paterson and *R. F. Farr*

Introduction

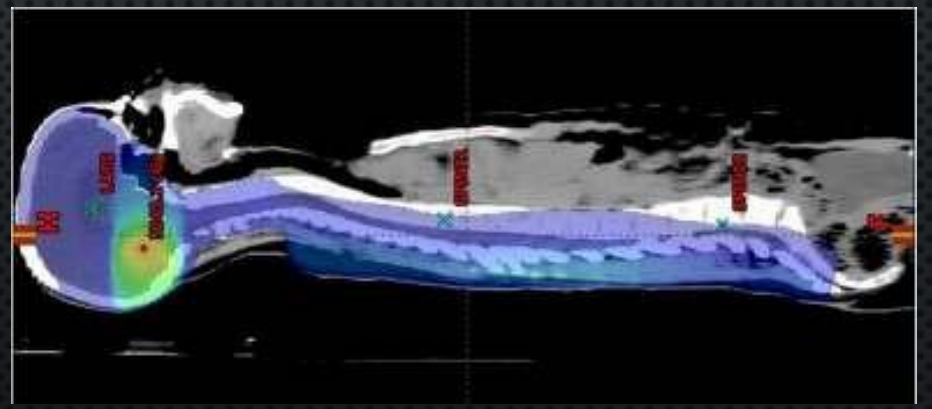
The prognosis in cases of medulloblastoma of the cerebellum has for many years been regarded as fairly hopeless. This viewpoint is expressed by DARGEON (1948) where he states that "medulloblastomas . . . have a consistently unfavourable prognosis". In their excellent book, "Intracranial tumours of infancy and childhood", BAILEY, BUCHANAN and BUCY come to the same conclusion. There are, however, a few authenticated cases reported with a long survival following treatment, cases which are almost historical in their rarity (PENFIELD and FEINDEL 1947; INGRAHAM, BAILEY and BARKER 1948).

For this reason it may be useful to describe the methods of treatment which have been used over the last ten years on proved cases of this disease, methods which have yielded over fifty per cent survival at three years following treatment. Over this period we have adopted, with these encouraging results, the principle of irradiation of the entire brain and cord as one undivided volume. This principle stems from the post-mortem findings in untreated cases of this disease in which it is almost universal to find deposits in the brain and cord which have seeded from

- First proposed in 1953 to irradiate "the entire brain and cord as one undivided volume"
- Principle from post-mortem findings of disease throughout the brain and cord

CRANIO-SPINAL IRRADIATION (CSI) + BOOST

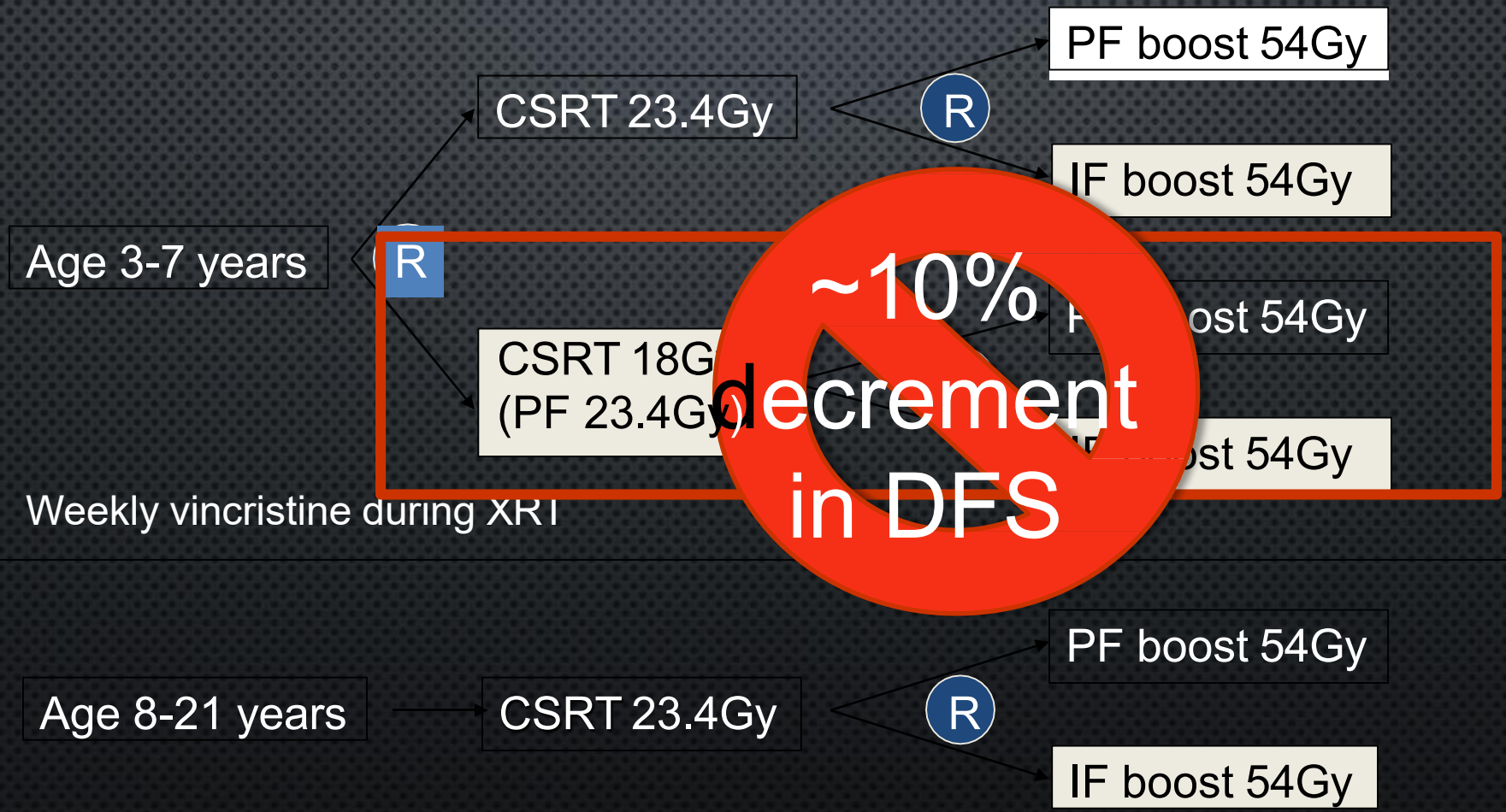
- Encompasses areas at high risk of recurrence.
  - **Target Volume for CSI**
  - Whole brain + Meninges
  - Spinal cord to include caudal end of thecal sac and sacral nerve roots and laterally to include meninges till exit of the nerve roots
  - **Target Volume for boost**
- Average risk : Tumor bed + 1-2cm margin
- High risk : Posterior Fossa



Children's Oncology Group

Average Risk Medulloblastoma

ACNS0331 Schema

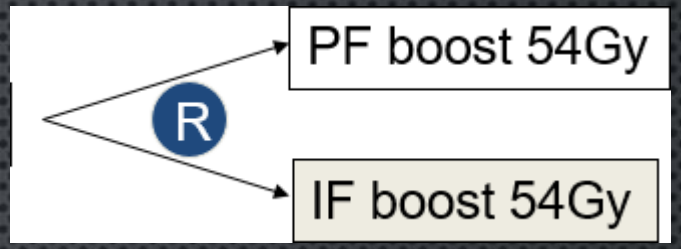


PF: Posterior fossa and IF: Involved field, tumor bed

Children's Oncology Group

AVERAGE RISK MEDULLOBLASTOMA

ACNS0331 Schema



NOTE: No difference in the IF vs WPF

- ***Involved field (Tumor bed boost) should be the standard at this point…***

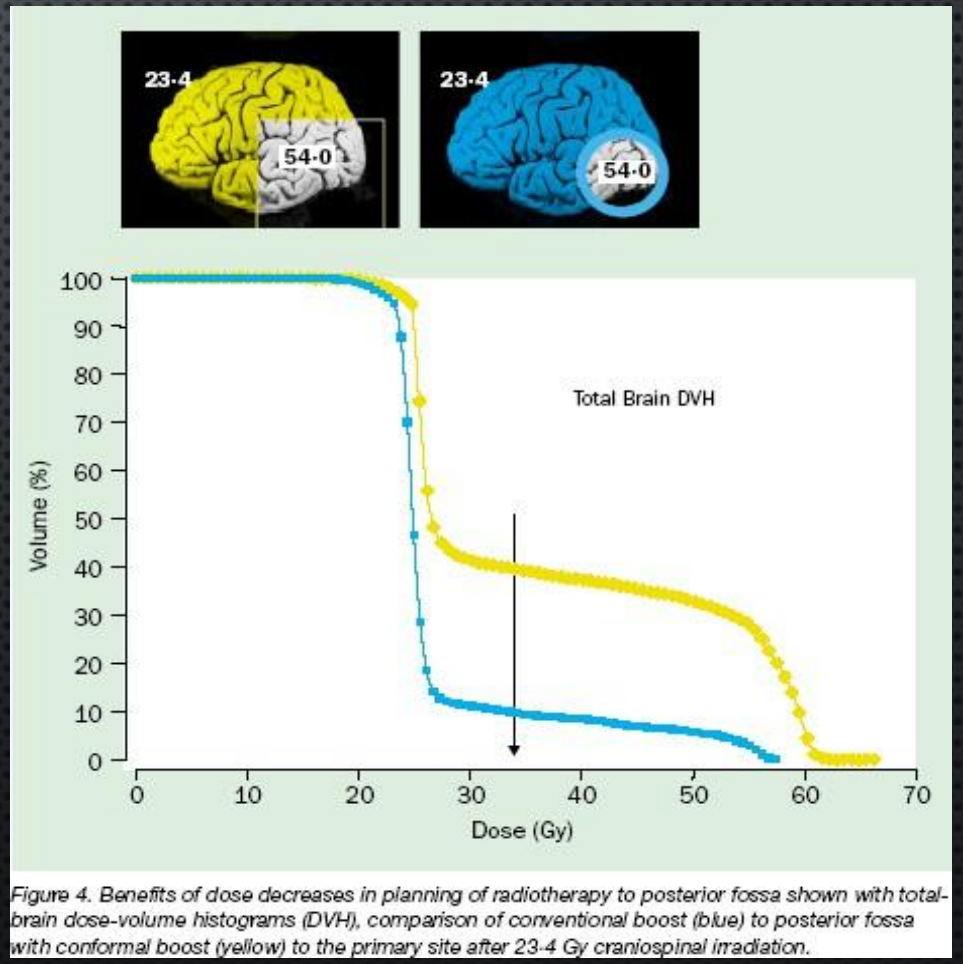
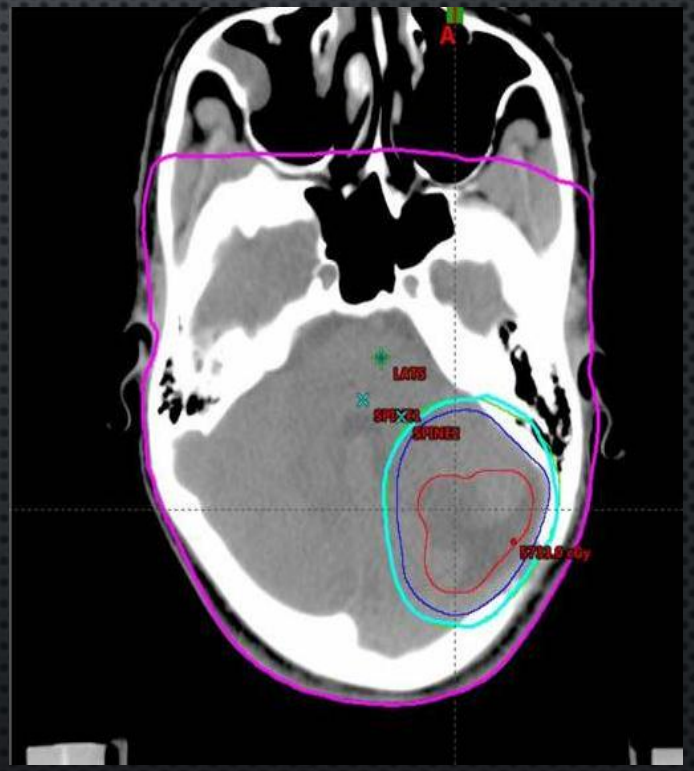


Figure 4. Benefits of dose decreases in planning of radiotherapy to posterior fossa shown with total-brain dose-volume histograms (DVH), comparison of conventional boost (blue) to posterior fossa with conformal boost (yellow) to the primary site after 23·4 Gy craniospinal irradiation.

COG RT GUIDELINES FOR IF BOOST

(with TY modifications, ANCS 0331)

- GTV: includes any residual enhancing or non-enhancing tumor **and** the wall of the resection cavity. ***(FUSE both post op and pre-op T1 post gad and T2 sequences)***
- CTV: is defined as the GTV plus a 1.5-cm margin except at bone or tentorial interface (*Buzz words: anatomically confined to posterior fossa, trim inside tentorium/boney PF)*
- **PTV:** an additional 0.3 to 0.5 cm around the CTV.



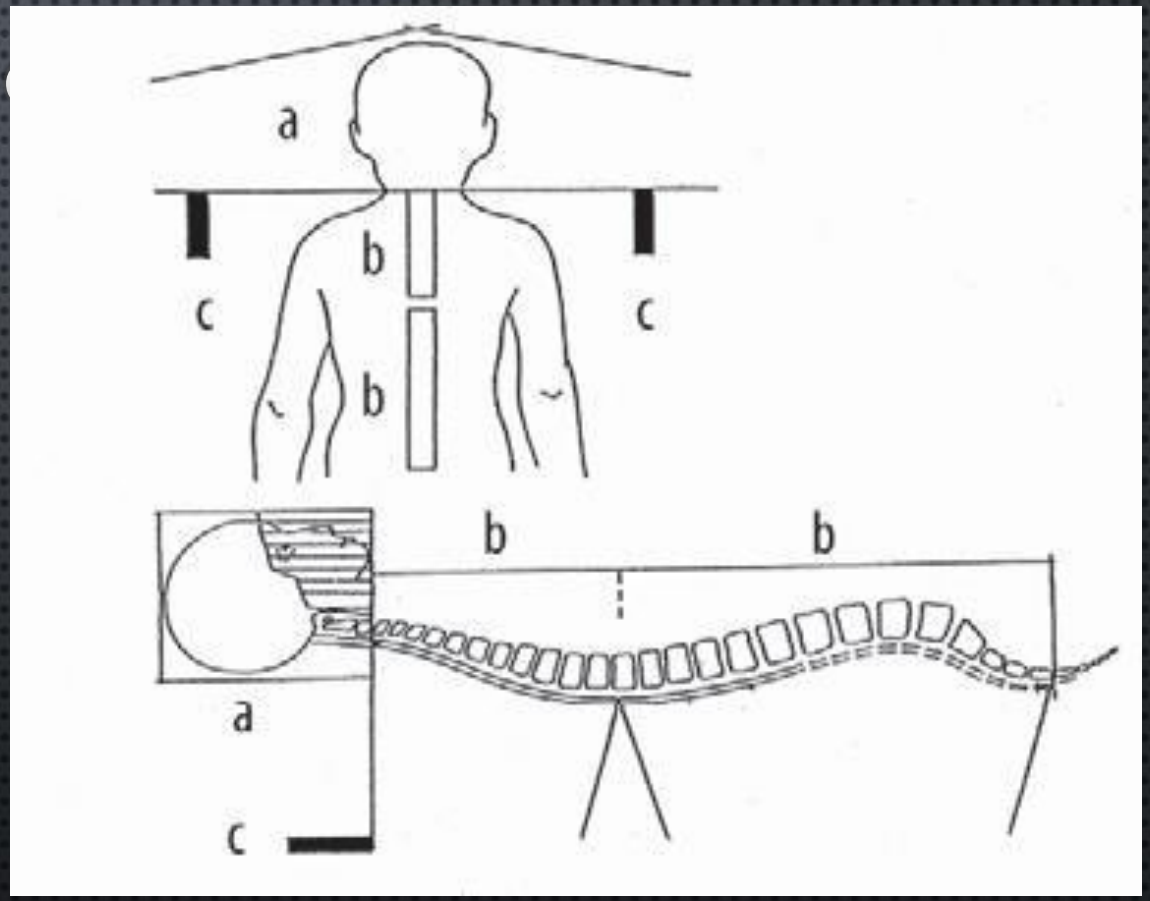
DOSES AND VOLUMES FOR MEDUL LOBLASTOMA

Risk Category	CSI dose	Boost dose
Average Risk	23.4 Gy/13#/2.5 weeks @1.8 Gy/#	30.6 Gy/17#/@1.8 Gy/# to tumor bed + margin
High Risk	35-36 Gy/21-20#/4 weeks @ 1.67-1.8 Gy/#	19.8 Gy/11#/2 weeks to posterior fossa
Gross focal spinal deposit	39.6 Gy/22# /4.5 weeks @1.8Gy/#	16.2Gy/9# to postr fossa &7.2-9 Gy/4-5#/1 week to spinal deposit

CRANIOSPINAL IRRADIATION (CSI)

Technically challenging:

- Large target area to be covered
- Irregular shape of the target
- Multiple fields with junction overlap
- Normal tissue exposure and late toxicities



CSI PLANNING STEPS

- Positioning & Immobilization
- Target/OAR Delineation
- Field Arrangement
- Doses
- Treatment Verification

PATIENT POSITIONING

PRONE:

Direct visualization of the field junctions on the patient.
Poor reproducibility
Scope of patient movement and Discomfort
Difficult anesthesia

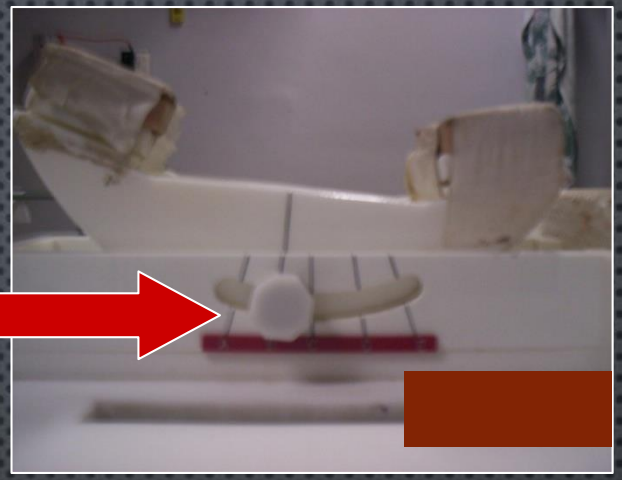
SUPINE:

Comfortable
Relative ease in anesthesia

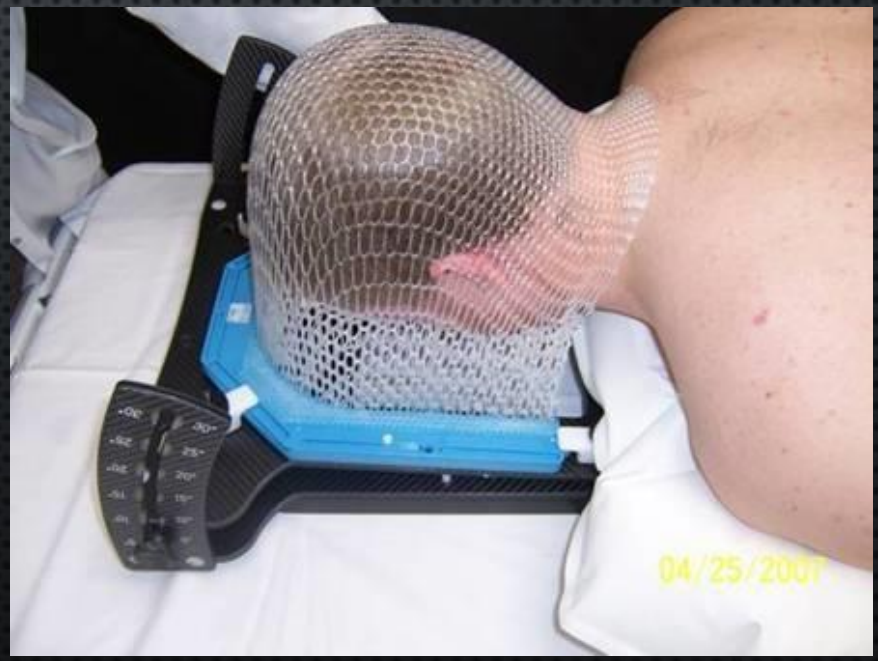
IMMOBILIZATION

Prone position:

Neck neutral to hyperextended
Arms by the side on a CSI board
Base plate with prone head and chin rest
Slots from A to E to allow various degrees of extension of neck
Thermocol wedge for supporting chest



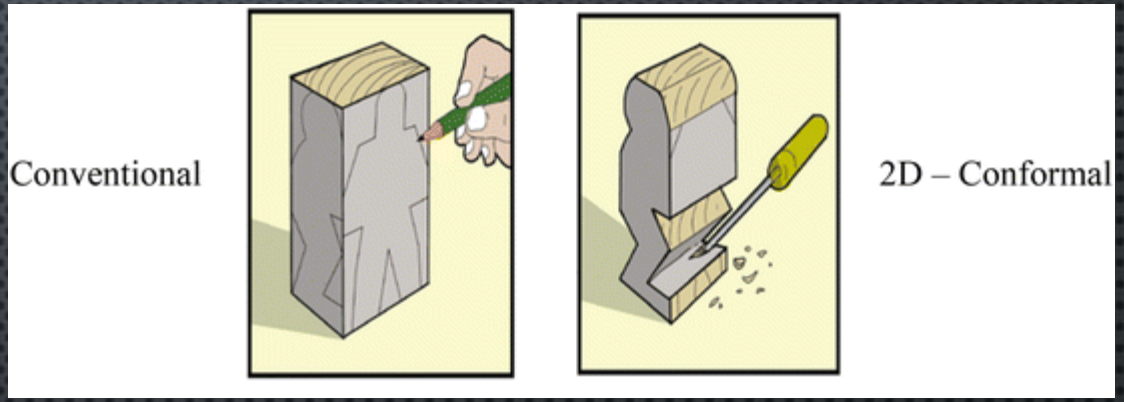
Prone Head Rest with Vacuum supports for trunk

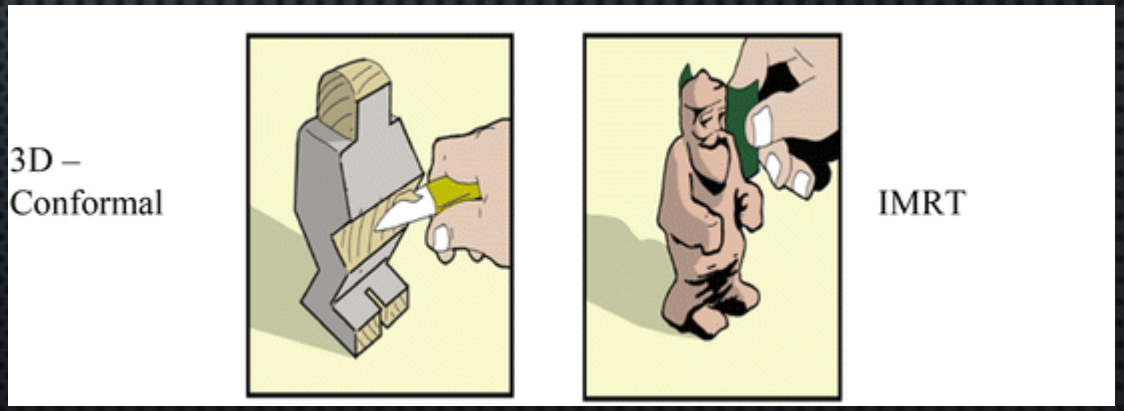


RT PLANNING

2D Fluoroscopic Simulation

3D CT based Volume delineation & Conformal dose delivery





2D SIMULATION AND FIELD PLACEMENT

CSI Fields:

- **Two lateral opposed cranial fields**
- **One or Two spinal fields**

Issues in Planning:

- **Divergence of Cranial and Spinal fields**
- **Field matching at junctions**

- Spinal field simulated first (get to know the divergence of the spinal field)
- SSD technique
- 2 spinal fields if the length is > 36 cm
- Upper border at low neck
- Lower border at termination of thecal sac or S2 /3 junction whichever is lower
- In case of 2 spinal fields , junction at L2/L3

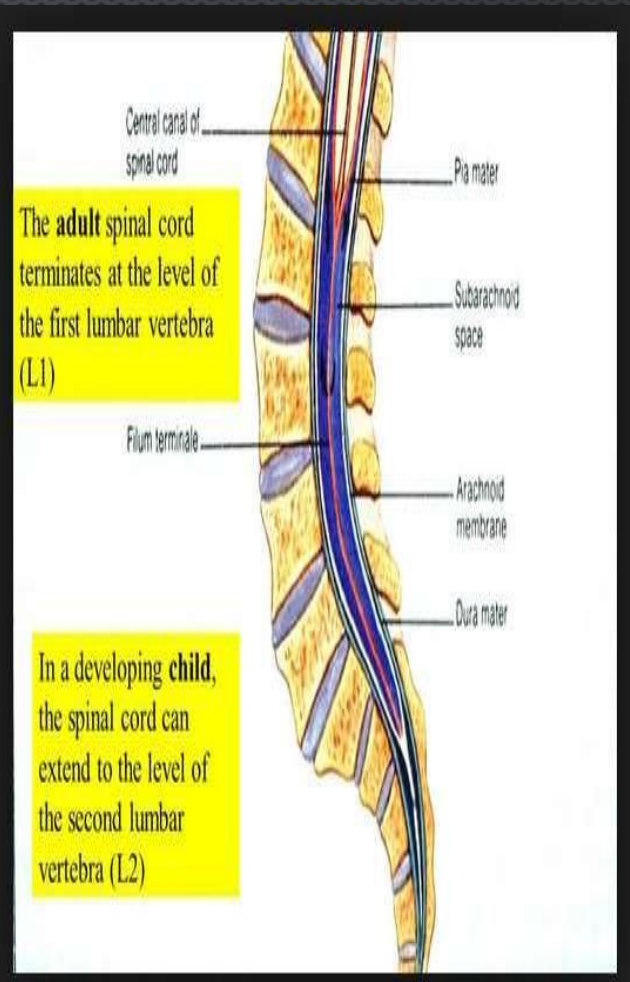
Junction of Cranio-Spinal Field:

Higher level - C1/C2 interspace, since overdose at cord is low as compared to low junction

Lower level - lowest level in the neck with exclusion of the shoulders in the lateral fields (from C5 to C7), lowers the exit dose to thyroid, mandible, larynx & pharynx

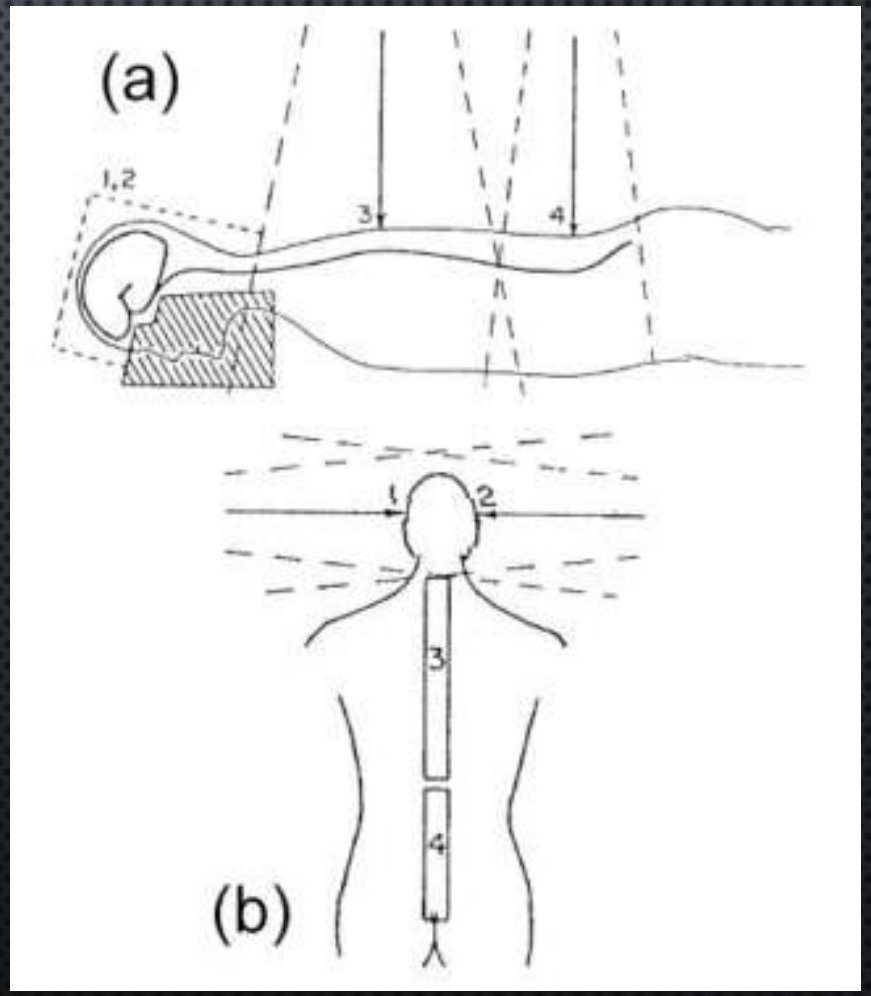
TERMINATION OF THECAL SAC

- **Traditional recommendation for lower border of spinal field is inferior edge of S2 (myelogram & autopsy studies).**
- **8.7% patients have termination below S2-S3 interspace.**
- **MRI accurately determines the level of termination of the thecal sac**
  - SA space ends at
    - S2 - 66%
    - S1 - 17%
  - **Recommendation: S2-S3 junction (covers 83%)**

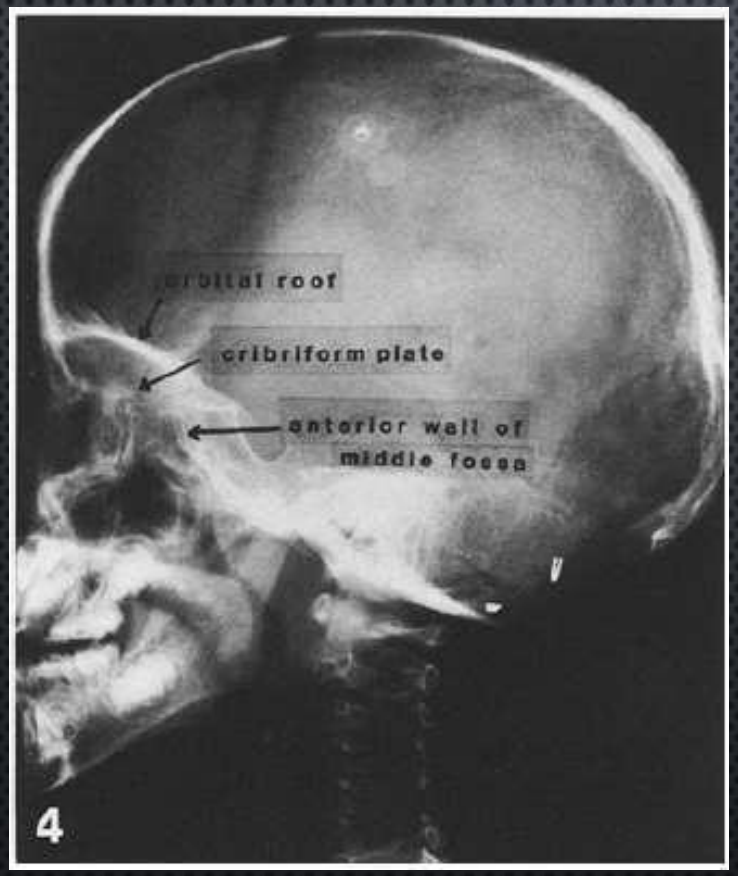


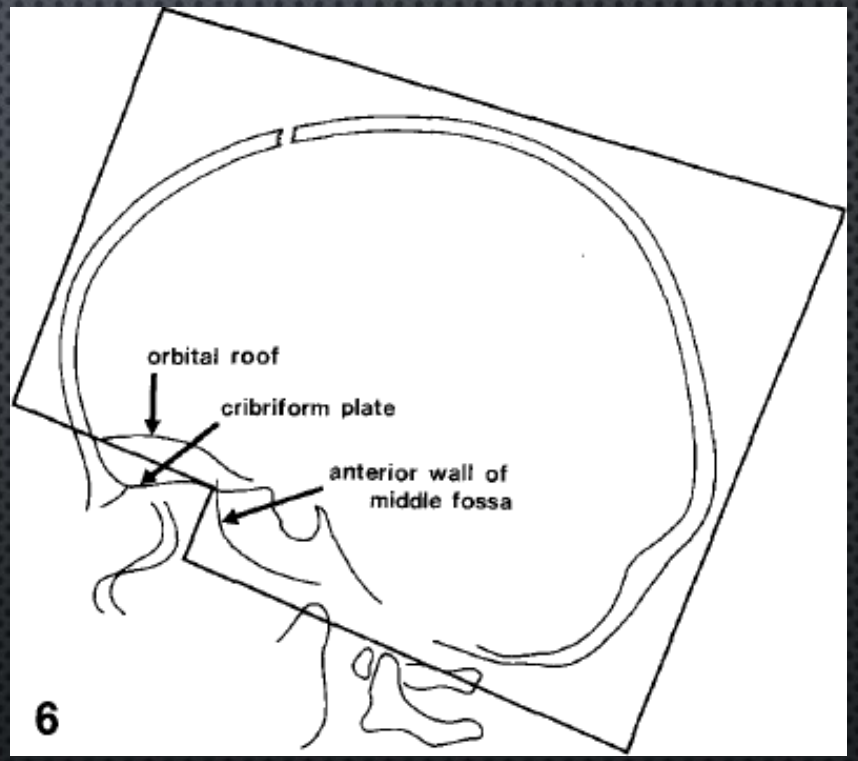
FIELDS TO ENCOMPASS TARGET VOLUME

- Phase I : Craniospinal radiotherapy (two parallel opposed lateral cranial fields orthogonally matched with the posterior spinal field to cover the entire length of the spinal cord)
- Phase II : Posterior fossa boost (whole posterior fossa irradiation or conformal boost to tumour bed)



CRANIAL FIELD





The lower border for a conventional cranial field if used with a block will result in a miss of the cribriform plate

Shielding

MORE IMPORTANT IS WHAT NOT TO SHIELD !

- Frontal (cribriform plate)
- Temporal region

Underdosage of basal areas, over generous use of eye shield, leads to higher supratentorial relapses

ELSEVIER

Int. J. Radiation Oncology Biol. Phys., Vol. 37, No. 3, pp. 523–529, 1997

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PII S0360-3016(96)00569-X

● *Clinical Investigation*

PEDIATRIC MEDULLOBLASTOMA: RADIATION TREATMENT TECHNIQUE AND PATTERNS OF FAILURE

RAYMOND MIRALBELL, M.D.,* ARNOLD BLEHER, M.D.,† PIA HUGUENIN, M.D.,‡ GERHARD RIES, M.D.,§ ROGER KANN, M.D.,‖ RENÉ O. MIRIMANOFF, M.D.,¶ MARKUS NOTTER, M.D.,# PHILIPPE NOUET, B.Sc,* SABINE BIERI, M.D.,* PETER THUM, M.D.** AND HECHMAT TOUSSI, M.D.††

Table 2. Medulloblastoma: first site of failure

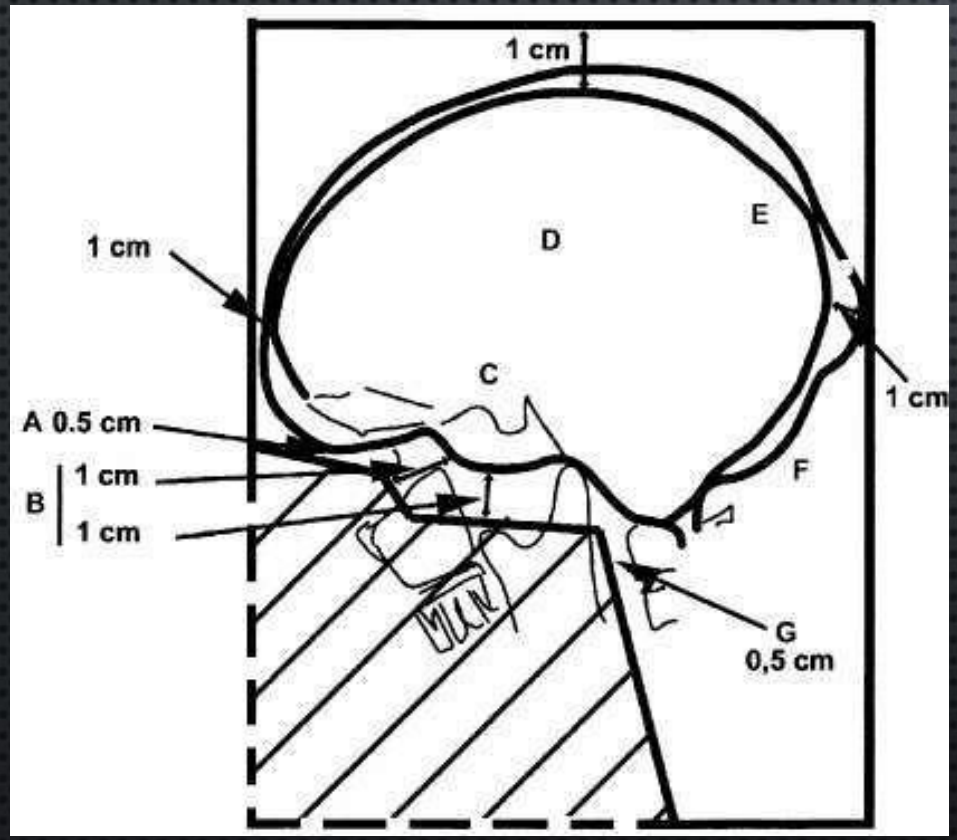
Posterior fossa	15 (31)
Supratentorial	12 (24)
Posterior fossa + supratent.	4 (8)
Spine	3 (6)
Posterior fossa + spine	3 (6)
Supratent. + spine	3 (6)
Posterior [illegible] + supratent. + spine	2 (4)
[illegible]s	7 (14)

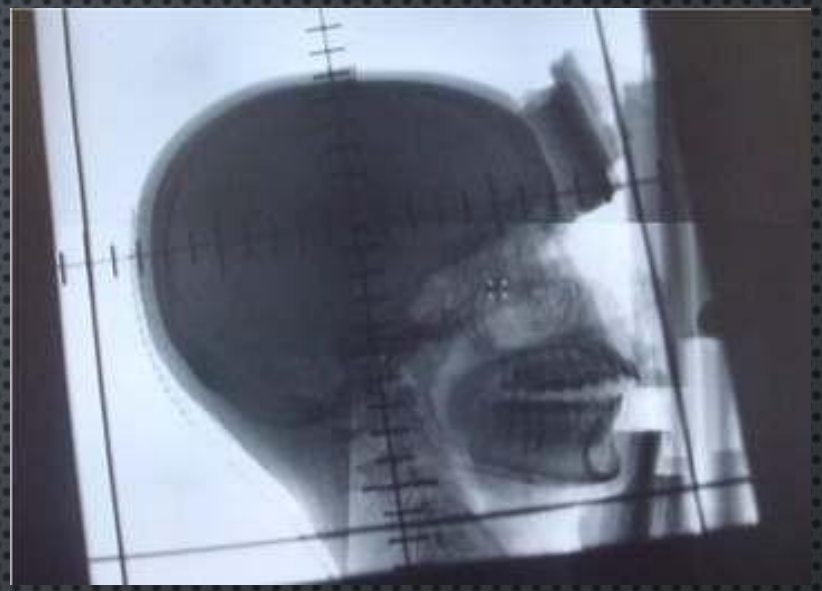
[illegible]nts and (%) rates.

Table 3. Supratentorial only failures: subsites of failure

Subfrontal	5 (42)*
Subtemporal	1 (8)
Subfrontal & subtemporal	2 (17)
Intraventricular	2 (17)
Hypothalamic	1 (8)
Diffuse meningeal	1 (8)

CRANIAL FIELD

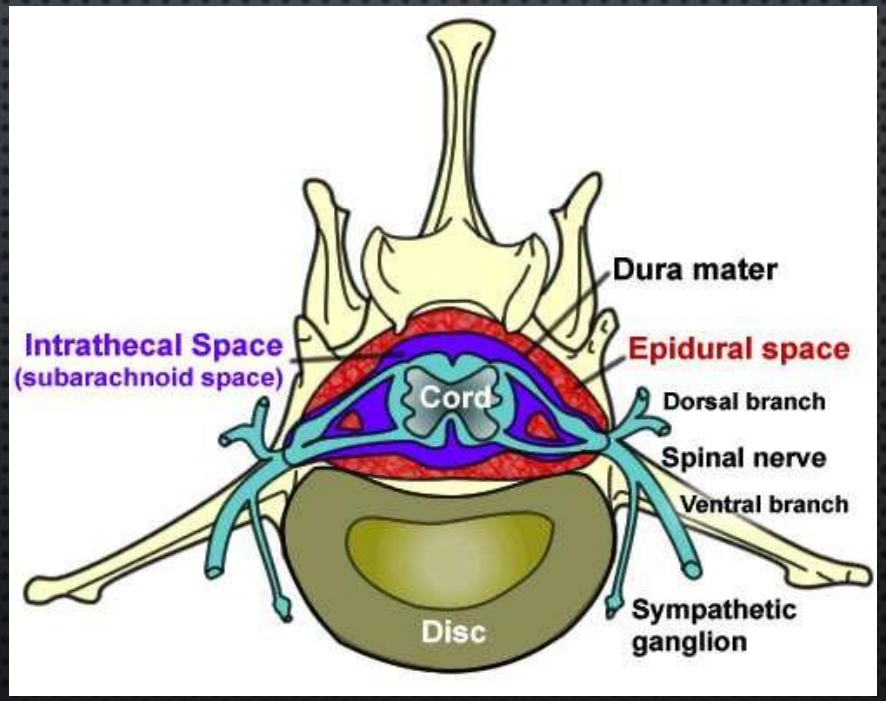


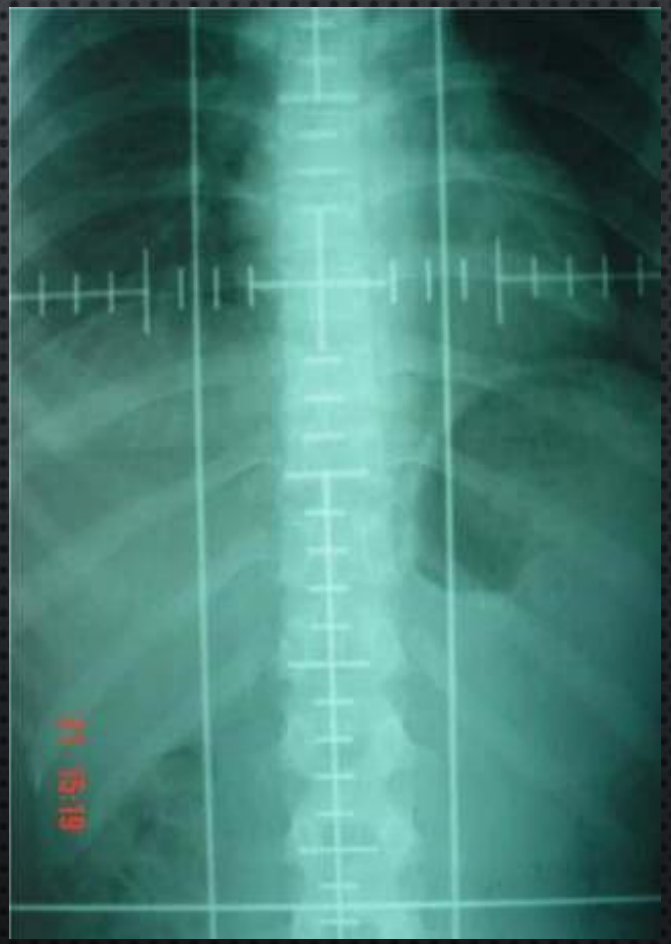


Shielding: SFOP guidelines are less stringent
The recommended placement of block is:
– 0.5 cm below the orbital roof
– 1 cm below and 1 cm in front of the lower most portion of the temporal fossa
– 1 cm away from the extreme edges of the calvaria.
– Note the flexion of the head.
Customized blocks are better than MLCs

SPINAL FIELD TARGET VOLUME

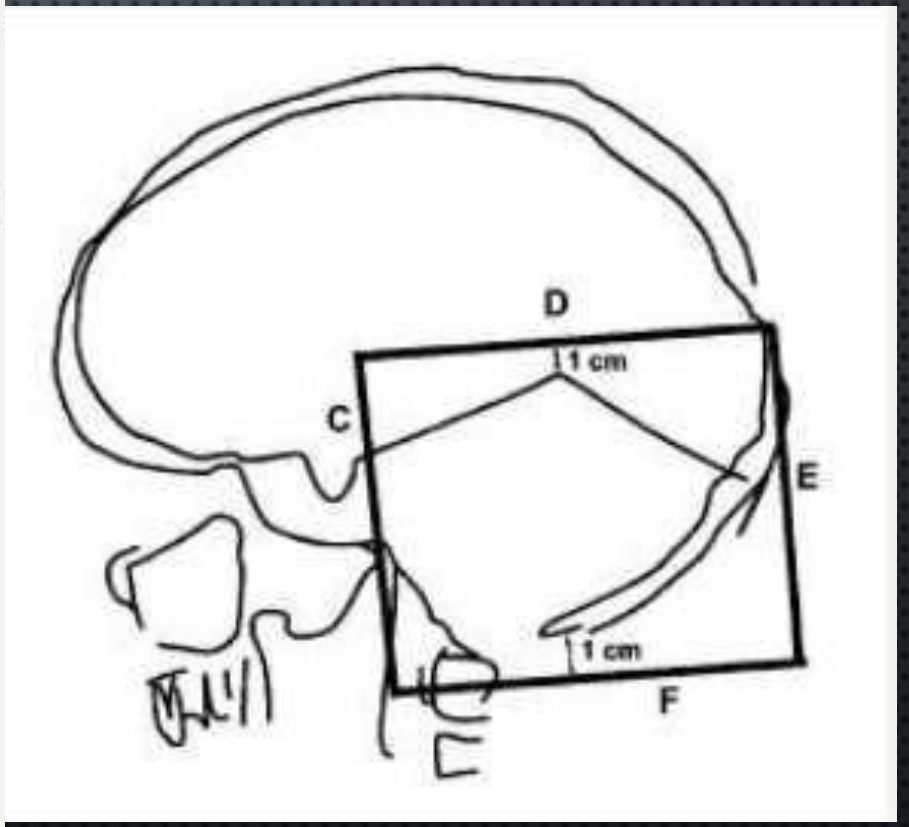
- WIDTH : VERTEBRAL BODY + 1 CM TO INCLUDE THE INTERVERTEBRAL FORAMINA , USUAL WIDTH 5 - 7 CM
- TO ENSURE THAT THE NERVE ROOT MENINGES EXITING FROM THE INTERVERTEBRAL FORAMINA ARE ADEQUATELY COVERED





BOOST- 2D PLANNING (POSTERIOR FOSSA)

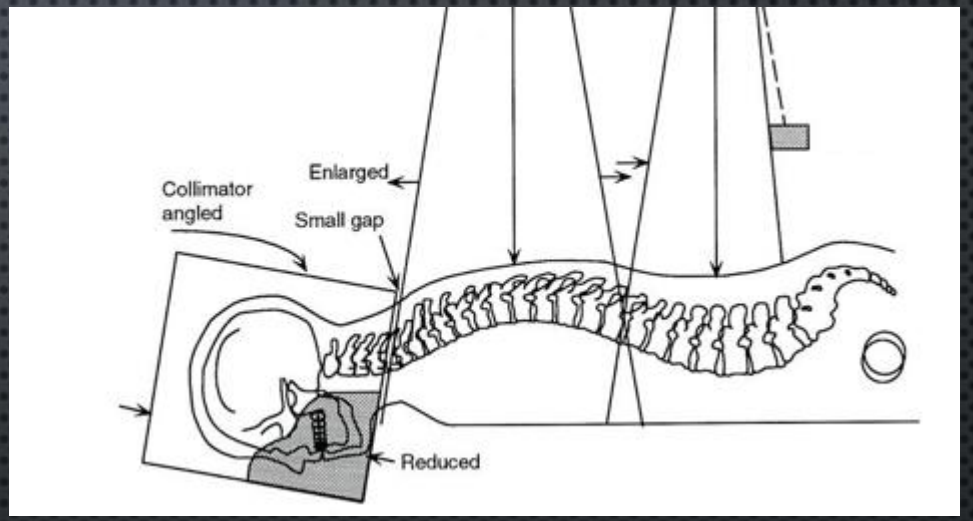
- **Field arrangement** - two lateral opposing fields
- **Anterior:** Posterior clinoid process (avoid pituitary)
- **Posterior:** Internal occipital protuberance
- **Inferior:** C1-C2 interspace
- **Superior:** Midpoint of foramen magnum & vertex or 1cm above the tentorium (as seen on MRI)



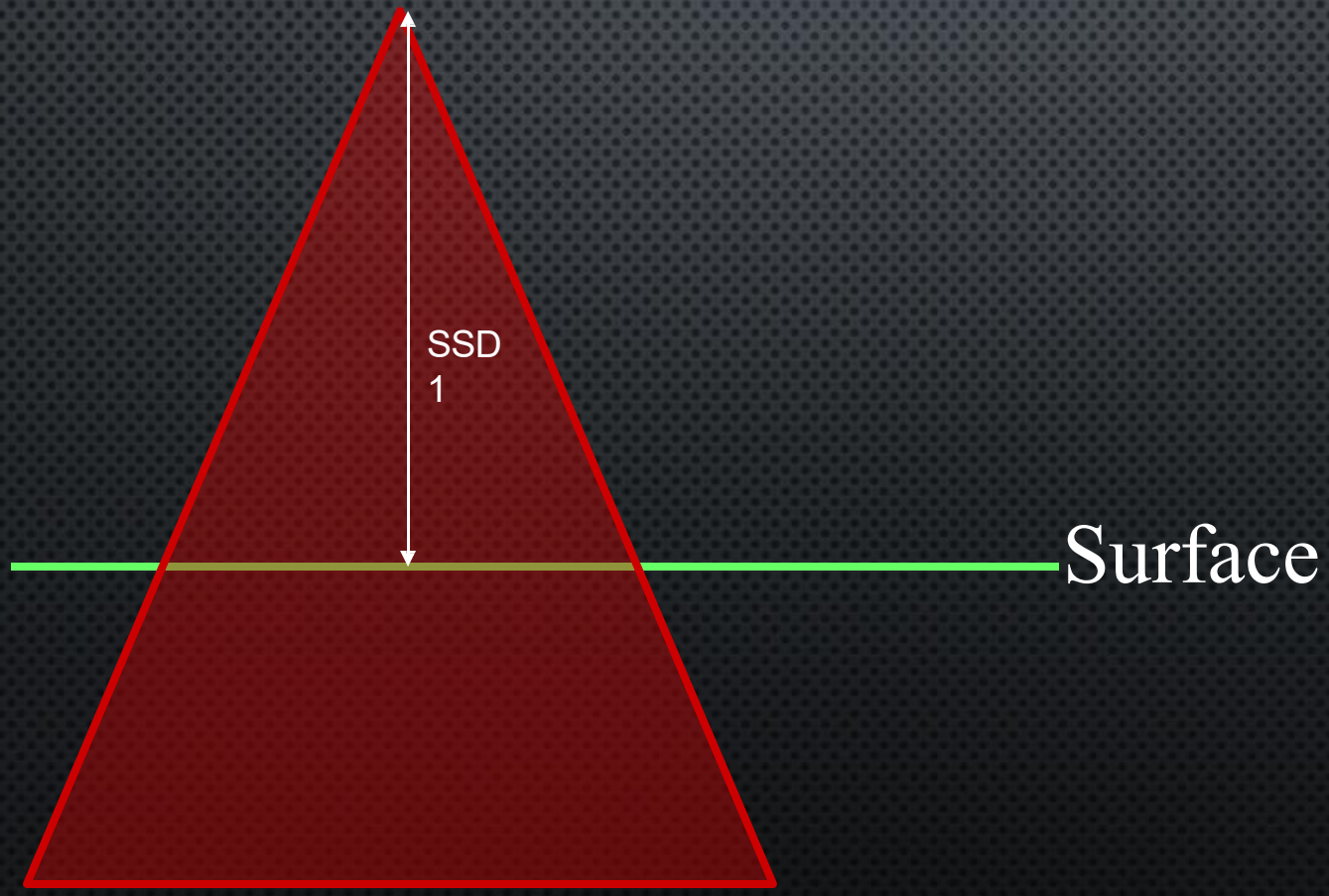
Gap vs No Gap?

- Medulloblastoma being a radiosensitive tumor, small reduction in dose per fraction or total dose to part of TV, owing to a gap, may produce significant difference in cell kill over a fractionated course of CSI, seen as local recurrences (*Tinkler, IJROBP 1995*)

- No gap risks overdose at the junction & cervical spine & may result in disabling late toxicity

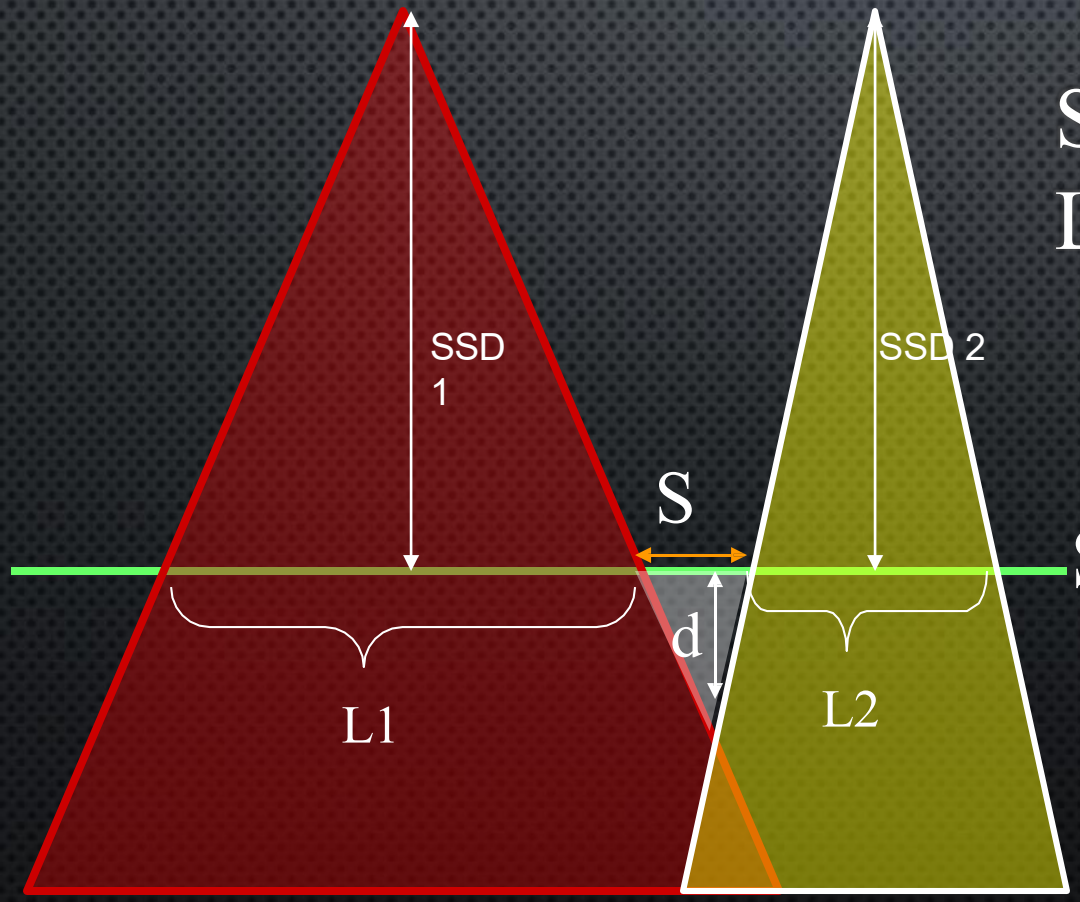


GAP CALCULATION-FORMULA



GAP CALCULATION-FORMULA

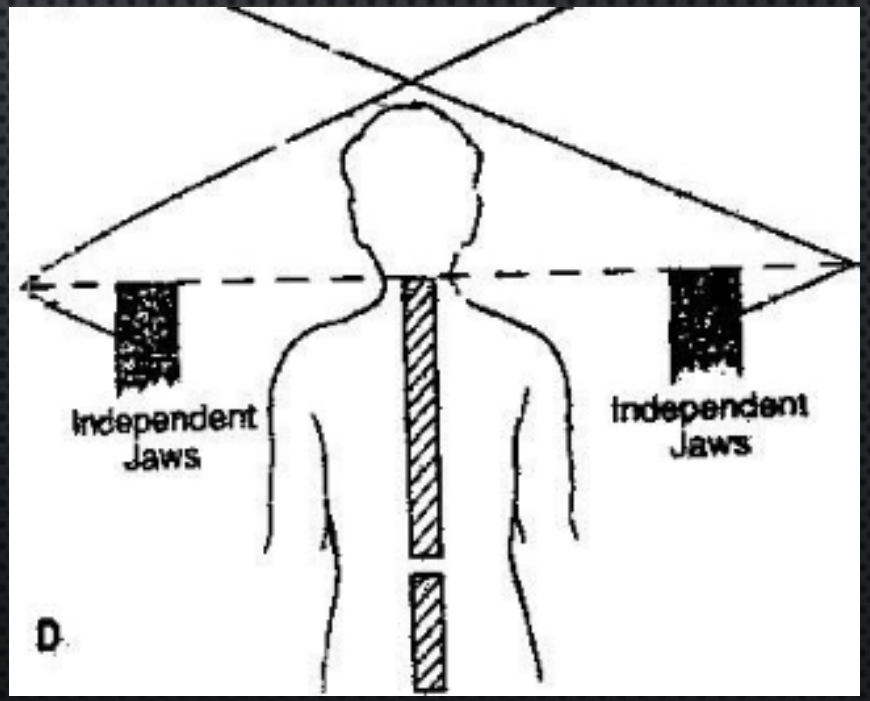
Gap calculation-formula



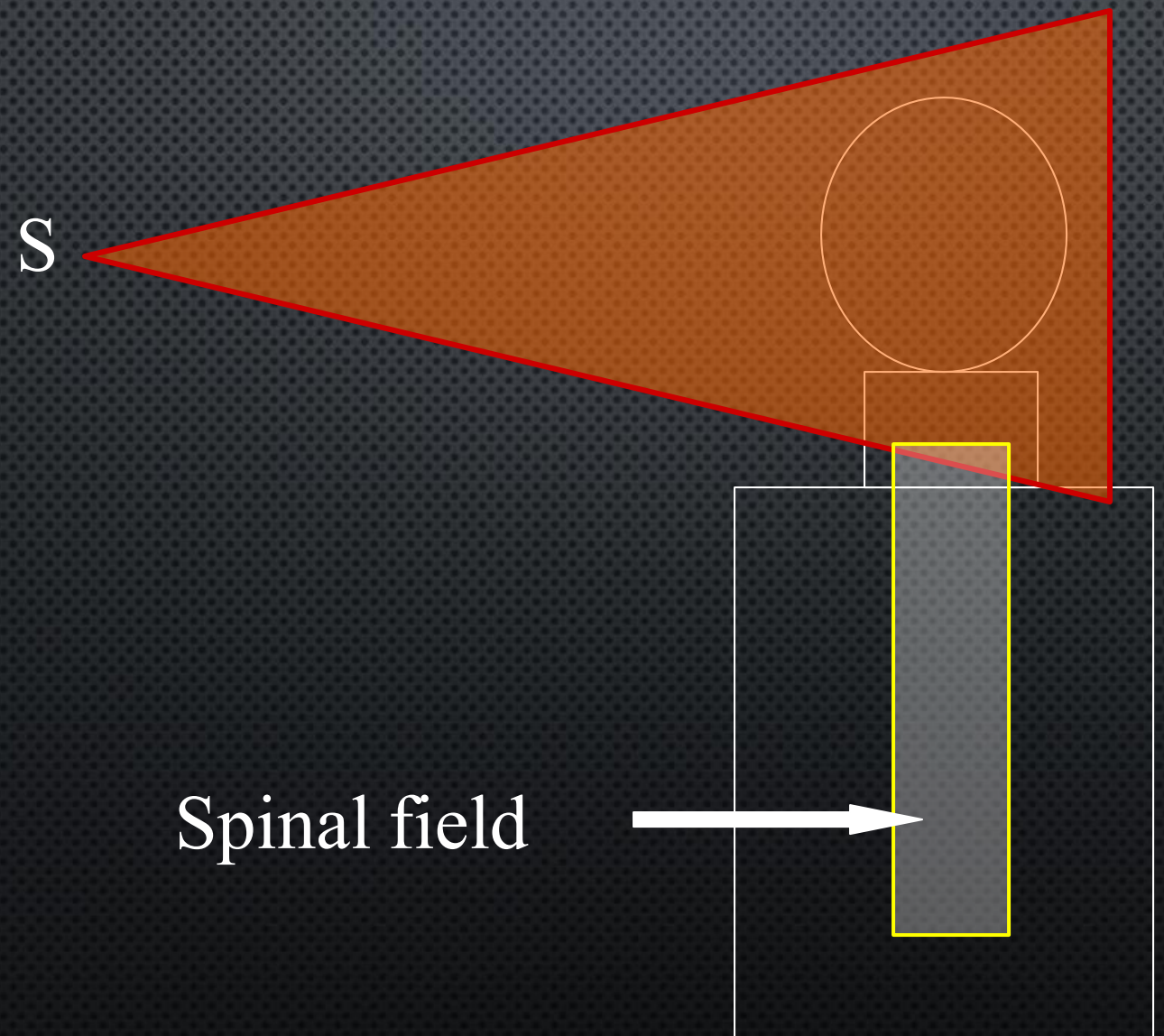
$$S = \tfrac{1}{2} L1(D/SSD1) + \tfrac{1}{2} L2(d/SSD2)$$

SIMULATION-CRANIAL FIELD

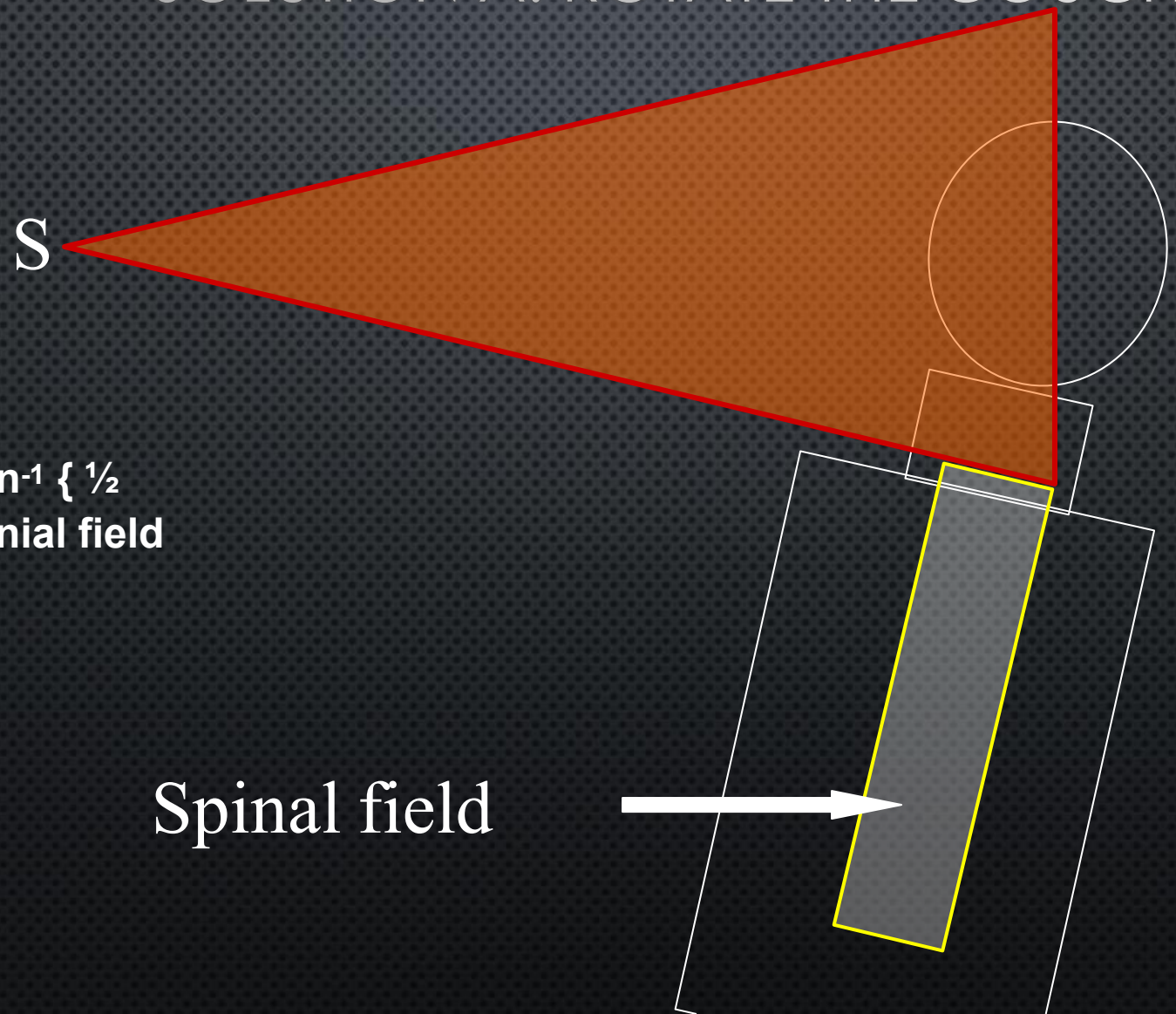
- Whole brain field is simulated & lower border is matched with the superior border of spinal field.
- AP width & superior border include the entire skull with 2 cm clearance.
- Techniques for matching craniospinal fields:
  - Collimator/couch rotation
  - Half beam block
  - Asymmetric jaws
  - Penumbra generators
  - Wedge
  - Tissue compensator

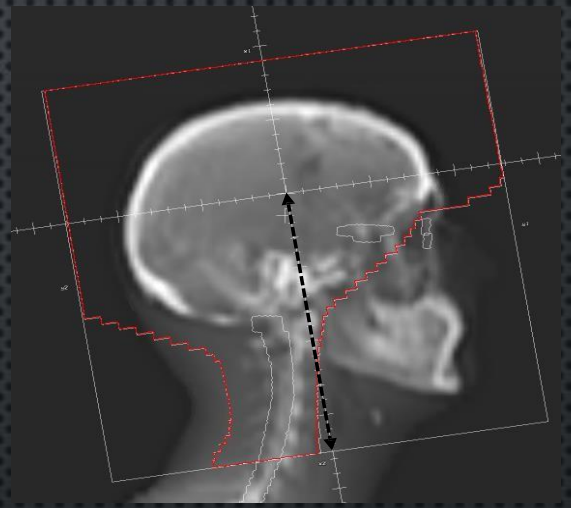


PROBLEM 1: DIVERGENCE OF CRANIAL FIELD



SOLUTION A: ROTATE THE COUCH





- **Couch angle = $\tan^{-1}$ { ½ L_2/SAD} L_2 is cranial field length**

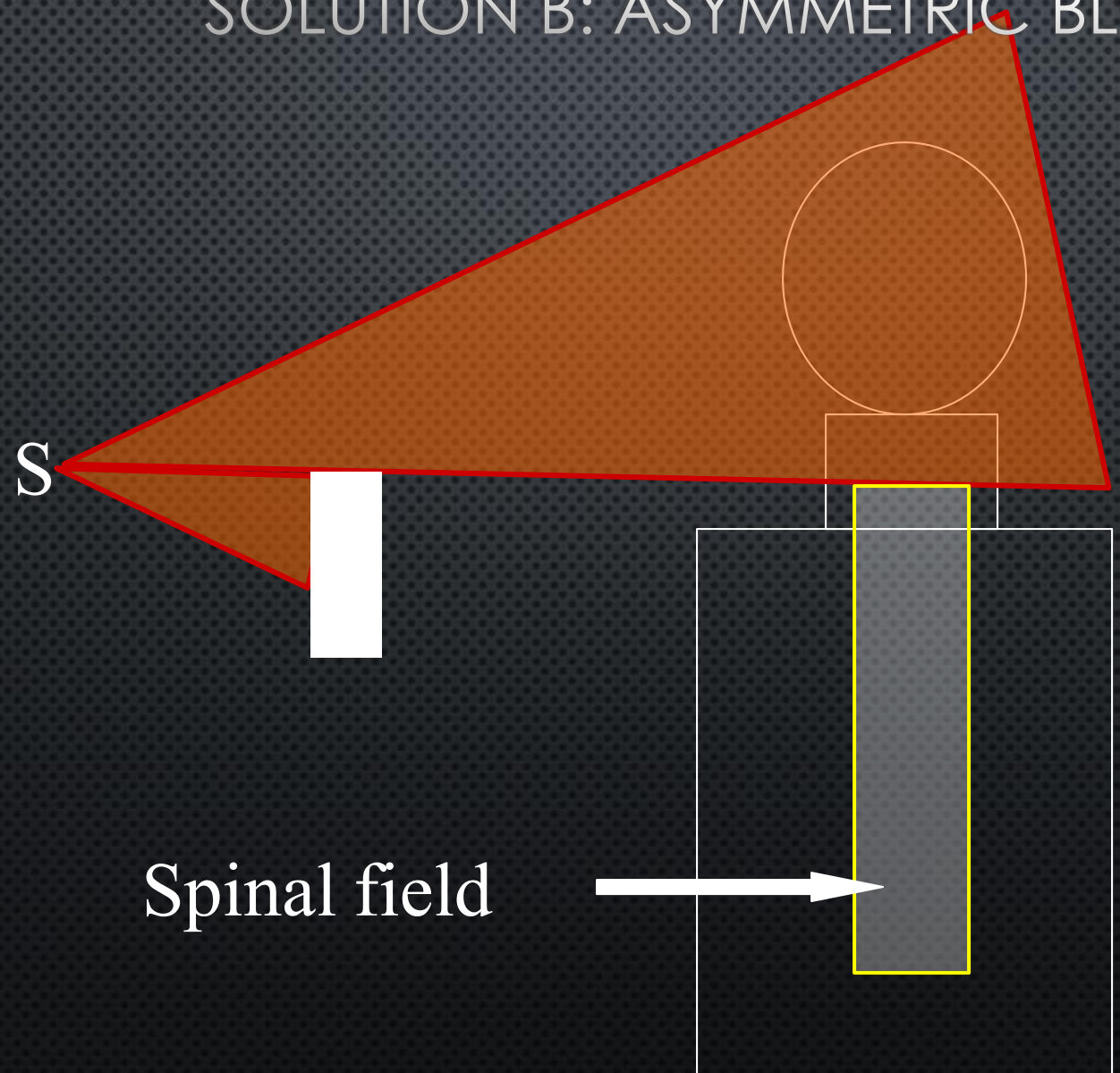
$$\tan a = \frac{y}{SAD}$$

$$\tan a = \frac{18\ cm}{100\ cm}$$

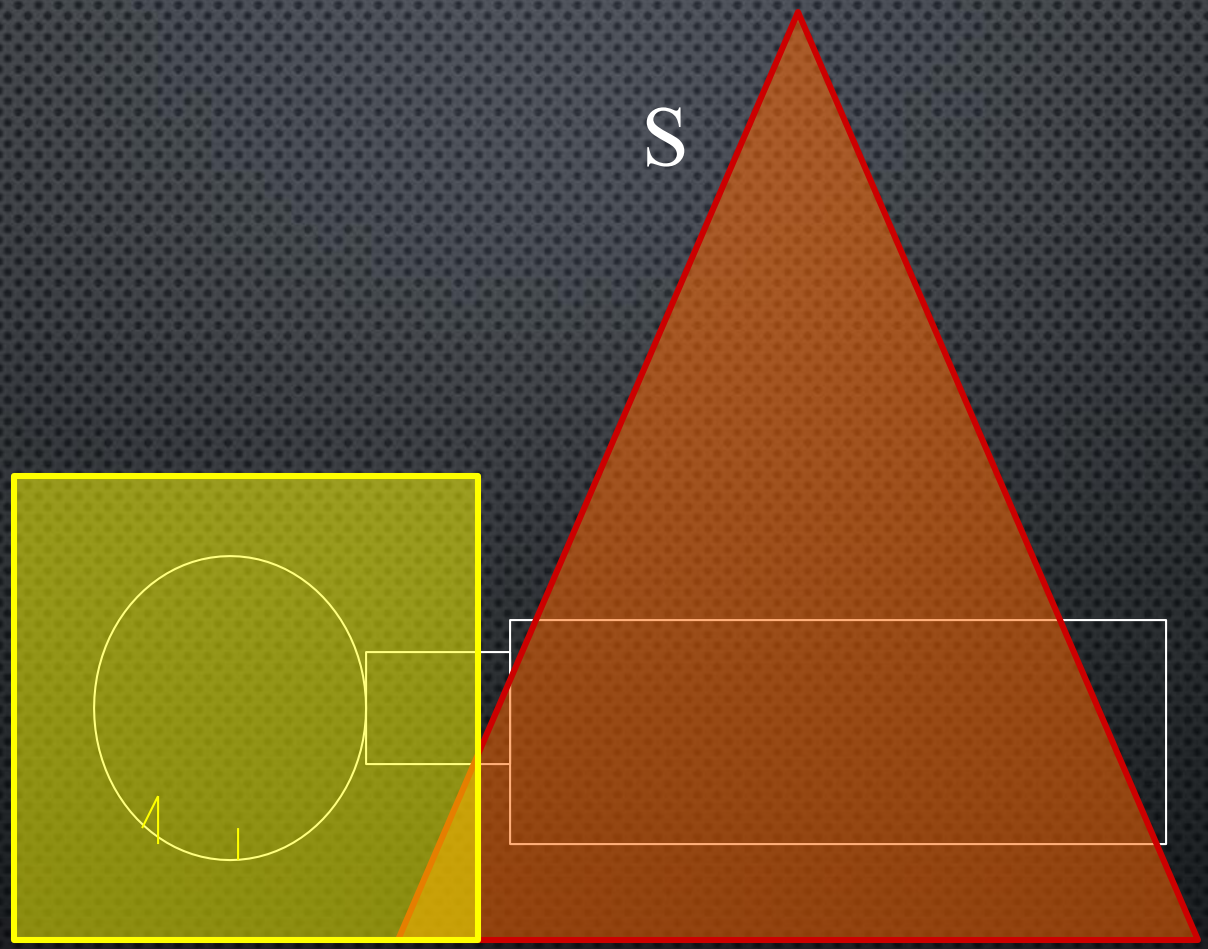
$$a = \tan^{-1}\frac{18\ cm}{100\ cm}$$

$$a = 10.2°$$

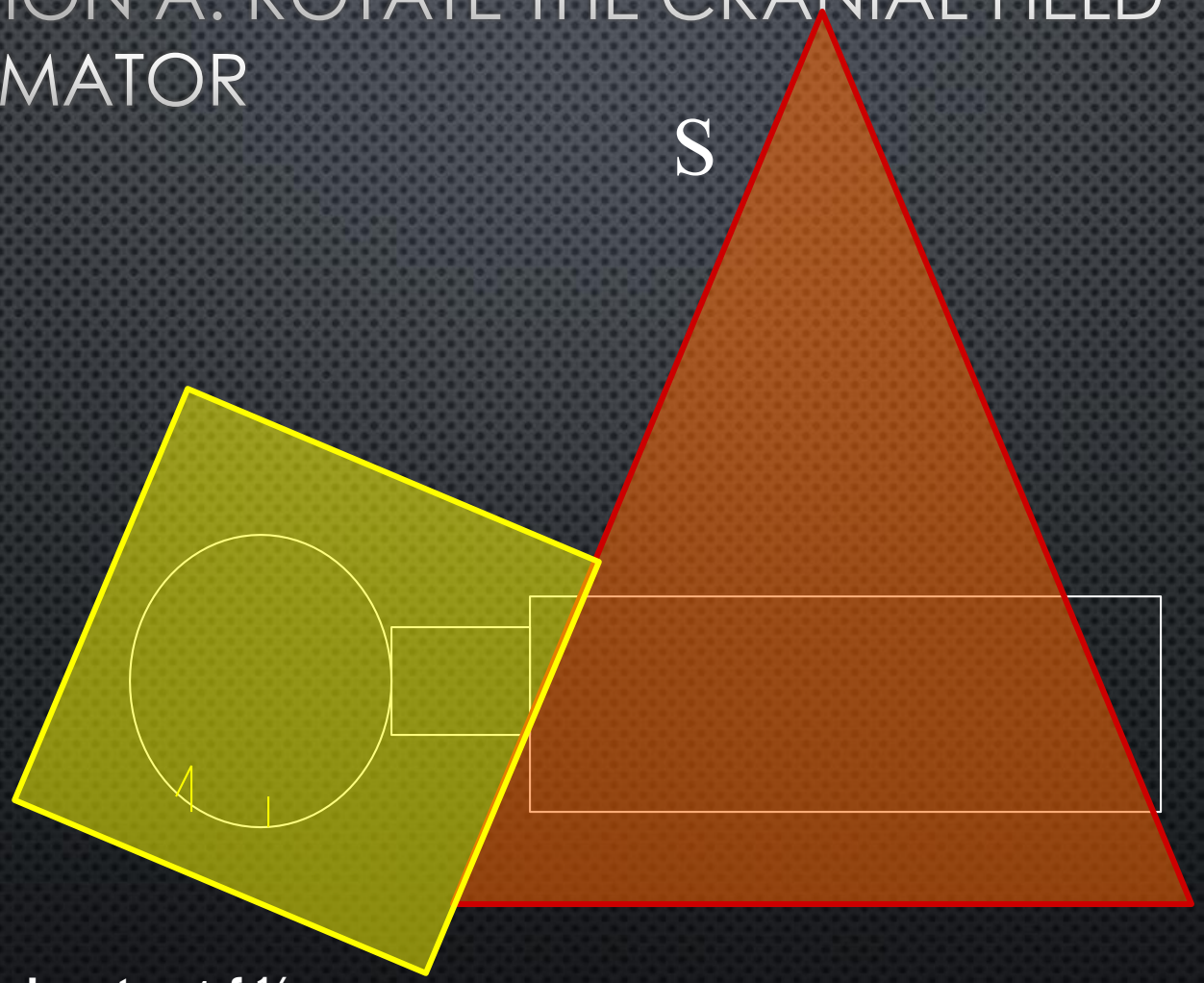
SOLUTION B: ASYMMETRIC BLOCK



PROBLEM 2 -DIVERGENCE OF SPINAL FIELD

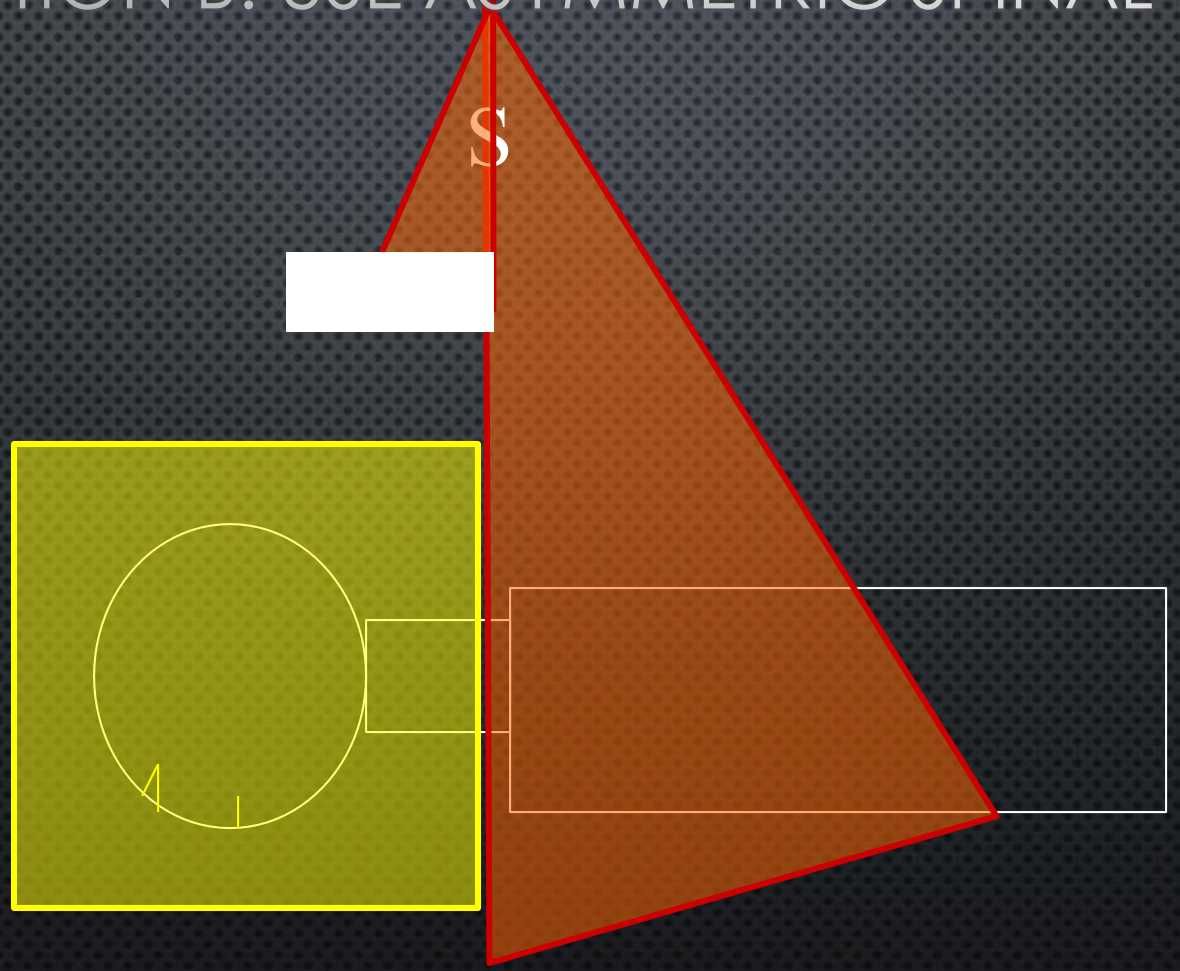


SOLUTION A: ROTATE THE CRANIAL FIELD COLLIMATOR



- **Cranial field Collimator angle = $\tan^{-1}$ { ½ L_1/SSD} L_1 is spinal field length**

SOLUTION B: USE ASYMMETRIC SPINAL BLOCK



CT SIMULATION- IS IT REQUIRED?

- Conventional Simulator films do not define:
  - Terminal location of the thecal sac.
  - Relationship between the optic globe and the cribriform plate.
- The cribriform plate may be located below or at the same level as the superior edge of the lens in 50% patients.
- Shielding the lens – underdosage of the cribriform plate.
- Nearly 25% of all recurrences occur in the supratentorial region.

CT SIMULATION-ADVANTAGES

- Virtual simulation of treatment fields without the patient.
- Better definition of critical organs and target volume.
- Graphical overlays of anatomic CT data onto digitally reconstructed radiographs (DRRs) and the viewing of all fields simultaneously in multiple CT-based planes improve field placement, matching, shielding accuracy & direct calculation of gap between the fields.

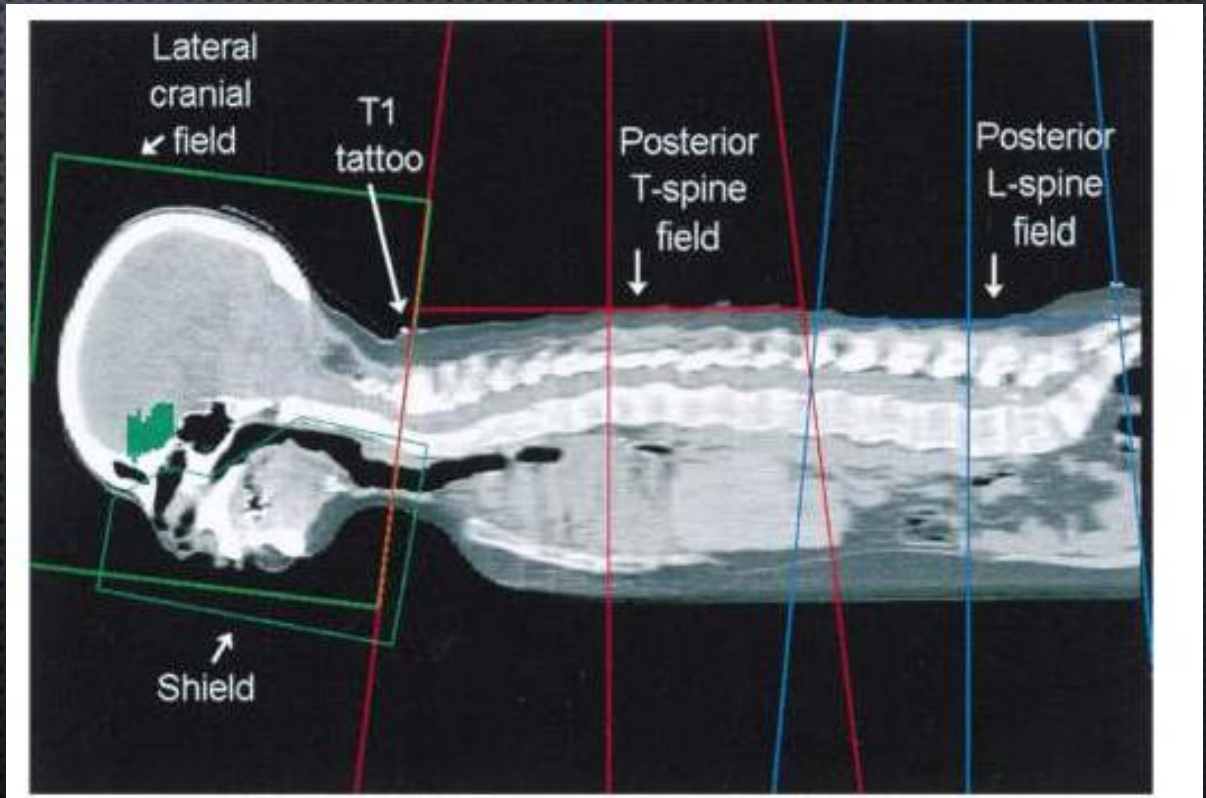
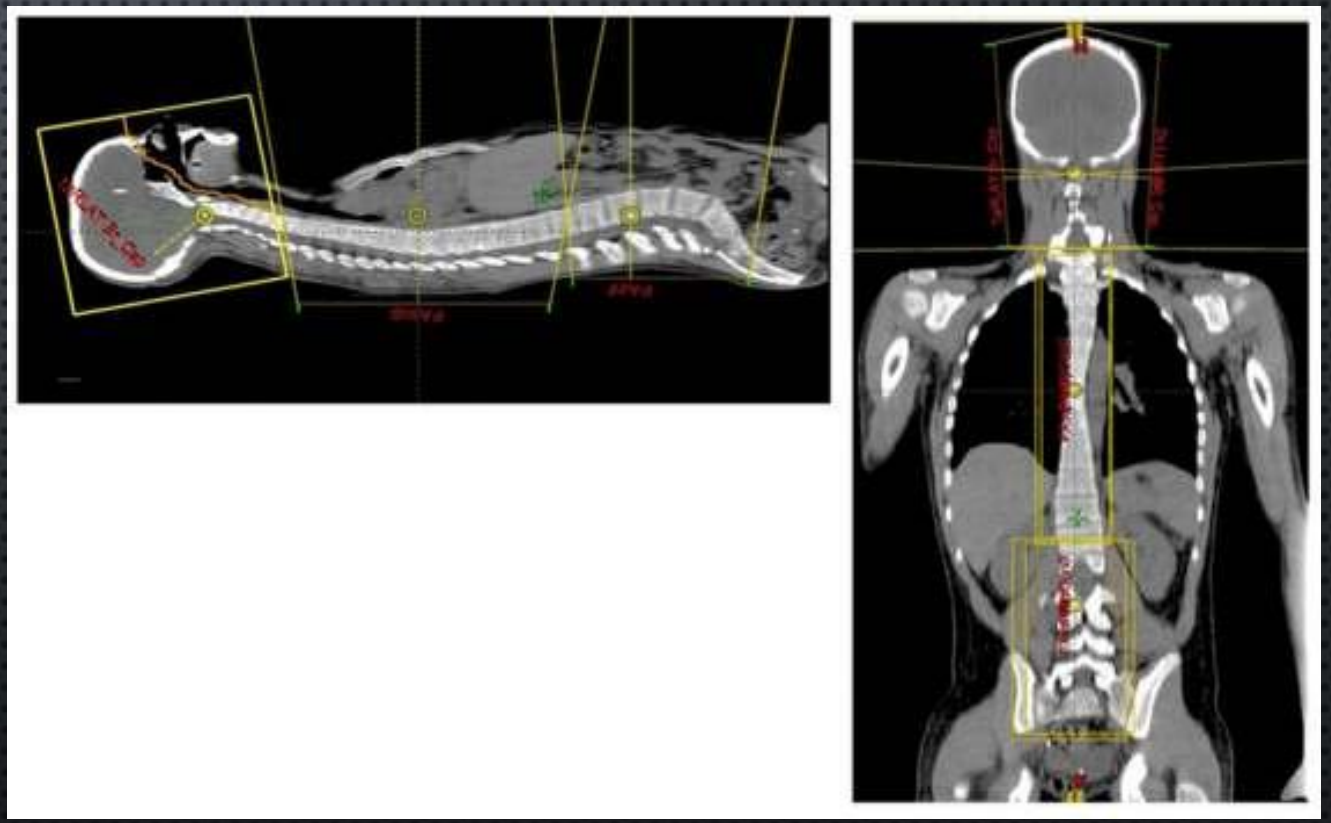


Fig. 2. A sagittal, isocentric, multiplanar reformatted (MPR) image of a 15-year-old male patient demonstrating virtual simulation of all fields and shielding. Accurate matching of the cranial and thoracic spine fields is achieved by interactive collimator rotation of the former directly on the workstation monitor.

STEPS IN CT SIMULATION

- Patient positioned using all ancillary devices and the spinal columns aligned with the sagittal external laser.
- Three-point reference marks drawn on the mask in a transverse plane at the center of the head with the aid of the external lasers.
- Two or three reference marks placed on the skin surface along the spinal column.
- Spiral CT images of 5 mm from the vault of skull – bottom of sacrum, with 3mm slices through the primary tumor/bed are acquired.
- Target volumes and organs at risk are contoured on images.
- Co-registered MRI and CT data sets are used for target volume delineation.

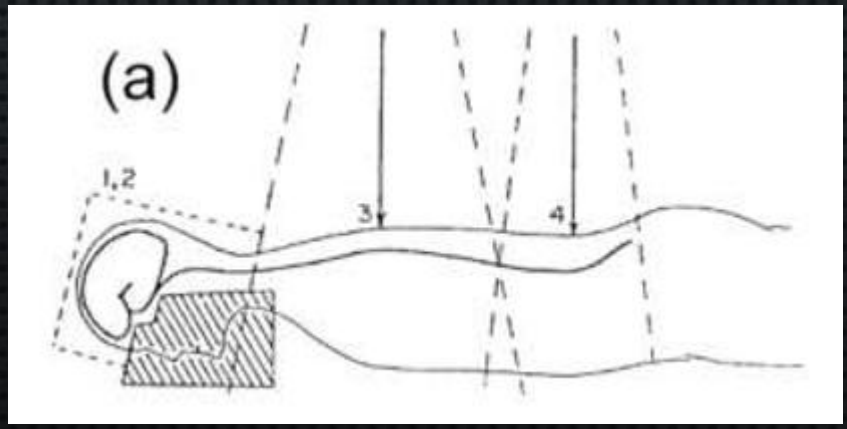


TREATMENT & VERIFICATION

- Port films after placing radio-opaque markers on the inferior border of cranial field can be used to verify craniospinal field matching.
- Electronic portal imaging has also played important role in verification & correction of set up errors.

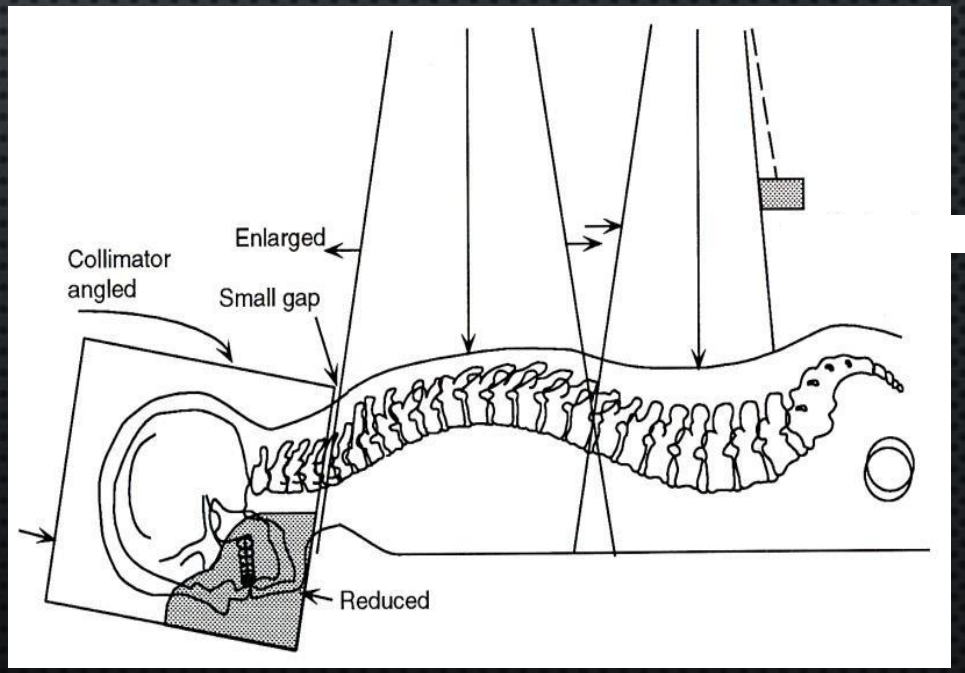
CRANIO-SPINAL JUNCTION: FIXED *VS* MOVING

- Owing to lateral scatter of photons & electrons, a gap on skin as defined by the light beam will be reduced by 1-2mm at depth (*Thatcher, 1989, IJROBP*).
- At doses relevant for medulloblastoma, a 5mm overlap at 4 MV photons can result in 30 to 40% overdose i.e. 14Gy for 36Gy prescribed dose, which may exceed cord tolerance (*Hopulka, 1993, IJROBP*)
- Systematic error during radiotherapy delivery could further lead to an overlap or gap. Acceptable systematic set up error for CSI is **2 mm**
- Concurrent CT recently being used for high risk patients can also result in long term neurotoxicity.

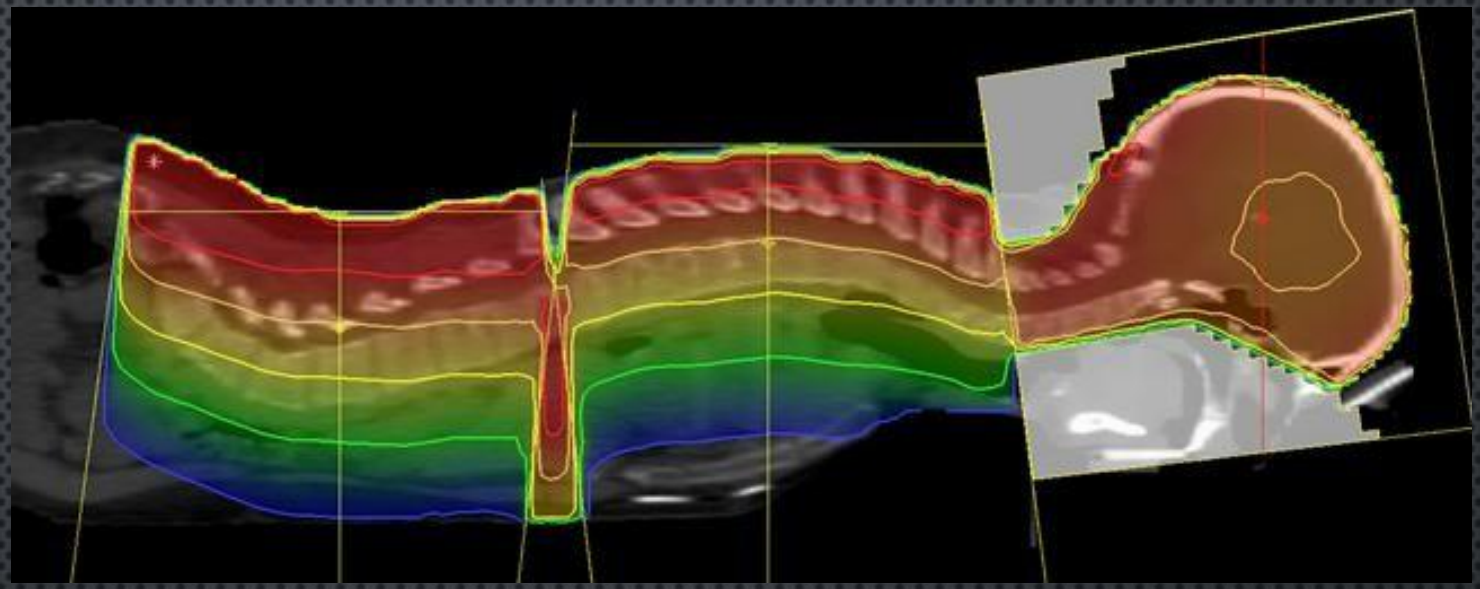


MOVING JUNCTION IN CSI

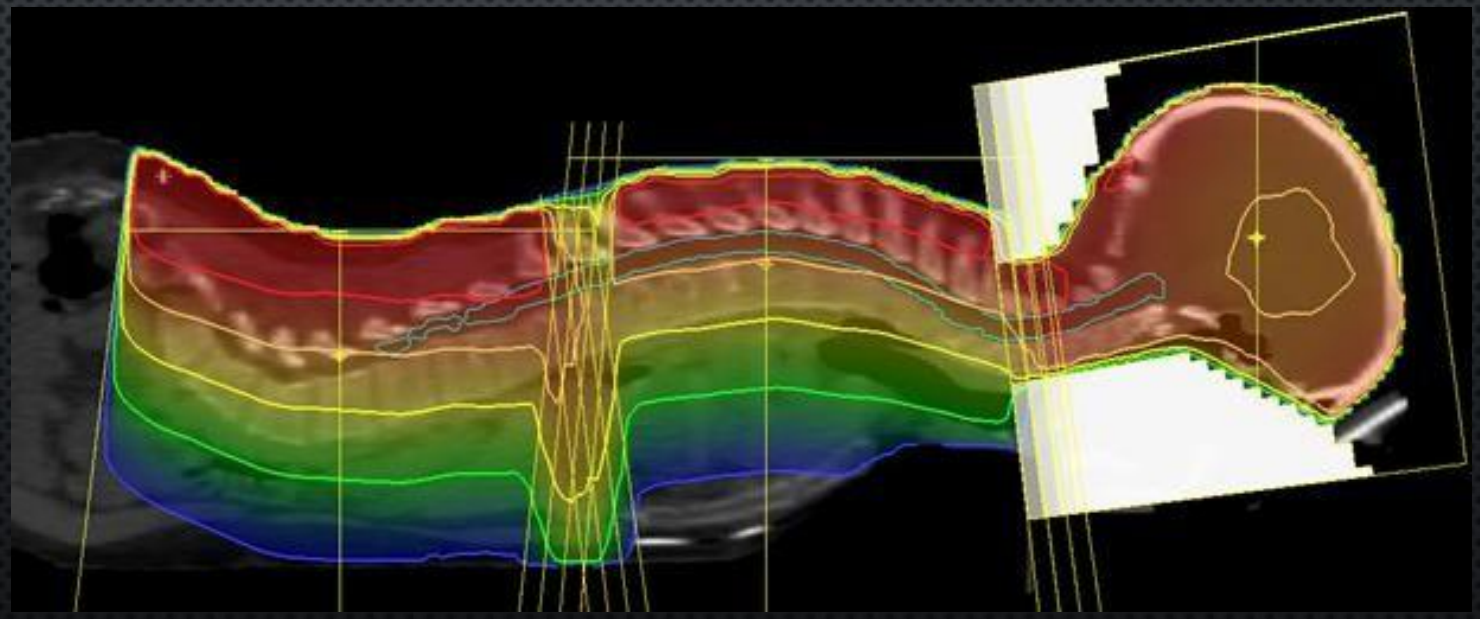
- Feathering after every 5 to 7 fraction (8-10 Gy) smoothes out any overdose or underdose over a longer segment of cord
  - Shift the field junction match lines throughout treatment
  - Needs to be accounted for during planning
  - Typically 1 cm shift



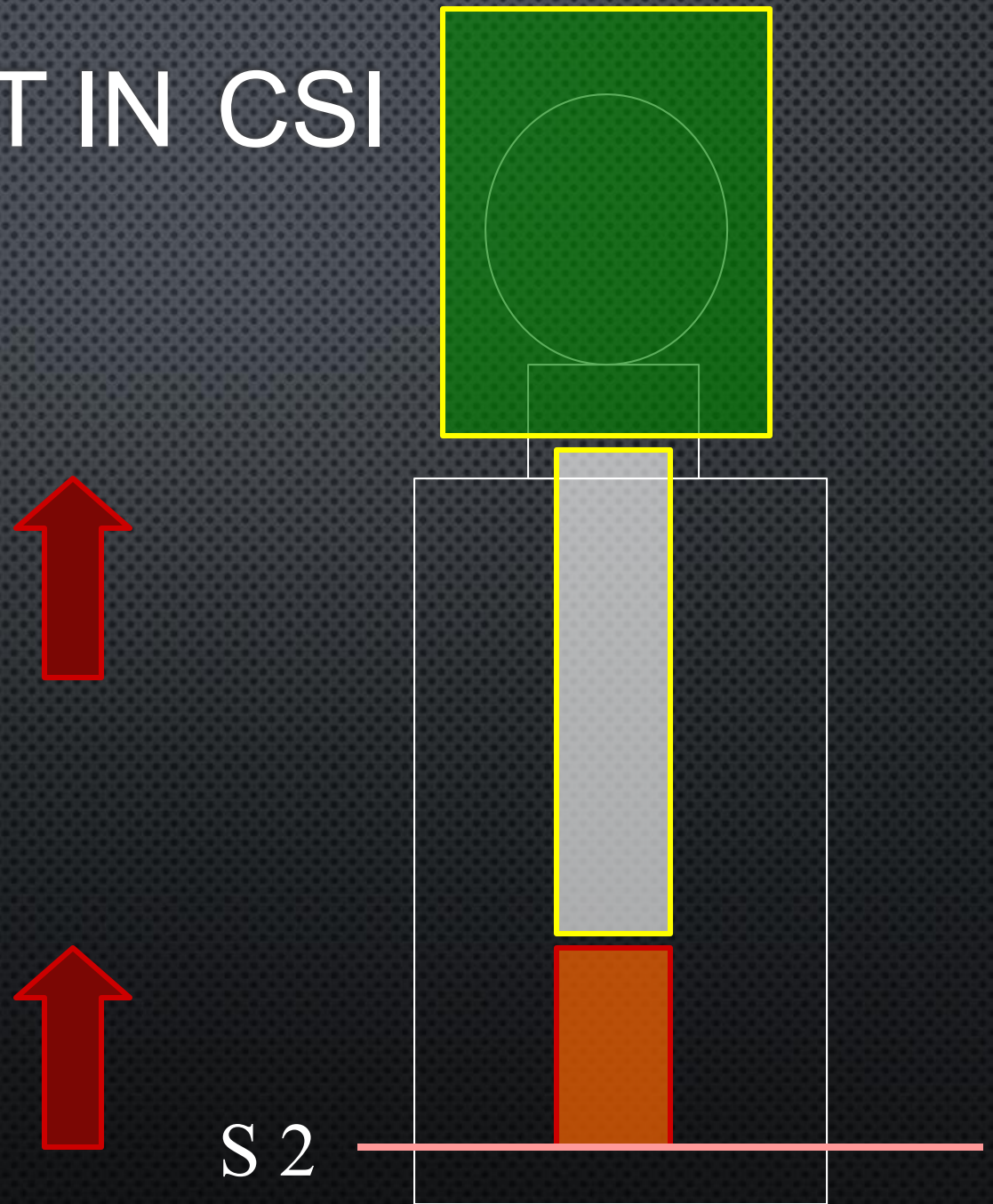
No feathering



With feathering

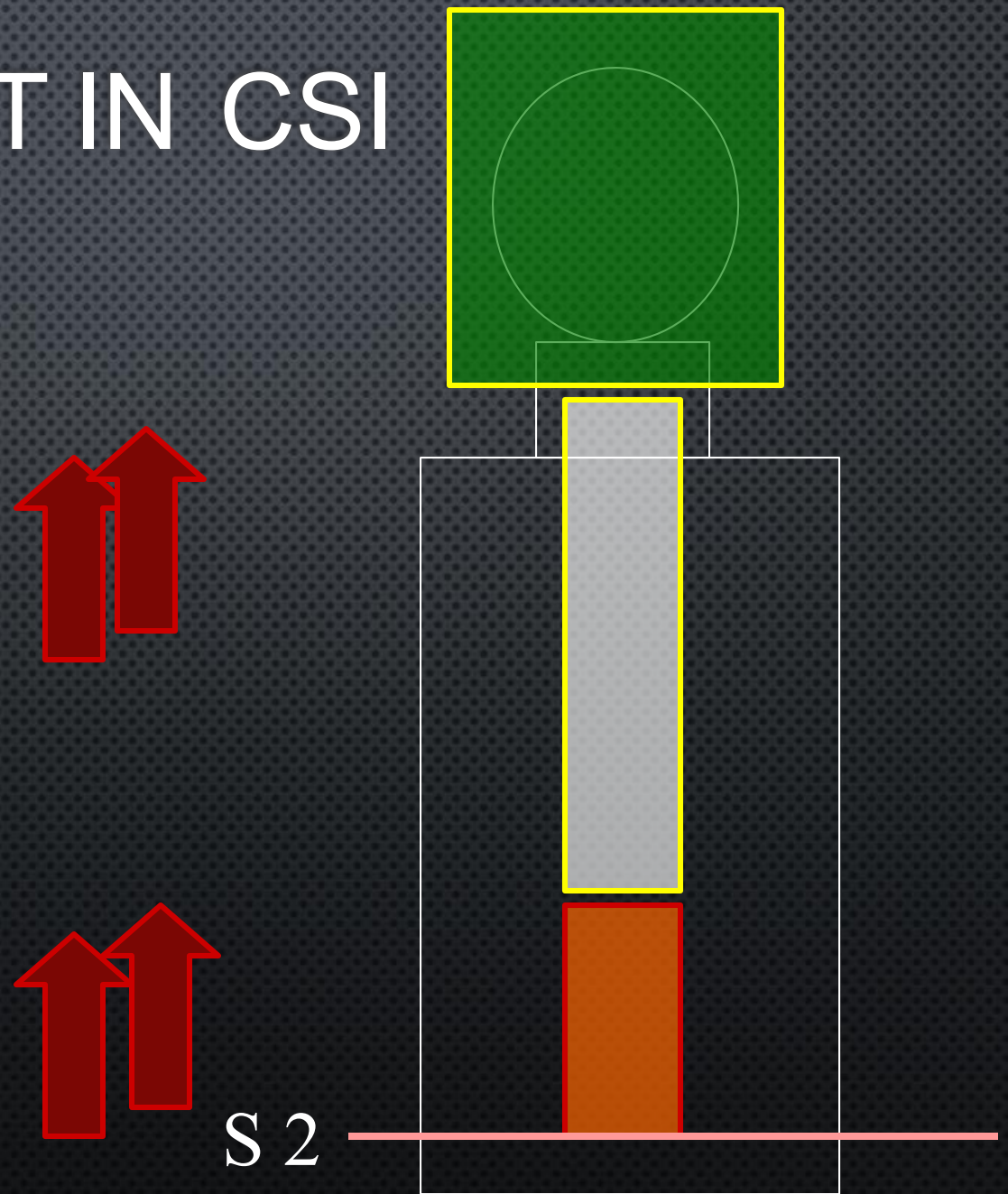


JUNCTION SHIFT IN CSI

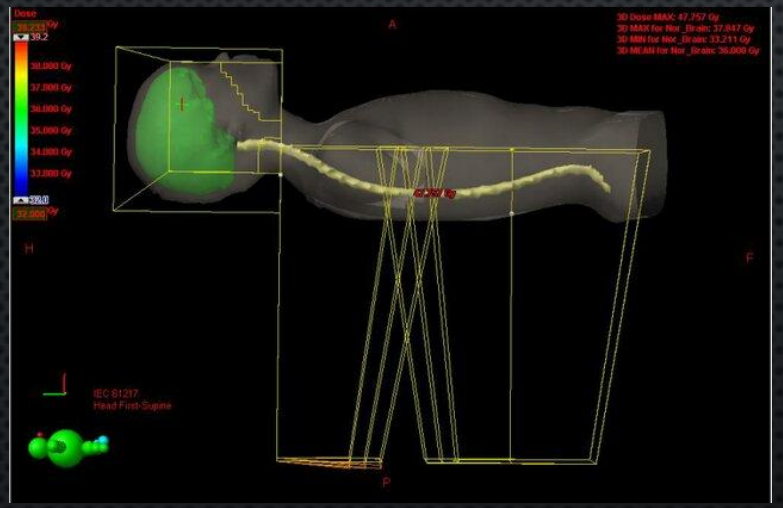


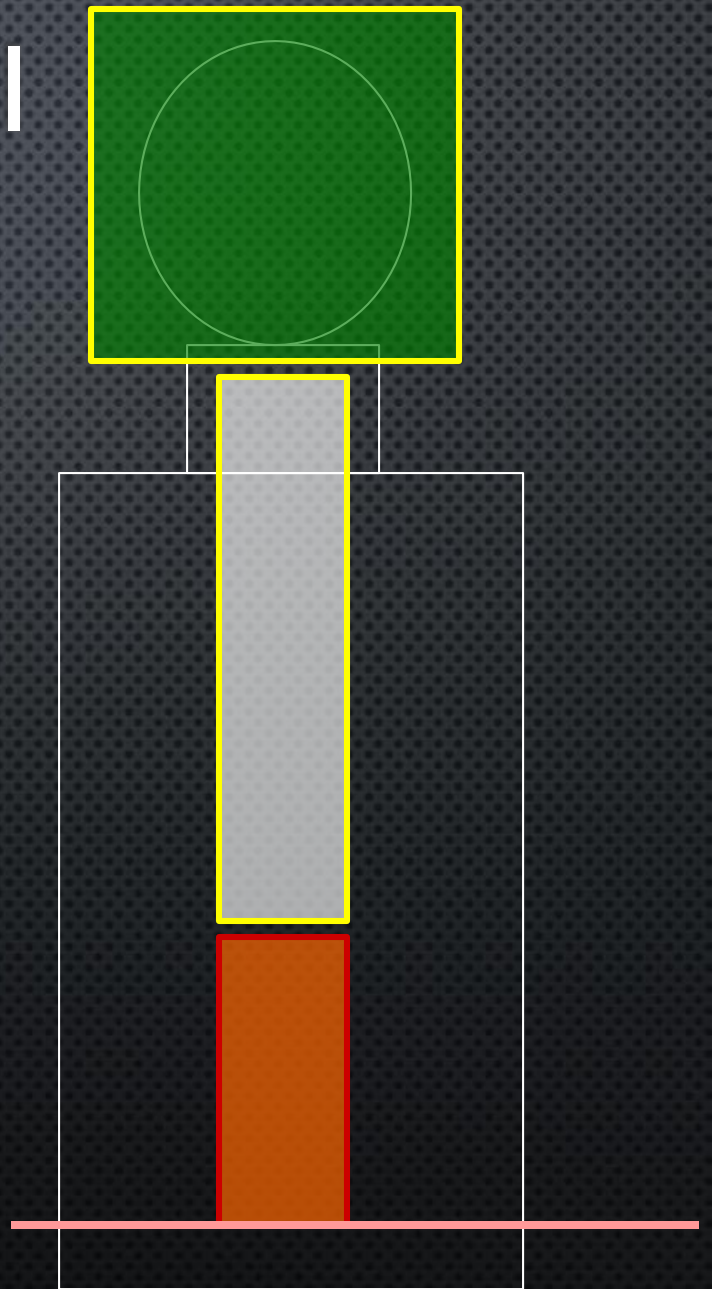
JUNCTION SHIFT IN CSI

- Cranial inferior collimator is closed & spinal superior collimator is advanced by the same distance superiorly (if junction to be shifted cranially)
- Similarly, lower border of superior spinal field & superior border of inferior spinal field are also shifted superiorly, maintaining the calculated gap between them



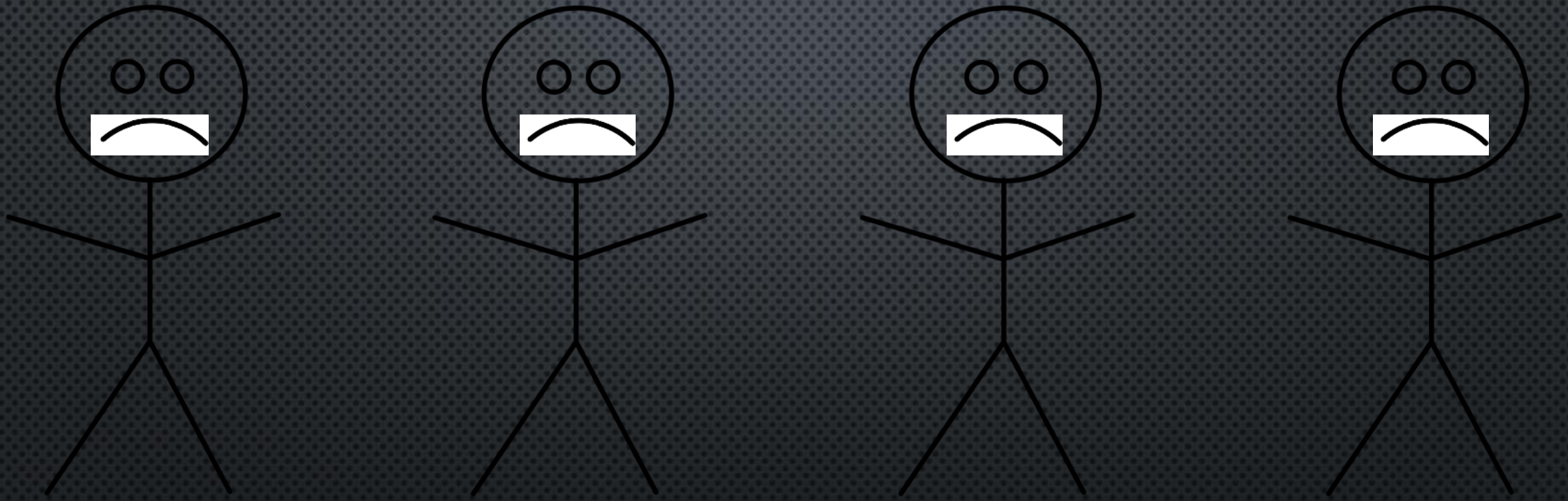
JUNCTION SHIFT IN CSI





S 2

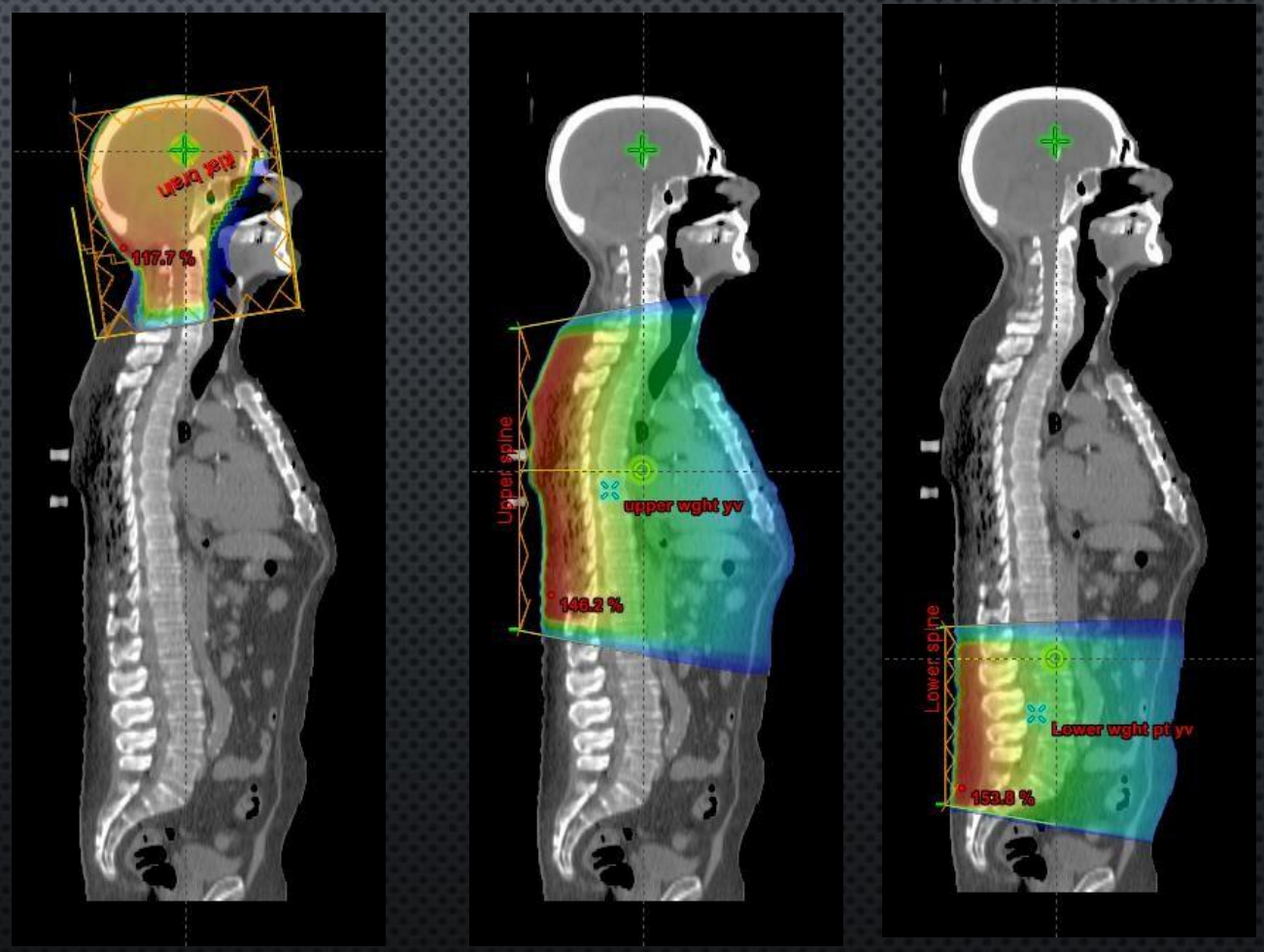
WORKLOAD



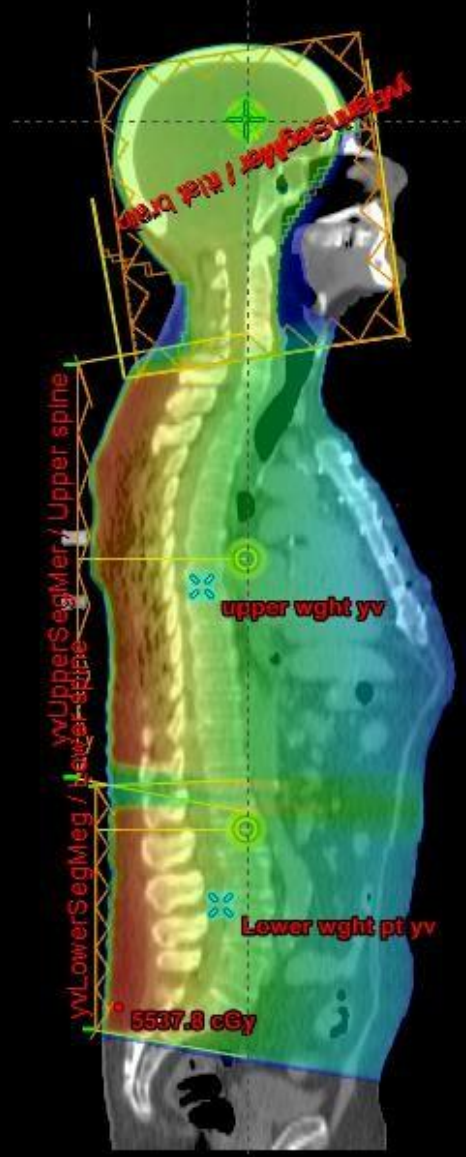
Dosimetrist Doctor Physicist Therapist

INTEGRATED FEATHERING

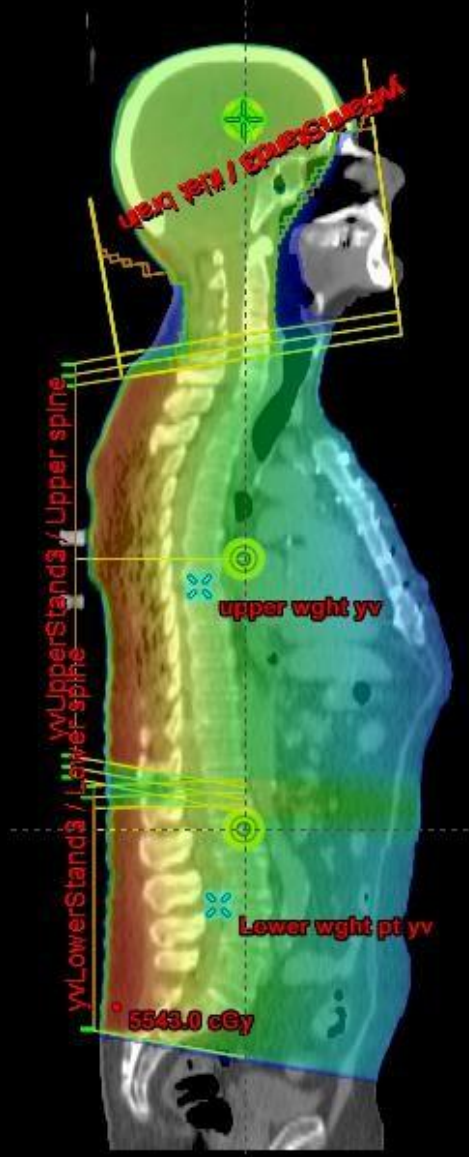
- Field-in-field beams
  - Feather across the match line region in **one plan**
  - 3 equally-weighted segments
  - 1 cm shift between segments
- Same plan throughout entire treatment



Integrated Feathering



CLASSIC FEATHERING



SUPINE CSI PLANNING CT BASED

Radiotherapy and Oncology 128 (2018) 192–197

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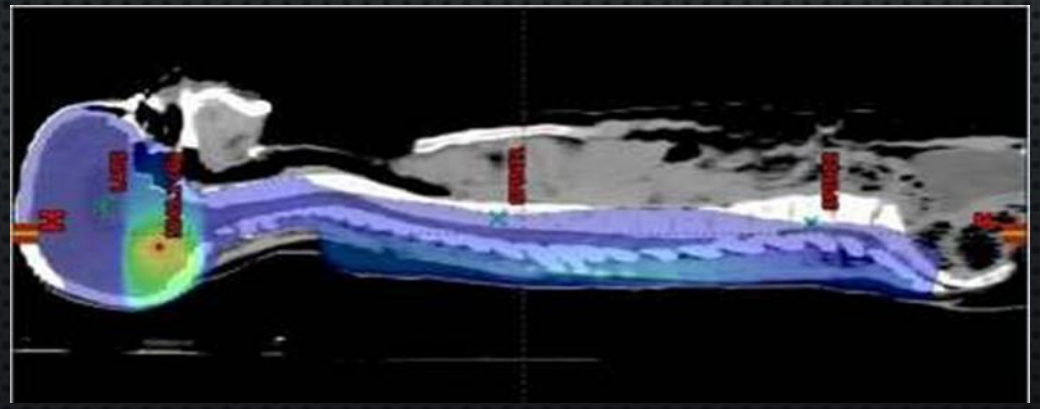
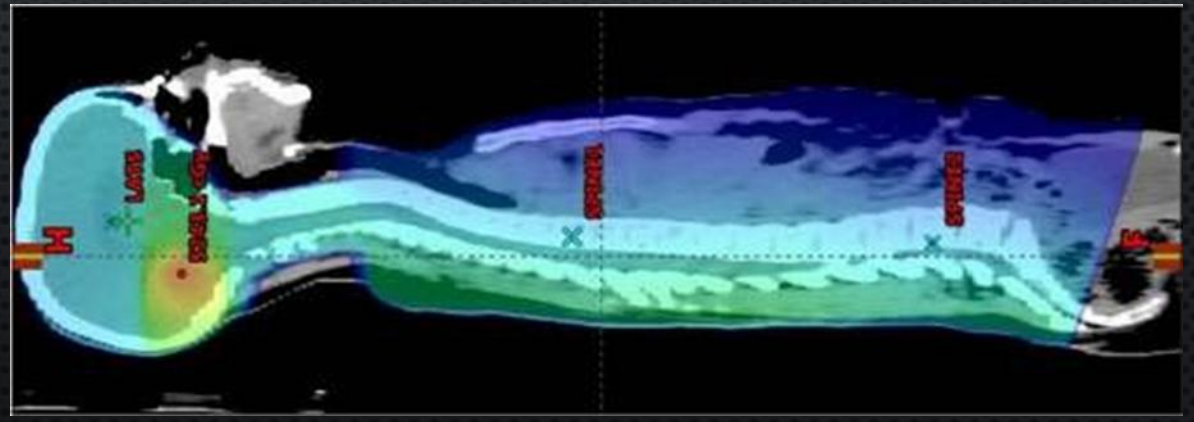
journal homepage: www.thegreenjournal.com

SIOPE Guideline

SIOPE – Brain tumor group consensus guideline on craniospinal target volume delineation for high-precision radiotherapy

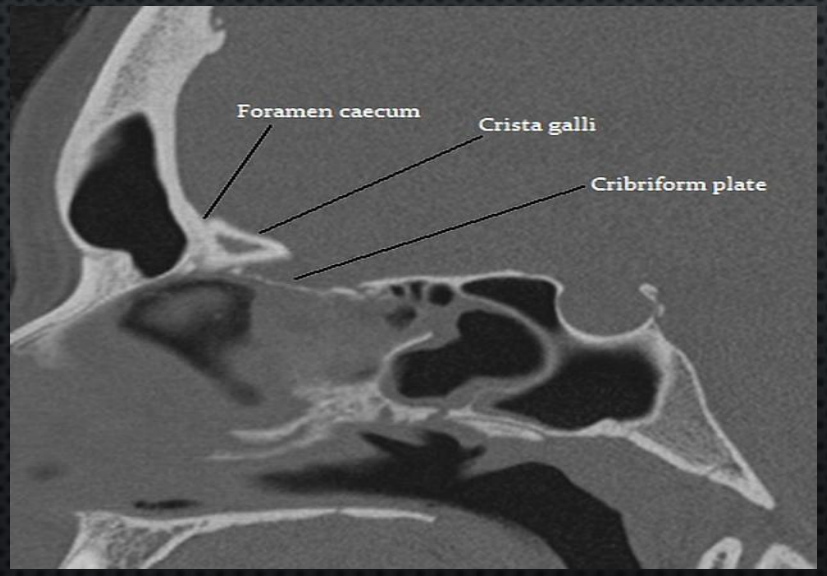
Thankamma Ajithkumar[a,*], Gail Horan[a], Laetitia Padovani[b], Nicky Thorp[c], Beate Timmermann[d], Claire Alapetite[e], Lorenza Gandola[f], Monica Ramos[g], Karen Van Beek[h], Melissa Christiaens[h], Yasmin Lassen-Ramshad[i], Henriette Magelssen[j], Kristina Nilsson[k], Frank Saran[l], Barbara Rombi[m], Rolf Kortmann[n], Geert O. Janssens[o], on behalf of SIOPE BTG Radiotherapy Group





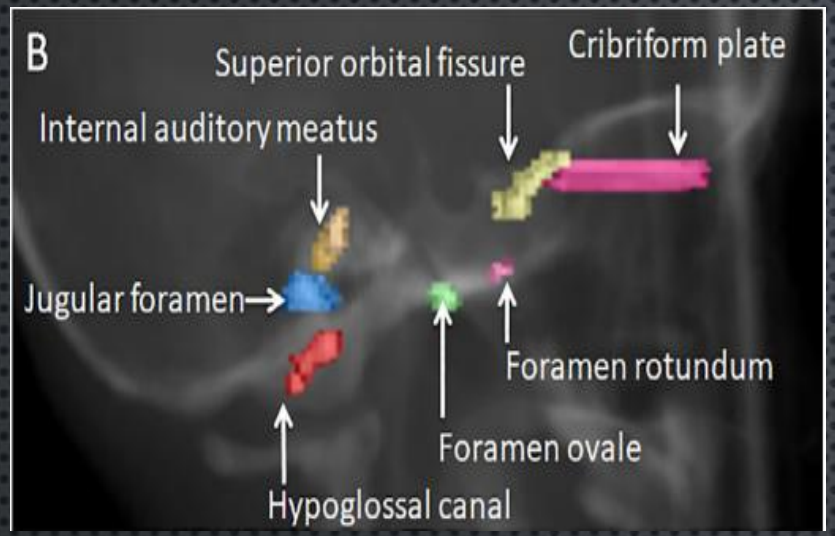
Guidelines for target delineation for CSI according to SIOPE and COG trials.

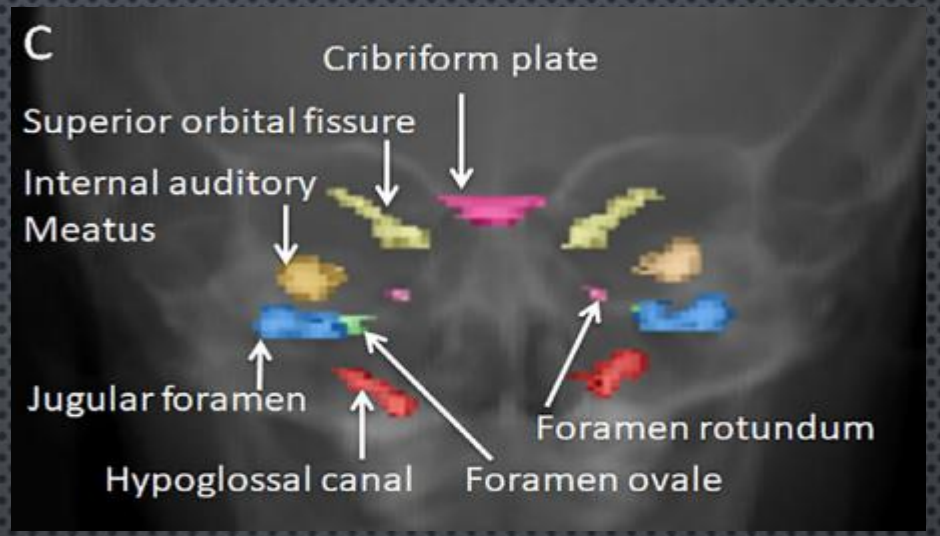
SIOPE (PNET4/5, SIOP CNS GCT II)	COG (ACNS0332, ACNS 0331, ACNS 0122)
Cranial CTV: 'includes brain with entire frontal lobe and cribriform plate. The geometric edge of the shielding should extend **at least 0.5 cm inferiorly below the cribriform plate and at least 1 cm elsewhere below the base of the skull**'	*Cranial CTV*: 'whole-brain field shall extend anteriorly to include the entire frontal lobe and cribriform plate region. Inferiorly, the CTV shall be at **least 0.5 cm below the base of the skull at the foramen magnum**'
Spinal CTV: 'extend laterally to cover the intervertebral formina. Inferior border of Spinal CTV must be determined by imaging the lower limit of the thecal sac on a spinal MRI; **inferior treatment field border should be set 1 cm below this**'	*Spinal CTV*: 'The spinal target volume will be the entire thecal sac. The field to cover this volume should extend laterally on both sides to cover the recesses of the entire vertebral bodies, with at least a 1 cm margin on either side. The inferior border of the treatment volume will be placed after review of the spinal MRI. **The border will be 2 cm below the termination of the subdural space**'
	Proton therapy 'For proton therapy, the spinal target volume will include the vertebral bodies for skeletally immature patients to minimise the risk of unequal vertebral growth. The spinal target volume in skeletally mature patients will include the spinal subarachnoid space with a margin of 3–5 mm into the vertebral body to allow for interfraction set up variation'

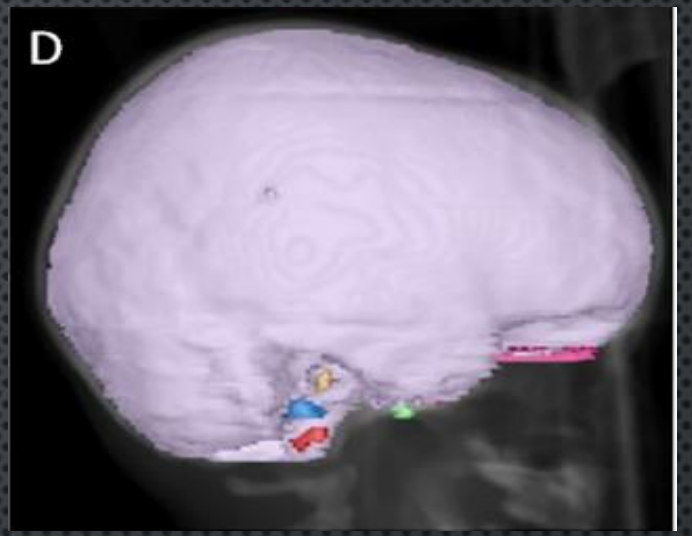


Description of the areas of interests that need to be include in the $CTV_{cranial}$ for CSI.*

Skull base foramen/Canal	Cranial nerve(s)	Anatomical description
Cribriform plate	Olfactory nerve	Cribriform plate is a thin horizontal plate of ethmoid bone which is bounded laterally by vertical lateral lamella
Optical canal of sphenoid	Optic nerve**	Optic canal is situated in the lesser wing of sphenoid, supero-medial to the superior orbital foramen
Superior orbital fissure	Oculomotor, trochlear, and first branch of trigeminal, and abducens nerves	Superior orbital fissure is located between the greater and lesser wings of sphenoid
Foramen rotundum	Second branch of trigeminal nerve	Foramen rotundum is located in the greater wing of sphenoid. It is supero-lateral to the vidian (pterygoid) canal and postero-infero-medial to the superior orbital fissure
Foramen Ovale	Third branch of trigeminal nerve	Foramen ovale is located in the greater wing of sphenoid and is postero-lateral to the foramen rotundum
Internal auditory meatus	Facial and vestibulo-cochlear nerves	Internal auditory meatus is located in the petrous temporal bone and is antero-superior to the jugular foramen
Jugular foramen	Glossopharyngeal, vagus, and accessory nerves	Jugular foramen is located supero-lateral to the foramen magnum and inferior to the carotid canal
Hypoglossal canal	Hypoglossal nerve	Hypoglossal canal is located in the occipital condyle and infero-medial to the jugular foramen







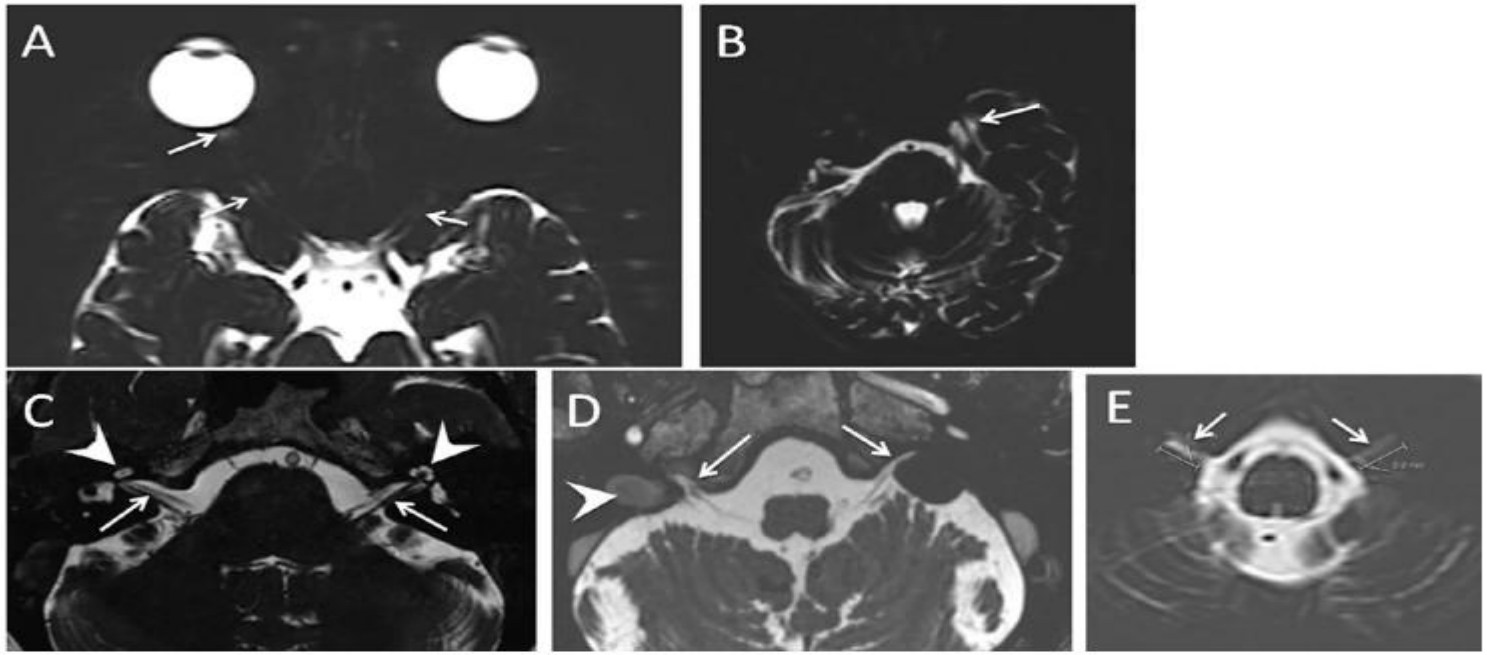


Fig. 1. (A) CSF tracks around the optic nerve and reaching up to the back of the globe (white arrows). (B) CSF in Meckel's cave (white arrow), adjacent to the medial site of the temporal lobe. (C) CSF in the IAM (white arrows) lies in close contact with the cochlea (white arrow head). (D) CSF flow in the jugular foramen JF (white arrows). Note carotid lies in the pars vascularis of jugular foramen (arrow head) (E) CSF in the hypoglossal canal (white arrows) (courtesy of Janssens and Noble et al.).

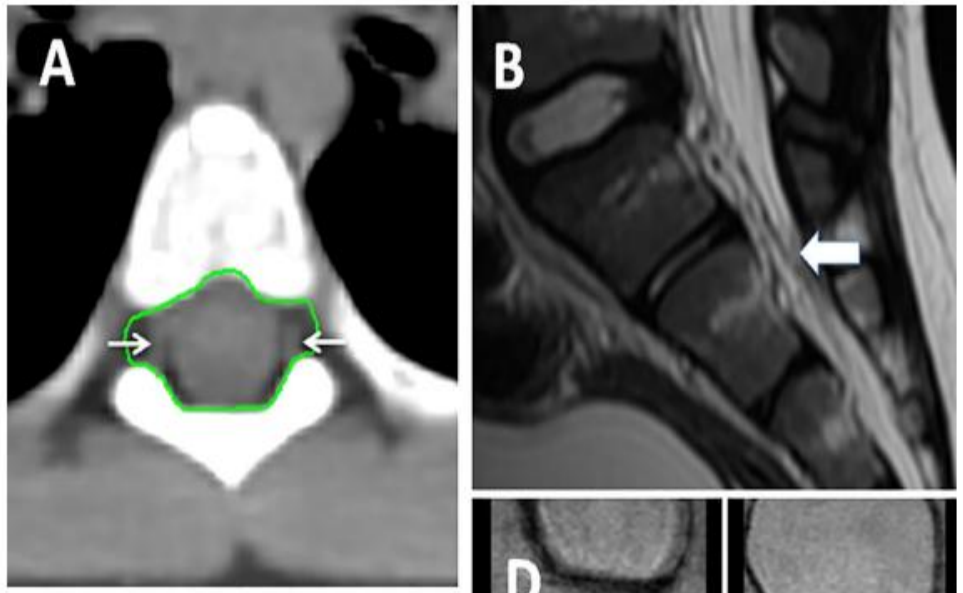


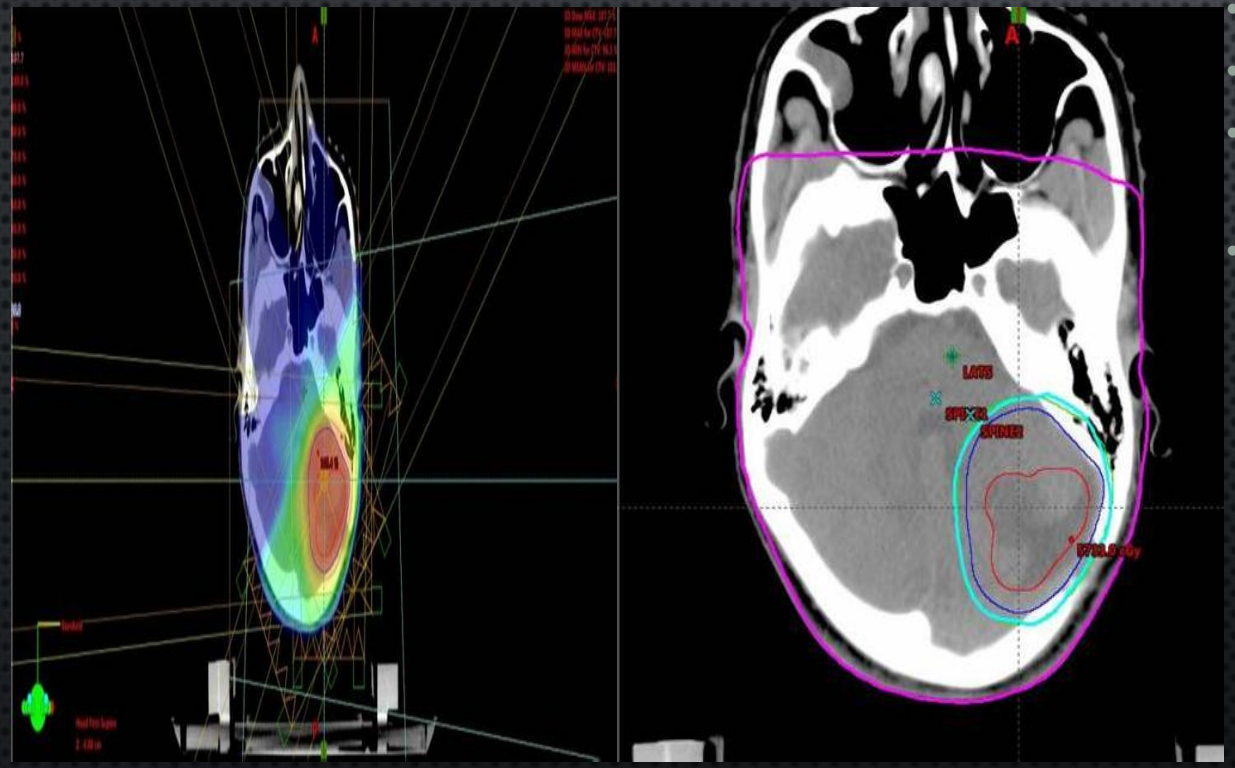
Fig. 4. (A) CTV_{spinal} including the entire arachnoid space with nerve roots (white arrows). (B) Lower level of CSF (white arrow) on sagittal T2W MRI, (C) Lower limit of CTV_{spinal} on planning CT scan, (D) Absence of CSF around sacral nerve roots (white arrows). Note CSF within spinal canal (arrow heads).

Organs-at-risk (OAR) :CTVcranial - Eye balls, lens, cochlea and the parotid and submandibular salivary glands.
CTVspinal : larynx, oesophagus, thyroid gland, breasts in females, lungs, heart, liver, stomach, intestine, pancreas, kidneys and the gonads

Growing vertebrae to the lowest uniform growth restraining dose vary between institutions (e.g. PTV covering uniform dose of 20 Gy, vertebra covering a fixed-isodose level etc.)

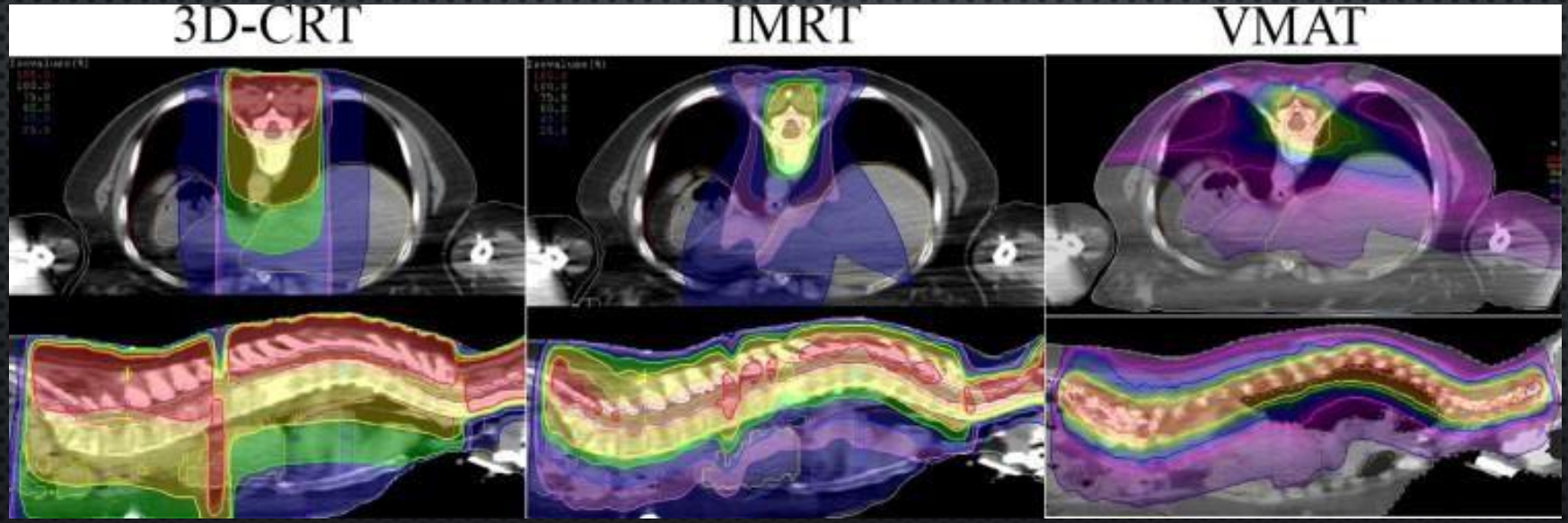
The PTV margin should be based on departmental data. Most institutions add a 3–5 mm margin to CTVcranial and a 5–8 mm margin to CTVspinal.

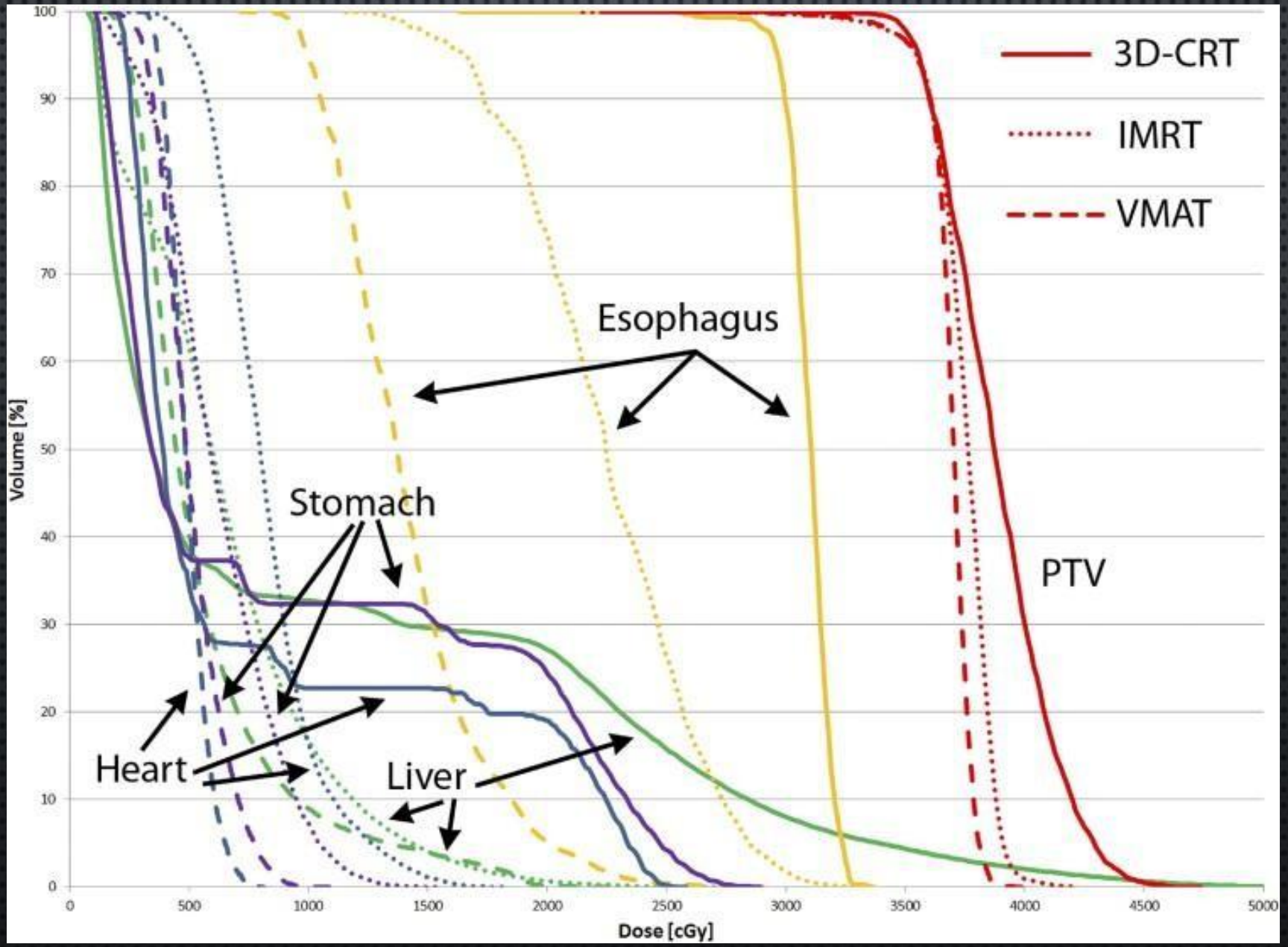
3D CRT / IMRT TUMOR BED BOOST



- GTV- Tumor bed on MRI
- CTV = GTV + 15 mm.
- PTV = CTV + 3-5 mm, modified only at sella.
- Immobilization accuracy +/- 3-5 mm.
- 95% of isodose covers 100% of CTV & 95% Of PTV.
- Homogeneity: no > 10% of target volume receives > 110% of boost dose.
- **Constraints:**
  - < 70% Supratentorial brain to receive > 50% boost dose.
  - < 80% Left & right cochlea to receive > 80% of boost dose.
  - < 50% Pituitary to receive > 30% of boost dose.
  - < 10% Left & right optic nerve & chiasma to receive > 50.4 Gy each.

CSI: 3D VS. IMRT/VMAT





Studenski, Matthew T., et al. "Intensity-modulated radiation therapy and volumetric modulated arc therapy for adult craniospinal irradiation--a comparison with traditional techniques." Medical Dosimetry 38.1 (2013): 48-54.

CSI: 3D VS. IMRT/VMAT

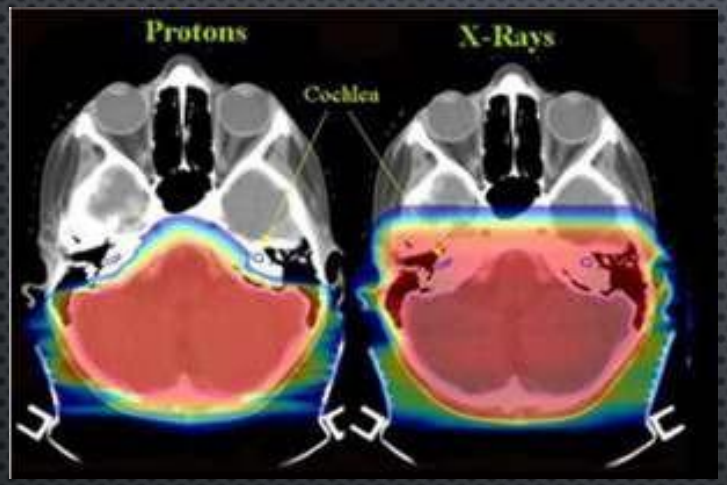
	3D	IMRT	VMAT
Pros	• Most efficient • Negligible OAR dose increase for cranial	• OAR sparing • Target coverage	• OAR sparing • Target coverage
Cons	• Higher dose to OARs for spinal fields	• Difficult to QA junctions • Hard to control hotspots outside of PTV • Longest treatment times	• Difficult to QA junctions • Hard to control hotspots outside of PTV • Low dose spread

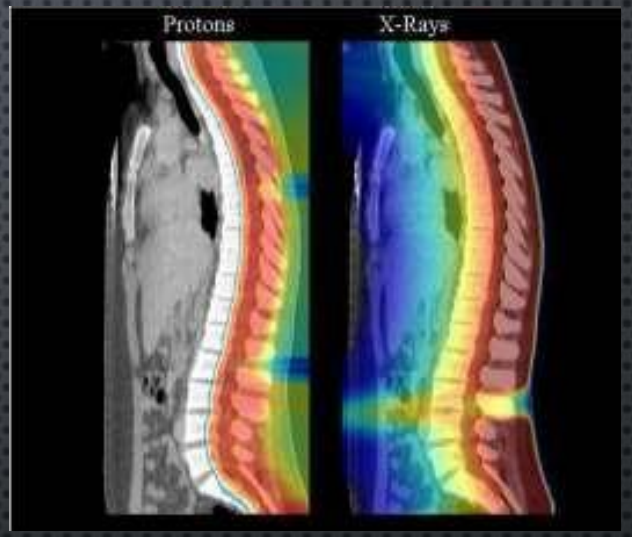
Studenski, Matthew T., et al. "Intensity-modulated radiation therapy and volumetric modulated arc therapy for adult craniospinal irradiation--a comparison with traditional techniques." Medical Dosimetry 38.1 (2013): 48-54.

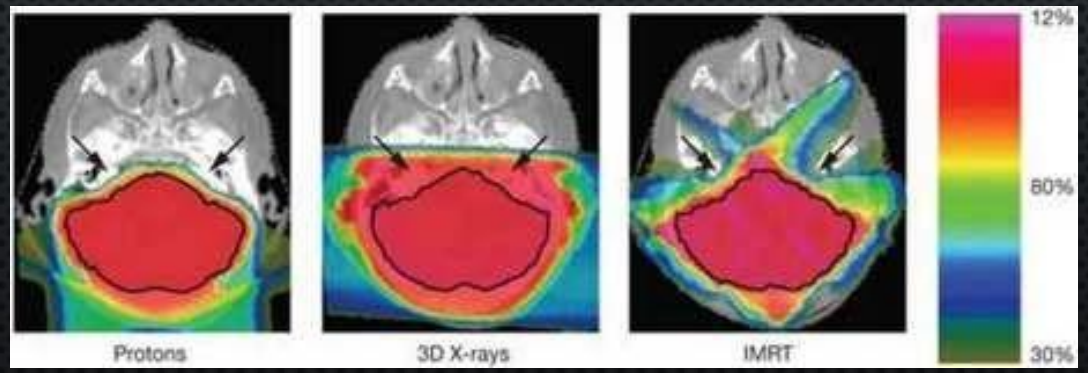
PROTON THERAPY

- Superior dose distribution for delivering a uniform dose of radiation to the posterior fossa and spinal cord within the thecal sac.
- Near complete organ sparing - lower probabilities of developing hearing, hormonal defects secondary to radiotherapy.
- Long term effects of secondary neutron spill - not quantified.

PHOTONS VS PROTONS







HYPER FRACTIONATION ?

- ***Average-risk disease***
- HIT-SIOP PNET 4 trial (n= 340) *Lannering B JCO 2012*
- Hyper-fractionated Radiation Therapy (HFRT) *vs* SFRT:
- CSI: 36 Gy/36#/48 days, 1 Gy BID, 8 hrs apart
- Tumor Boost: 32 Gy/32#/2.5 wks, 1 Gy BID, 6 hrs apart, 5 days/wk
- *Similar survival and toxicity*
- ***High-risk disease***
- Hyper-fractionated Accelerated Radiation Therapy (HART):
- CSI: 36 Gy/36#/3 wks, 1 Gy BID, 6 hrs apart, 6 days/wk
- Boost: 24 Gy/20#/2 wks, 1.2 Gy BID, 6 hrs apart, 6 days/wk
- *5Yr EFS 59-70%*

RT INDUCED NORMAL TISSUE EFFECTS

Acute Toxicity

- Hair loss
- Vomiting +/- Headache
- Skin reactions especially over ears
- Somnolence
- Hematological toxicity (prophylactic growth factor support is **NOT** indicated)

Long term Sequelae

- Neurocognitive & neurophysiological dysfunction
- Endocrine abnormalities
- Growth retardation
- Ototoxicity- particularly with platinum based adj CT
- Cerebrovascular accidents
- Gonadal toxicity & reduced fertility
- Second malignancies

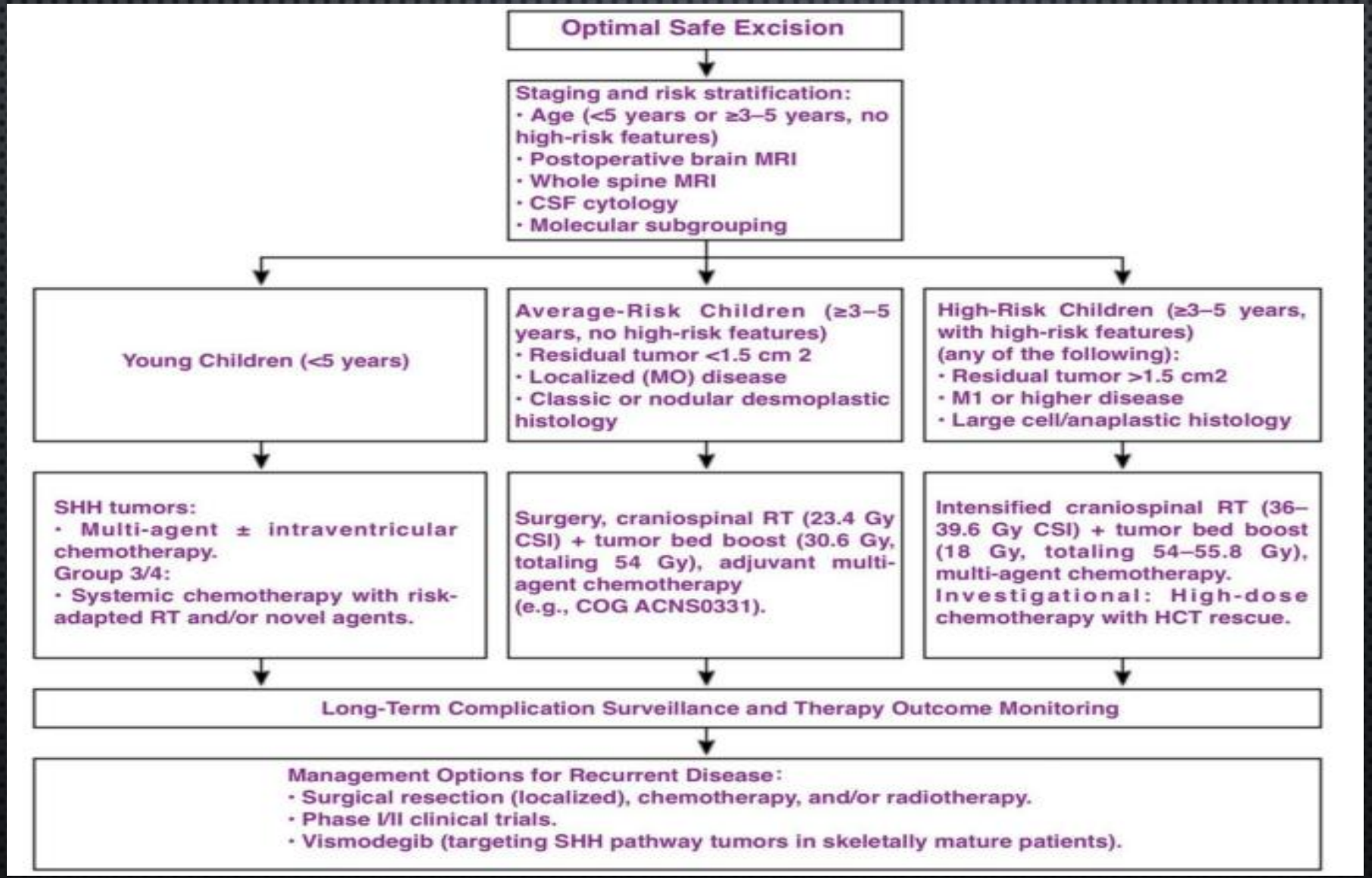
Recommendations for Follow up

- 3 monthly - first 2 years
- 6 monthly - next 5 years
- Annually thereafter

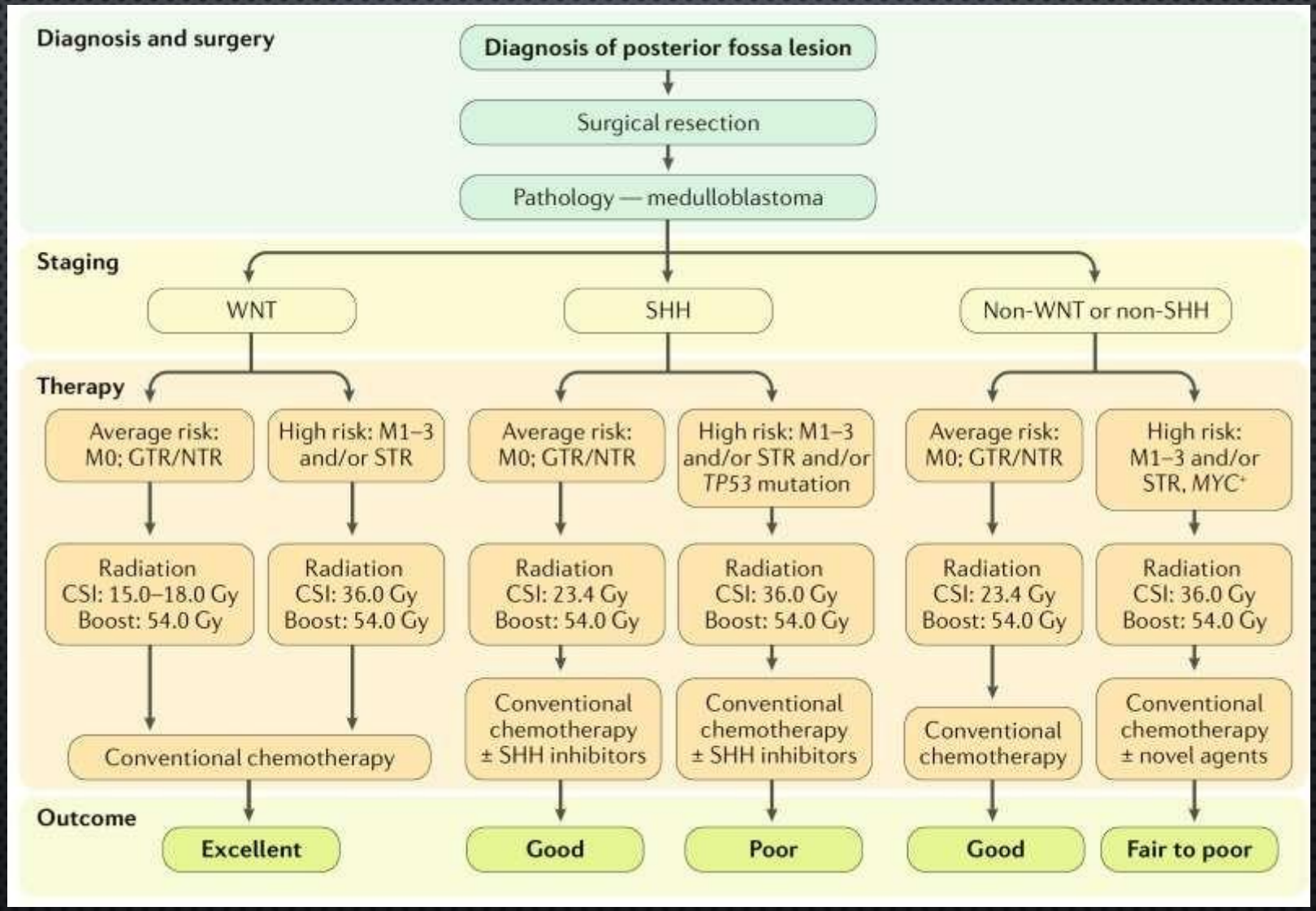
- Contrast-enhanced MRI of the brain and spine
  - 6-12 weeks after completion of all therapy
  - to serve as a baseline for future comparison.

- Routine imaging surveillance should be ordered only if neurologic worsening occurs, recurrence/progression of disease is suspected

KEY TREATMENT STEPS AND STRATEGIES

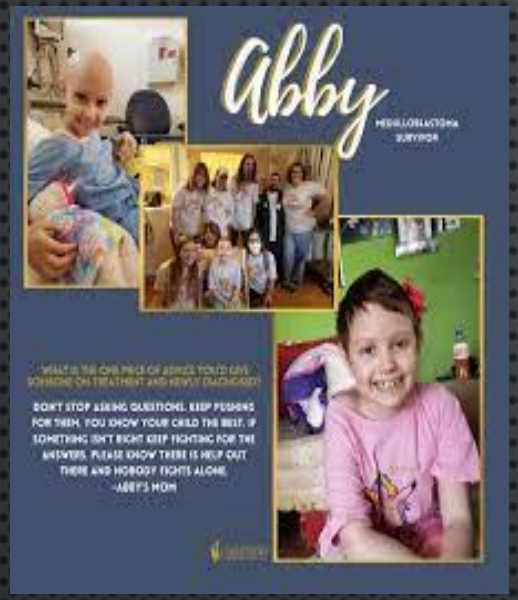


MOLECULAR RISK-ADAPTED MANAGEMENT



Dose decrease of
RT and CT

SMO inhibitor (vismodegib)
BET inhibitors
CDK4/6 inhibitor (ribociclib)
MET inhibitor (foretinib)


Abby
MEDULLOBLASTOMA SURVIVOR
DON'T STOP ASKING QUESTIONS. KEEP PUSHING FOR THEM. YOU KNOW YOUR CHILD THE BEST. IF SOMETHING ISN'T RIGHT KEEP FIGHTING FOR THE ANSWERS. PLEASE KNOW THERE IS HELP OUT THERE AND NOBODY FIGHTS ALONE.
-ABBY'S MOM


MEDULLOBLASTOMA
DOESN'T
COME
WITH A
MANUAL
IT COMES WITH A
MOTHER WHO
NEVER GIVES UP


Jillian
ACUTE LYMPHOBLASTIC LEUKEMIA SURVIVOR
"GOD GIVES HIS HARDEST BATTLES TO HIS STRONGEST SOLDIERS"
- YOU CAN SIT DOWN AND YOU CAN LET CANCER CONTROL YOUR LIFE, OR YOU CAN GET UP, DUST OFF, AND FIGHT
-JILLIAN DUFFY, 2011 MISS CONNECTICUT


MEET SOPHIA SANDOVAL, 3-YEAR-OLD MEDULLOBLASTOMA WARRIOR WHO CELEBRATED HER LAST DAY OF CHEMO DRESSED AS WONDER WOMAN. DROP A ❤ #IMAGESYOUWONTSEEONTV
My Last day of Chemo
IT Was A Tough. But I Did Tonight


Emma
MEDULLOBLASTOMA SURVIVOR
FIND THE GOOD, EVEN ON THOSE CRAP DAYS - ITS OK TO BE SAD FOR A LITTLE BIT, BUT GET UP AND DO SOMETHING FOR SOMEONE ELSE. ALWAYS GIVE BACK.
-EMMA

THANK YOU