Pediatric Radiotherapy Planning and Delivery

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Overview of this Presentation

- Differences between childhood tumors and their formation compared to adult tumors
- Normal tissue tolerance differences between children and adults
- Secondary cancer risk from radiotherapy
- General treatment planning issues
- Craniospinal irradiation techniques
- Total Body irradiation techniques
- Immobilization and isocenter verification
- Interesting clinical cases
- Clinical trial issues

Tumorigenesis

- Cancers in adults result from a multistep process and often progress over many years or decades.
  - Treatment based on high proliferation rate in low proliferation rate context
- Children's tumors develop over a much briefer time course,
  - not likely to be caused by environmental factors, genetic mutations are common.
  - Treatment is in context of rapidly growing normal tissues, highly susceptible to damage from radiation and chemotherapy and induction of new cancers.

Childhood Cancers are Different than Adult Cancers

Childhood Cancer Incidence (2% of all cancers)

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

Adult Cancer Incidence

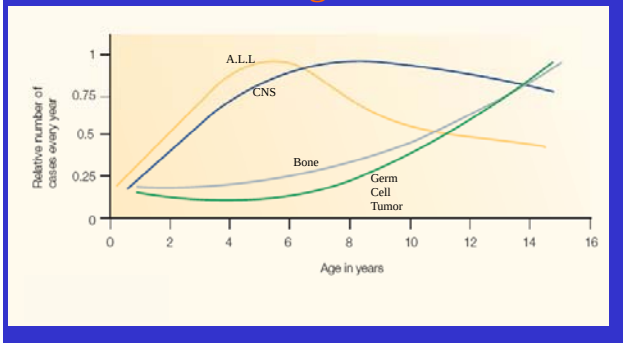
Male	Female
Prostate	Breast
Lung/Bronchus	Lung/Bronchus
Colon.Rectum	Colon/Rectum
Bladder	Uterus
Lymphomas	Ovary
Oral cavity	Skin Melanoma
Skin Melanoma	Cervix
Leukemia	Leukemia

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)

Adult cancers are predominantly Carcinomas

Relative Number of Cancers by Age



Childhood Cancer Survival Rate

- Has steadily increased from the 1960's
- 3 year survival rate = 80%, 5 year = 75%
- But Brain Stem Gliomas nearly always fatal
- Treatment Intent nearly always for cure as opposed to palliation.

Secondary Malignancy Rate: RT vs. Chemo vs. Both Hodgkin's Disease

Clinical Characteristic	All Patients (N = 1,380)	Patients With Second Neoplasms					
		Solid Tumors (n = 104)		Leukemia (n = 27)		Non-Hodgkin's Lymphoma (n = 6)	
	No. of Patients	No. of Patients	%	No. of Patients	%	No. of Patients	%
Treatment modalities							
Radiation alone	314	31	30	0	0	1	17
Chemotherapy alone	106	2	2	5	19	1	17
Radiation and chemotherapy	960	71	68	22	81	4	67

RT-induced solid tumors mostly breast and thyroid

Induction of Second Cancer for Pediatric Patients Treated with RT

- Overall rate 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
- Solid cancers accounted for 81% of all SM.
- The average latency period was about 15 years
- Risk is higher for younger age at Dx. RR is 3-6 fold than adults.
- RR is a nearly linear function of dose, up to very high doses.
- Sixty-five % of SM occur in the radiation field, 20% adjacent, 15% distant
- Risk continues to increase over time, 20, 30 years +

Hereditary Retinoblastoma

RT Treatment Produces Highest Incidence of Induced Second Malignancy

- 58% incidence of SM after 50 years for irradiated patients,
- 27% for non-irradiated patients.
- Abramson, 1997: 1500 patients, no increased risk for tumors created outside the field. In-field SM occurred for patients treated under 1 y.o.

E. Hall and others:

IMRT may increase SM rate from 1% to 1.75%

Due to multiple beams spreading out low doses to large volumes and increased head leakage

Risk models based on the assumption that low doses of radiation cause SM, higher doses (>3Gy) sterilize any transformed cells.

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 distant from the high dose region where head leakage dose dominates.
- 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.

CHLA Patient Population

- Sedation every day for < 7 y.o.
- Treat about 12 pts/day
- 70% IMRT
- 40% Brain/CNS tumors
- Remaining 60% could be to any body site
- Prescribed doses range from 10Gy to 70Gy depending on disease and site.

Overview of Planning Issues for Conformal Treatments

- Non-coplanar vs. coplanar beams: spread low dose area around to lessen mid-dose volume
- Normal structure tolerance dose- % of target dose
- IMRT vs. 3-D Conformal
- Immobilization techniques for head and body
- We don't use radiosurgery – tumors are usually too big and organs at risk wouldn't tolerate large single fraction dose

Features of Clinical Material

- Sites brain, pelvis, abdomen, head and neck
- 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%

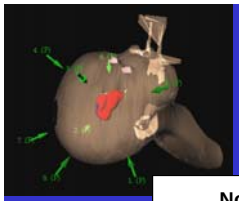
Comparison of Critical Structure Dose for Children vs. Adults

Structure	Children	Adult
Whole Brain	18 Gy	35 Gy
Bones	10 Gy	>65 Gy
Pituitary (growth hormone)	20 Gy	none
Ovary/testes (reproduction)	10 Gy	none
Breast (ca induction 40 Gy)	RR = 20	RR = 2

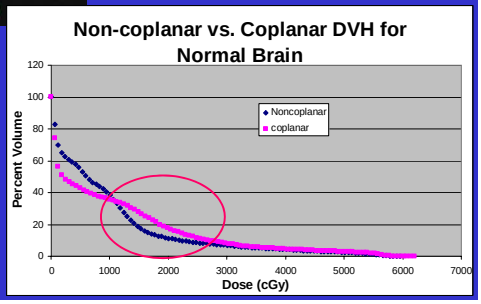
Cardiac toxicity may be higher for children, more years for problem to develop than in adults

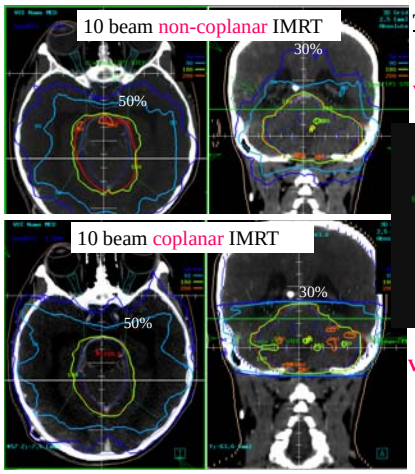
Reasons to use IMRT

- Tissue compensator
- Concave targets
- Multiple targets
- Better normal tissue sparing/low dose region shaping.
- Target conformality - better than "3D conformal"



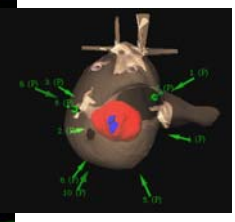
Non-coplanar beams may reduce cognitive deficits for brain targets





Temporal Lobe Dose

Volume of 50% dose = 30%



Volume of 50% dose = 53%

Treatment of Medulloblastoma

Craniospinal Irradiation Plus Posterior Fossa Boost

- 7-8 % of all intracranial tumors but…
- 30% of pediatric brain tumors
- ¾ of all cases occur in children, median age 9 y.o.

Craniospinal Axis Treatment

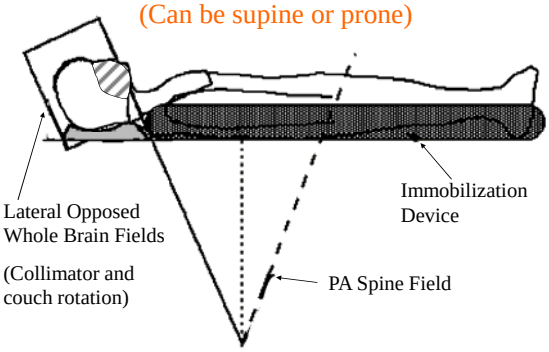
Treat whole spine and whole brain to either 2340 cGy (aver. risk) or 3600 cGy (high risk)
Boost posterior fossa to total of 54 Gy

CSI Planning issues:

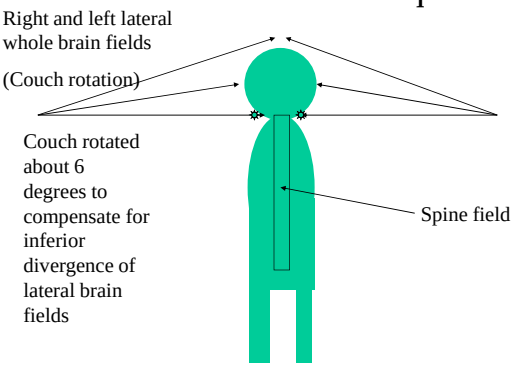
- Prone vs. Supine
  - Supine is better for reproducibility and for anesthesiologist, but method for verifying junction must be developed.
- Junction dose spine-brain
  - Junction level and shifts- C2 (jaw and thyroid exit) vs C5 (inferior cord dose from lat beams)
- Exit doses: gut, throat, heart

Conventional Craniospinal Irradiation Technique

(Can be supine or prone)

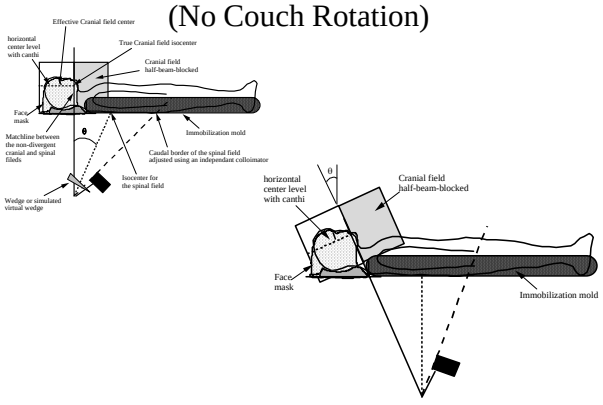


Conventional Craniospinal Irradiation Technique

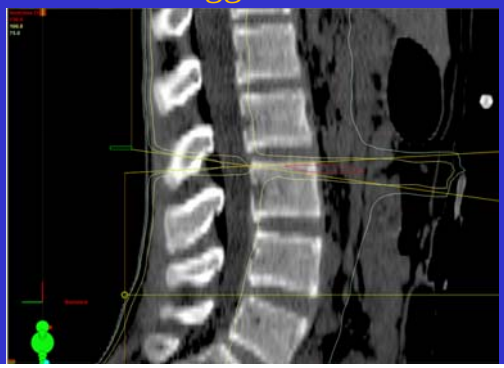


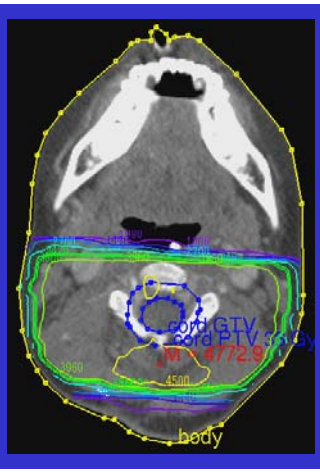
Split beam CSI technique

(No Couch Rotation)



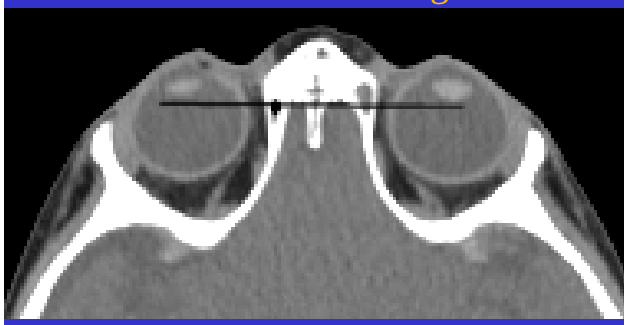
Need abutted Spine fields for bigger kids





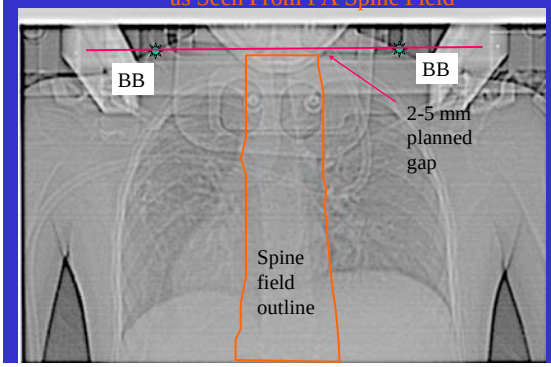
Dose to Mouth and Airway Kept Low by Shaping Whole Brain Fields

Spare lenses But Don't Block the Cribriform Plate Region



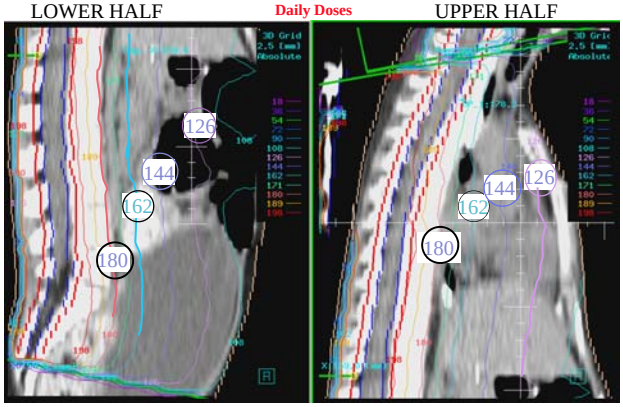
Verification of Brain/Spine Junction for Supine Position

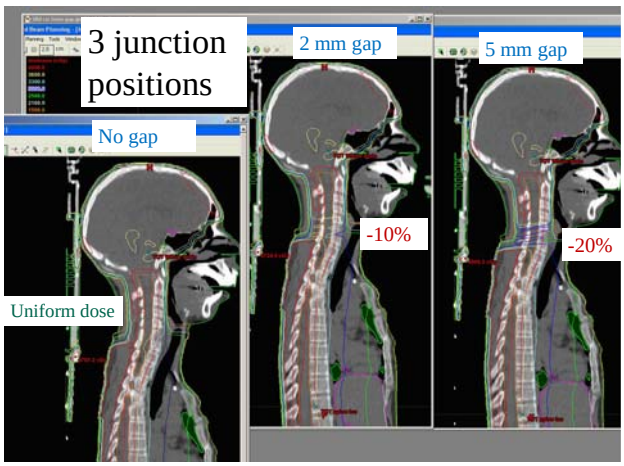
as Seen From PA Spine Field



Conventional Craniospinal Irradiation Technique - Dosimetry for PA Spine before jct shifts

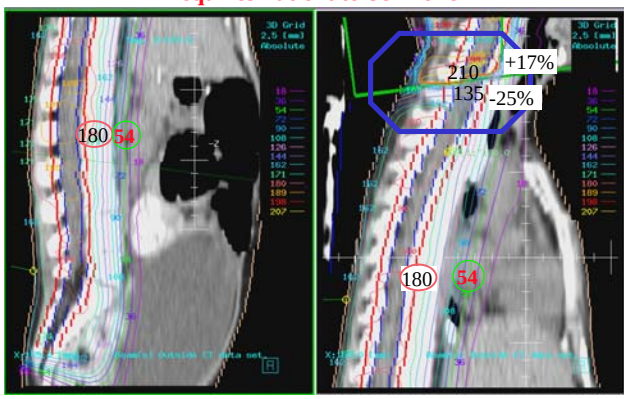
LOWER HALF Daily Doses UPPER HALF





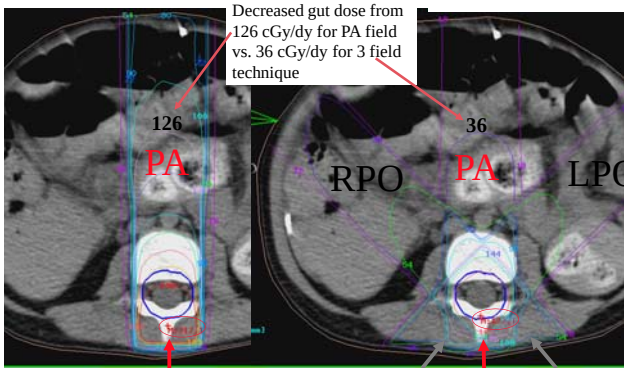
16 MeV PA Electron Beam Spine Field

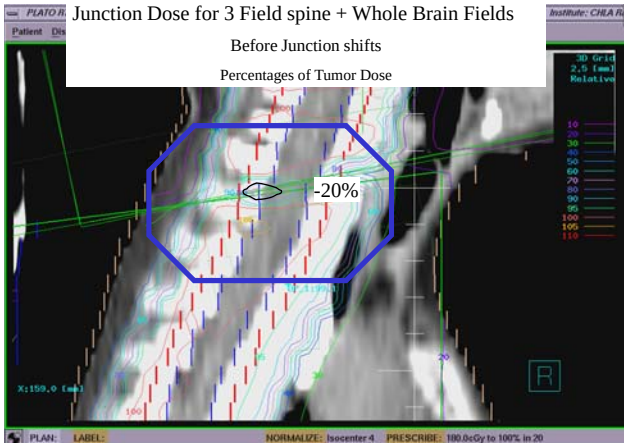
*****Requires Patient to be Prone *****



Spine Treated by PA, RPO, and LPO

Spine Treatment
Conventional vs. 3-Field Technique

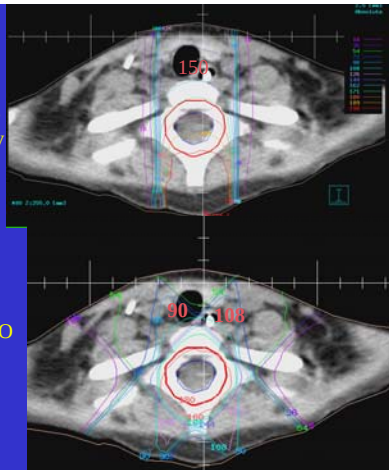




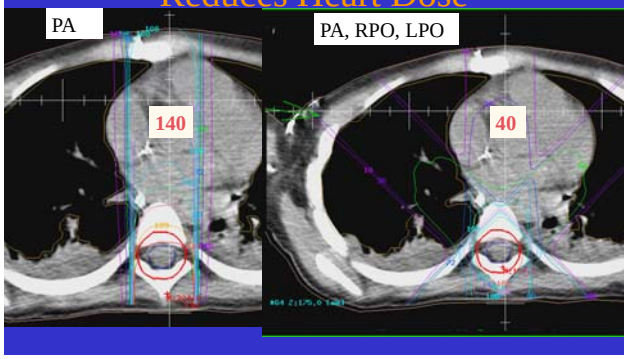
PA Spine field only

3 Field Spine Technique Protects Trachea and Esophagus

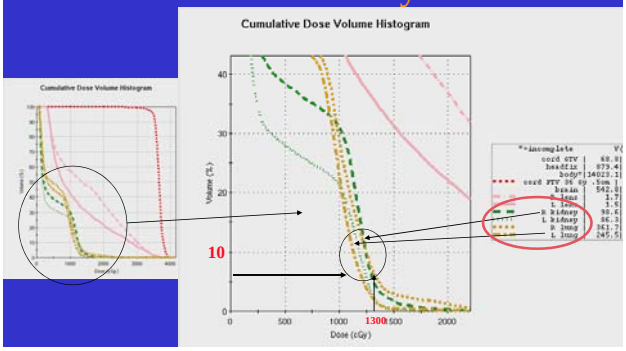
PA, RPO, LPO spine fields



3 Field Spine Technique Reduces Heart Dose



Less than 10% of Kidneys and Lung Get 1300 cGy



Head to Foot Immobilization

Changing the Boost Treatment for Medulloblastoma

- Reduce severe cognitive and hearing losses associated with this treatment.
- Test whether reducing the boost volume and dose (for less than 8 y.o.) to just the surgical bed + margin will change recurrence and morbidity patterns.
- Nearly all C.O.G. (U.S.) treatment facilities have 3-D conformal and >90% have IMRT capability so it is feasable to use these technologies in a clinical trial.

Children's Oncology Group ACNS0331

Image-Based Conformal Boost Treatment of Whole Posterior Fossa vs. Local Volume

- 3D conformal image-based planning and delivery is required.
- IMRT is allowed.
- At least 95% of either target must be covered by at least 95% of 30.6 Gy prescribed boost dose.

ACNS0331 Cont.

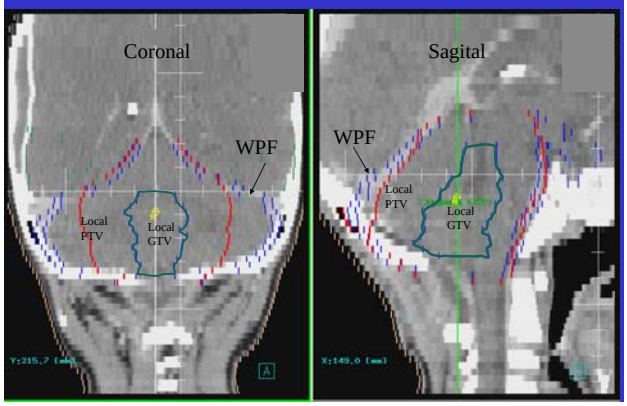
•Whole Posterior Fossa boost - 3mm margin on CTV

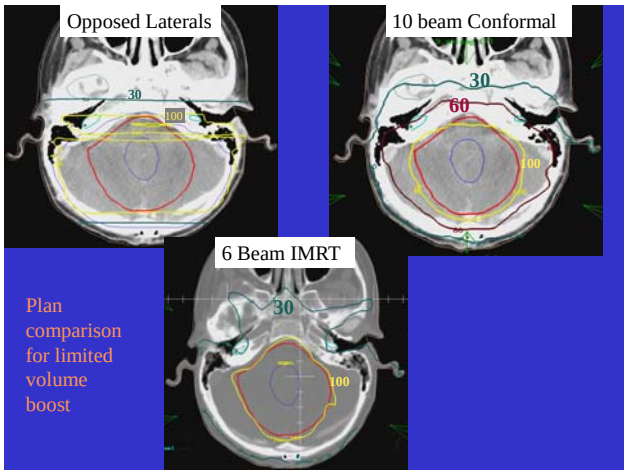
• Local Boost - 15 mm margin on GTV + 3mm for PTV = 18 mm total 3-dimensional margin.

• In all cases at least 95% of the PTV receives at least 95% of 30.6 Gy

•In all cases, optic chiasm dose less than 27 Gy (50 Gy total)

Whole Posterior Fossa and Local Target Volumes





Sites>>>> Technique Whole post. Fossa to 30.6Gy	Cochlea Mean Dose Gy	Pituitary Mean dose Gy	% Supr. Tent Brain 10 Gy	% Supr. Tent Brain 20 Gy	% Temp. Lobe 10 Gy	% Temp. Lobe 20 Gy
Opposed Laterals WPF	31	4	20	17	74	69
IMRT 6 Beam WPF	13	8	25	6	59	17
IMRT 10 Beam WPF	10	7	27	6	36	6
Conformal 10 Beam WPF	24	16	33	11	81	27

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

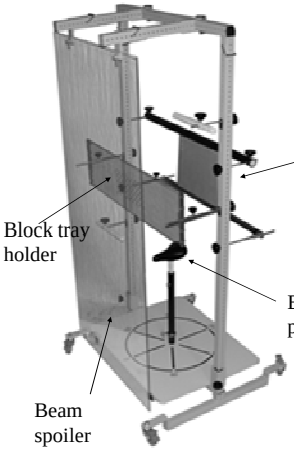
also A.M.L. and some other diseases

- Most common childhood cancer – 3000 new cases per year.
- Total Body Radiation (12-13.5 Gy = lethal dose) is used as a secondary conditioning regimen after chemo to kill all cancer cells as well as all immune system cells.
- Patients then get bone marrow transplant. Lack of immune system lessens the chance of rejection of the new bone marrow.

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 feasable.
    - **Cons:** Patient required to stand, lung blocks hung on external tray
  - 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 problem.
- Beam spoiler typically used to bring full dose to skin surface
- Dose rate kept ≤ 10 cGy/min at patient midplane

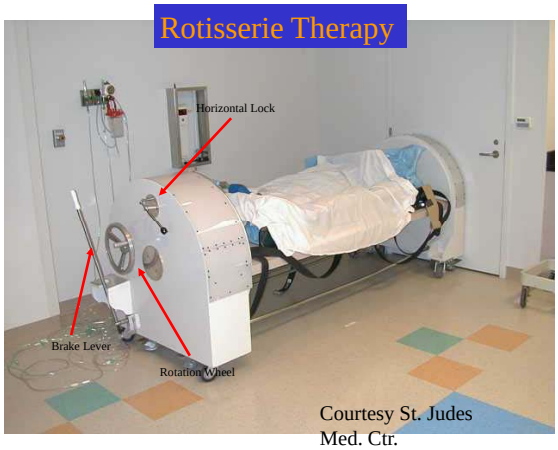
Total Body Irradiation for Leukemia



TBI stand

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

Rotisserie Therapy



Courtesy St. Judes Med. Ctr.

Physics Measurement for Commissioning and Calibration

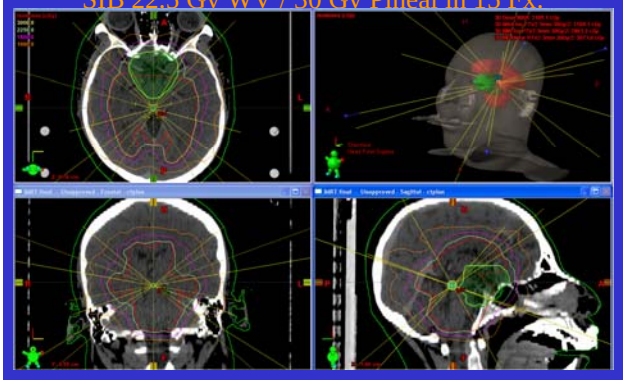
- Setup a phantom system which simulates patient and treatment geometry
- Measure central axis PDD or TMR and OPFs. 30x30x30 cm calibration phantom suitable, make corrections for **smaller** irradiated area for patient treatment
- Measure off axis ratios-large field across diagonal, function of depth.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

Interesting Clinical Cases

Intracranial Germinoma

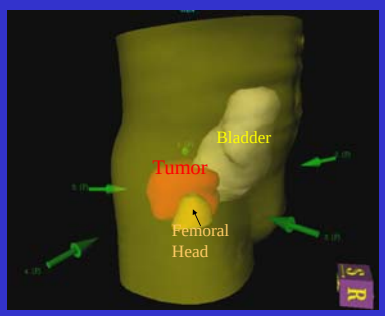
(10% of ped brain tumors)

SIB 22.5 Gy WV / 30 Gy Pineal in 15 Fx.

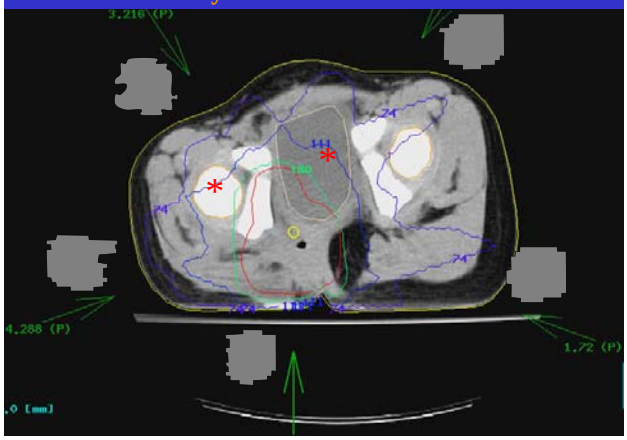


Pelvic Germ Cell Tumor

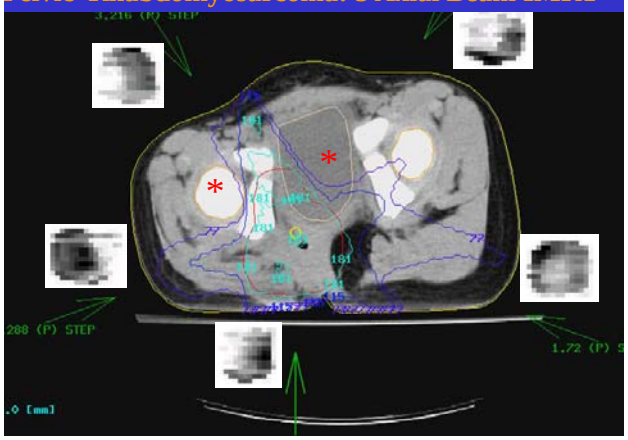
Pelvic Rhabdomyosarcoma and Surrounding Organs



Pelvic Rhabdomyosarcoma: 5 Beam Conformal RT

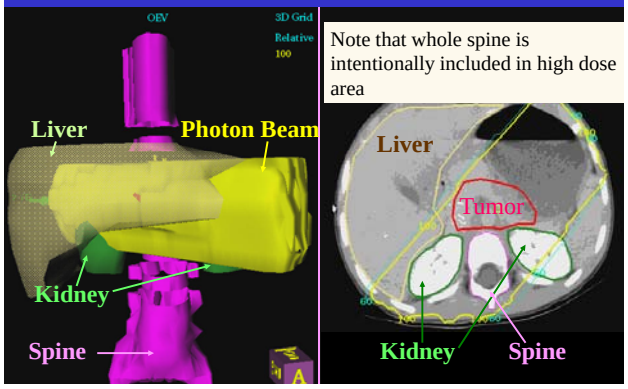


Pelvic Rhabdomyosarcoma: 5 Axial Beam IMRT

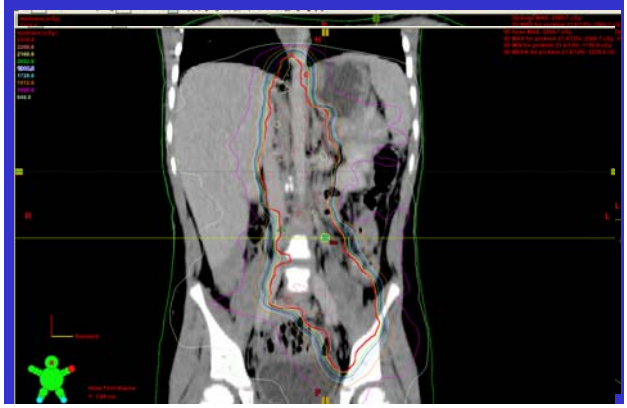


Neuroblastoma

Neuroblastoma: Opposed Oblique Beams

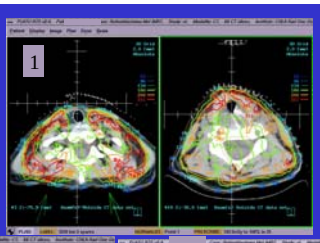


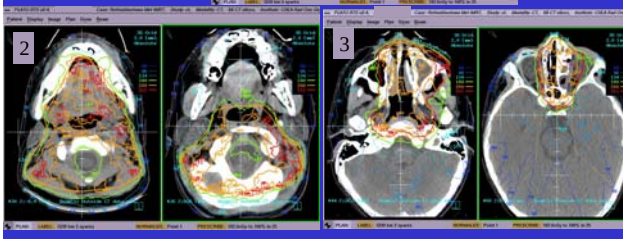
Neuroblastoma: 9 Axial Beam IMRT



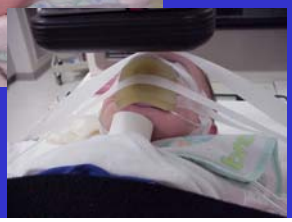
Other Head and Neck

Metastatic Retinoblastoma





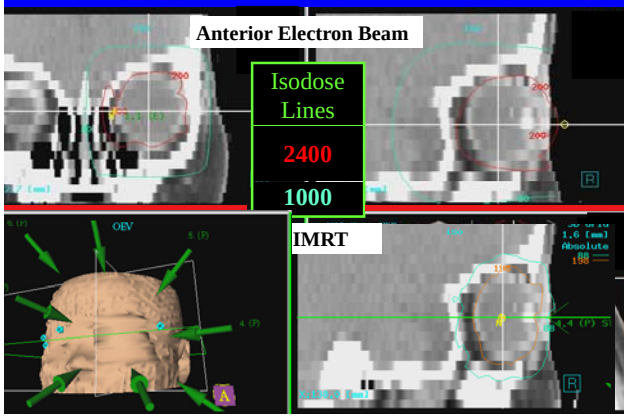
Lead with bolus backing under lip to protect teeth



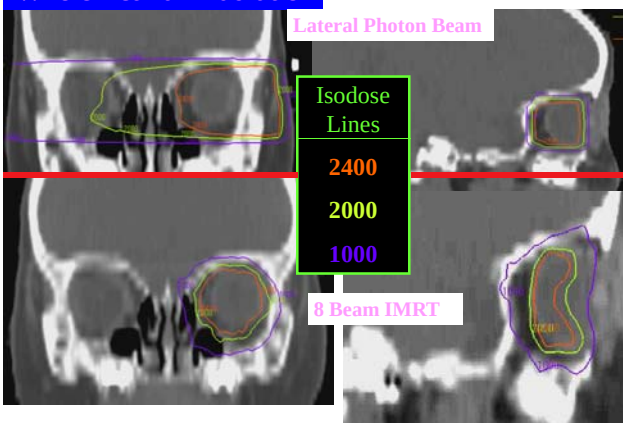
Keloid Treatment in Infant (Electron Beam)

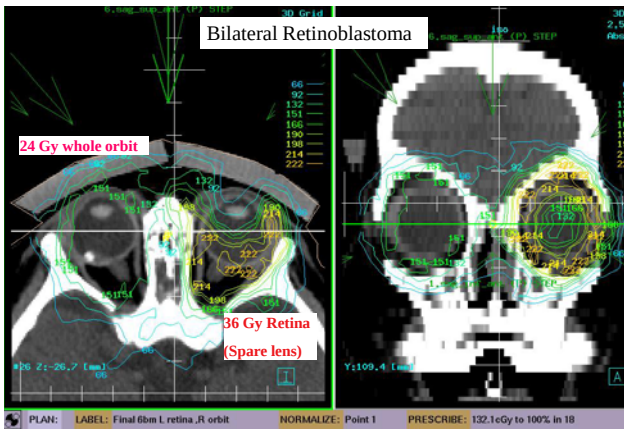
Orbital Tumors

Whole Globe Irradiation by



Whole Retina Irradiation





Relocatable Immobilization

Medical Intelligence : HeadFix and BodyFix

Radionics: Tarbell-Loeffler-Cosman Pediatric Headframe

Materials - VBH HeadFix Arc

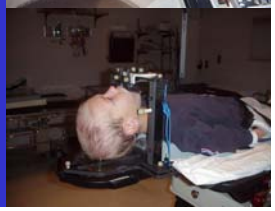
(Childrens Hospital LA and Medical Intelligence, Germany)

1) All carbon fiber, open structure.

2) Vacuum-assisted mouthpiece with vacuum gauge.

3) <1mm average daily reproducibility in each direction.

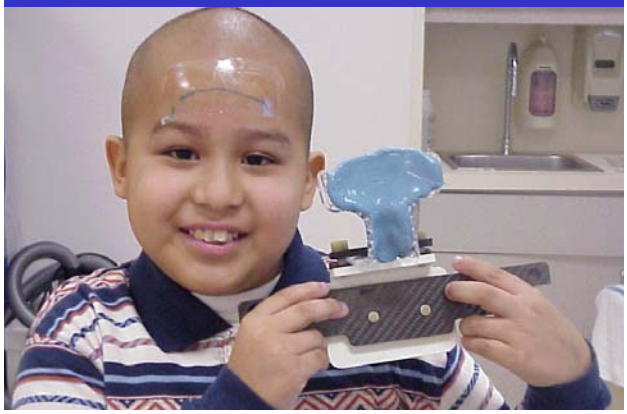
4) For adults or children



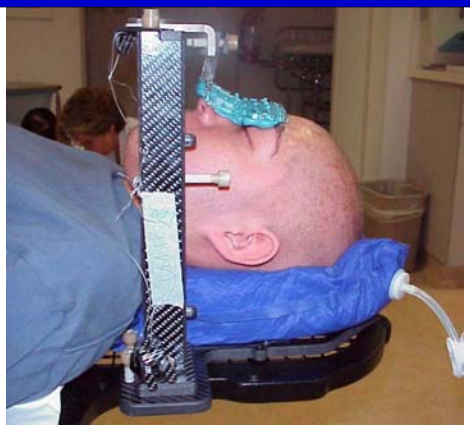
HeadFix^{R} Assembly with Custom Headrest

Custom Dental Fixation Device with Vacuum

Naso-Frontal Head Immobilization Device

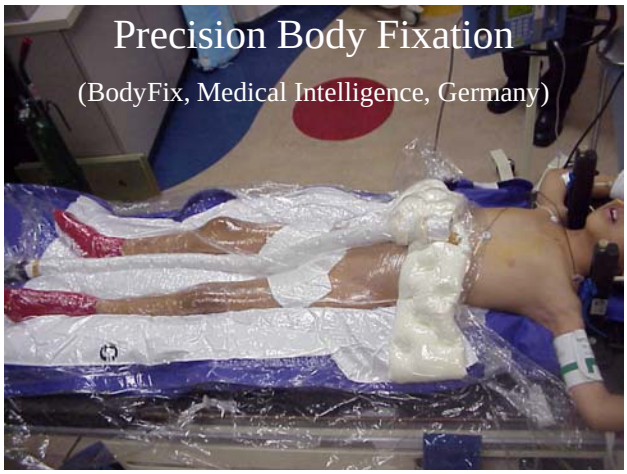


Naso-Frontal Immobilization Assembly



Precision Body Fixation

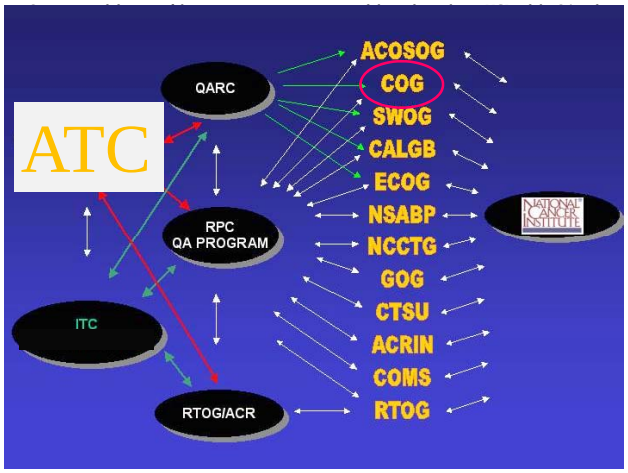
(BodyFix, Medical Intelligence, Germany)



Clinical Trials

Many Children are Treated on Protocol

- Children's Oncology Group (COG)
- RPC – Radiological Physics Center
- Quality Assurance Review Center – QARC
- Advanced Technology Consortium - ATC
- Various ongoing COG studies that allow IMRT, encourage digital data submission, require isodoses and DVH data submitted.



Quality Assurance Review Center (QARC – www.QARC.org)

- QARC was created in the late 1970's.
- Provides wide range of QA services for:
  - Children's Oncology Group (COG),
  - The Pediatric Brain Tumor Consortium (PBTC),
  - The Cancer and Leukemia Group B (CALGB),
  - The Eastern Cooperative Oncology Group (ECOG),
  - the American College of Surgeons Oncology Group (ACOSOG) and
  - The Southwest Oncology Group (SWOG).

Benchmarking and Credentialing

- RPC TLD monitoring
- Standard Treatment Planning Benchmark Package
  - 3-D conformal brain
  - Irregularly shaped field (Mantle)
  - Cranio-spinal irradiation
- IMRT Questionnaire and Benchmark (may also include phantom irradiation)
- Total Body Irradiation Benchmark
- Image Fusion Benchmark
- Proton Therapy Benchmark

Protocol Data Submission

- Rapid review – submit data 24-72 hours after start of RT.
- Pre-treatment review- must get ok to treat.
- ALL new protocol data submission is now required to be electronic, DICOM RT or RTOG format.

Summary

- Treating children with radiotherapy is more challenging than adults.
- Children get different cancers 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.

A few of our former patients (and current friends)