Planning and Delivery in Pediatric Radiotherapy

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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,
  – may require fewer events to progress,
  – mechanisms underlying initiation might therefore differ from adult cancers – genetic mutations,
  – not likely to be caused by environmental factors.
  – 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

<table>
<thead>
<tr>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostate</td>
<td>Breast</td>
</tr>
<tr>
<td>Lung/Bronchus</td>
<td>Lung/Bronchus</td>
</tr>
<tr>
<td>Colon/Rectum</td>
<td>Colon/Rectum</td>
</tr>
<tr>
<td>Bladder</td>
<td>Uterus</td>
</tr>
<tr>
<td>Lymphomas</td>
<td>Ovary</td>
</tr>
<tr>
<td>Oral cavity</td>
<td>Skin Melanoma</td>
</tr>
<tr>
<td>Skin Melanoma</td>
<td>Cervix</td>
</tr>
<tr>
<td>Leukemia</td>
<td>Leukemia</td>
</tr>
</tbody>
</table>
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

- A.L.L
- CNS
- Bone
- Germ Cell Tumor
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.
Comparison of Critical Structure Dose for Children vs. Adults

<table>
<thead>
<tr>
<th>Structure</th>
<th>Children</th>
<th>Adult</th>
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</thead>
<tbody>
<tr>
<td>Whole Brain</td>
<td>18 Gy</td>
<td>35 Gy</td>
</tr>
<tr>
<td>Bones</td>
<td>10 Gy</td>
<td>&gt;65 Gy</td>
</tr>
<tr>
<td>Pituitary (growth hormone)</td>
<td>20 Gy</td>
<td>none</td>
</tr>
<tr>
<td>Ovary/testes (reproduction)</td>
<td>10 Gy</td>
<td>none</td>
</tr>
<tr>
<td>Breast (ca induction 40 Gy)</td>
<td>RR = 20</td>
<td>RR = 2</td>
</tr>
</tbody>
</table>

Cardiac toxicity may be higher for children, more years for problem to develop than in adults
Secondary Malignancy Rate: RT vs. Chemo vs. Both Hodgkin’s Disease

<table>
<thead>
<tr>
<th>Clinical Characteristic</th>
<th>No. of Patients</th>
<th>Patients With Second Neoplasms</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Solid Tumors (n = 104)</td>
</tr>
<tr>
<td>All Patients (N = 1,380)</td>
<td></td>
<td>No. of Patients</td>
</tr>
<tr>
<td>Radiation alone</td>
<td>314</td>
<td>31</td>
</tr>
<tr>
<td>Chemotherapy alone</td>
<td>106</td>
<td>2</td>
</tr>
<tr>
<td>Radiation and chemotherapy</td>
<td>960</td>
<td>71</td>
</tr>
</tbody>
</table>

RT-induced solid tumors mostly breast and thyroid
Induction of Second Cancer for Pediatric Patients Treated with RT

- Osteogenic sarcoma is most often seen SM after RT. There are some cases (25% in one study) where the SM occurs outside the RT field (in long bones).
- Chemo usually used with RT, both increase risk of SM
- Brain tumor irradiation (children): 4% after 15 years
- A.L.L. survivors receiving radiation: estimated risk of SM = 21% vs. 1% for those pts not getting RT. Mostly benign or low grade ca. Long term survival was only slightly less than for matched children in general population.
- Doses less than 10 Gy generally were not associated with increased risk of SM. Kun et al: No SM for doses less than 48 Gy
- Donaldson et al.: risk for SM in survivors of Ewing’s sarcoma: 2.7 relative risk of bone sarcoma, 40 for doses > 60 Gy. **Don’t use orthovoltage due to higher bone dose.**
- Risk continues to increase over time, 20, 30 years +
- E. Hall- IMRT may increase SM rate from 1% to 1.75% (adults)
- Peacock (adults): 3-10% vs. 1% conventional RT due to 10 fold increase in MUs.
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.
CHLA Patient Population

- Sedation every day for < 7 y.o.
- Treat about 16 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
- BEV to miss low dose critical structures, i.e. lens, pituitary
- IMRT vs. 3-d conformal: total body dose
- 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%
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 vs. Coplanar DVH for Normal Brain
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

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)

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

• Treat posterior fossa to total of 54 Gy by separate boost fields
Conventional Craniospinal Irradiation Technique
(Can be supine or prone)

- Lateral Opposed Whole Brain Fields
  (Collimator rotation)
- Immobilization Device
- PA Spine Field
Dose to Mouth and Airway Kept Low by Shaping Whole Brain Fields
Conventional Craniospinal Irradiation Technique

Right and left lateral whole brain fields

(Couch rotation)

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

Spine field
Verification of Brain/Spine Junction for Supine Position as Seen From PA Spine Field

- BB
- Spine field outline
- 2-5 mm planned gap
Conventional Craniospinal Irradiation Technique - Dosimetry for PA Spine

**Daily Doses**

**LOWER HALF**
- 180
- 162
- 144
- 126

**UPPER HALF**
- 180
- 162
- 144
- 126

3D Grid 2.5 [mm] Absolute
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

Decreased gut dose from 126 cGy/dy for PA field vs. 36 cGy/dy for 3 field technique
Junction Dose for 3 Field spine + Whole Brain Fields

Before the 2 Junction shifts

Percentages of Tumor Dose

-20%
PA Spine field only

3 Field Spine Technique Protects Trachea and Esophagus

PA, RPO, LPO spine fields
3 Field Spine Technique
Reduces Heart Dose

PA, RPO, LPO
Less than 10% of Kidneys and Lung Get 1300 cGy
Skin Marks Lined Up to Marks on Immobilization Bag for Daily Treatment
Split beam CSI technique
(No Couch Rotation)

- True Cranial field isocenter
- Effective Cranial field center
- Cranial field half-beam-blocked
- Face mask
- Immobilization mold
- Horizontal center level with canthi
- Matchline between the non-divergent cranial and spinal fields
- Isocenter for the spinal field
- Caudal border of the spinal field adjusted using an independent colliomator
- Wedge or simulated virtual wedge
- Horizontal center level with canthi
- Face mask
- Immobilization mold
- Cranial field half-beam-blocked
Changing the Boost Treatment for Medulloblastoma

- Reduce cognitive and hearing losses associated with this treatment.
- Test whether reducing the boost volume 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 50% have IMRT capability so it is feasible 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

Coronal

- WPF
- Local PTV
- Local GTV

Sagital

- WPF
- Local PTV
- Local GTV
Plan comparison for limited volume boost
<table>
<thead>
<tr>
<th>Sites</th>
<th>Technique</th>
<th>Cochlea Mean Dose Gy</th>
<th>Pituitary Mean dose Gy</th>
<th>% Supr. Tent Brain 10 Gy</th>
<th>% Supr. Tent Brain 20 Gy</th>
<th>% Temp. Lobe 10 Gy</th>
<th>% Temp. Lobe 20 Gy</th>
</tr>
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<tbody>
<tr>
<td>Opposed</td>
<td>Laterals WPF</td>
<td>31</td>
<td>4</td>
<td>20</td>
<td>17</td>
<td>74</td>
<td>69</td>
</tr>
<tr>
<td>IMRT</td>
<td>6 Beam WPF</td>
<td>13</td>
<td>8</td>
<td>25</td>
<td>6</td>
<td>59</td>
<td>17</td>
</tr>
<tr>
<td>IMRT</td>
<td>10 Beam WPF</td>
<td>10</td>
<td>7</td>
<td>27</td>
<td>6</td>
<td>36</td>
<td>6</td>
</tr>
<tr>
<td>Conformal</td>
<td>10 Beam WPF</td>
<td>24</td>
<td>16</td>
<td>33</td>
<td>11</td>
<td>81</td>
<td>27</td>
</tr>
</tbody>
</table>
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.

• 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 feasible.
    • 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
Total Body Irradiation for Leukemia
TBI stand

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

Brake Lever
Horizontal Lock
Rotation Wheel

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
Pelvic Germ Cell Tumor
Pelvic Rhabdomyosarcoma and Surrounding Organs

[Image of a 3D anatomical diagram showing the tumor and surrounding organs]
Pelvic Rhabdomyosarcoma: 5 Beam Conformal RT
Pelvic Rhabdomyosarcoma: 5 Axial Beam IMRT
Neuroblastoma
Neuroblastoma: Opposed Oblique Beams

Note that whole spine is intentionally included in high dose area.
Neuroblastoma: 8 Axial Beam IMRT
Other Head and Neck
Metastatic Retinoblastoma
PNET of Neck
Keloid Treatment in Infant (Electron Beam)

Lead with bolus backing under lip to protect teeth
Orbital Tumors
Whole Globe Irradiation by

Anterior Electron Beam

Isodose Lines

2400

1000

8 Beam IMRT
Whole Retina Irradiation

Isodose Lines

2400
2000
1000

8 Beam IMRT
Bilateral Retinoblastoma

24 Gy whole orbit

36 Gy Post Globe

PLAN: Final 6bm L retina, R orbit
NORMALIZE: Point 1
PRESCRIBE: 132.1 cGy to 100% in 18
Whole Globe Irradiation: IMRT vs Electrons

### 24 Gray Minimum Dose to Whole Globe

<table>
<thead>
<tr>
<th>Dose</th>
<th>Volume Outside Globe Getting Dose</th>
<th>Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;20 Gy</td>
<td>28.3 cc</td>
<td>83%</td>
</tr>
<tr>
<td>&gt;15 Gy</td>
<td>47.4 cc</td>
<td>78%</td>
</tr>
<tr>
<td>&gt;10 Gy</td>
<td>72.3 cc</td>
<td>71%</td>
</tr>
<tr>
<td>&gt; 5 Gy</td>
<td>113.5 cc</td>
<td>48%</td>
</tr>
</tbody>
</table>

*12 MeV e- IMRT*
Whole Retina Irradiation: IMRT vs Lateral Beam

<table>
<thead>
<tr>
<th>Dose</th>
<th>Volume Outside Retina Getting Dose</th>
<th>Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Lateral Beam</td>
<td>IMRT</td>
</tr>
<tr>
<td>20 Gy</td>
<td>25.3 cc</td>
<td>3.0 cc</td>
</tr>
<tr>
<td>15 Gy</td>
<td>45.4 cc</td>
<td>5.0 cc</td>
</tr>
<tr>
<td>10 Gy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lens only</td>
<td>11.3 %</td>
<td>0.3 %</td>
</tr>
<tr>
<td>Total volume</td>
<td>59.7 cc</td>
<td>11.7 cc</td>
</tr>
<tr>
<td>5 Gy</td>
<td>71.2 cc</td>
<td>44.7 cc</td>
</tr>
</tbody>
</table>
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\textsuperscript{R} Assembly with Custom Headrest
Custom Dental Fixation Device with Vacuum
HeadFix® Assembly with Target Localizer Box
Naso-Frontal Immobilization Assembly
Precision Body Fixation

(BodyFix, Medical Intelligence, Germany)
Isocenter Verification

• Simulation as QA for TPS
  • Compare AP and LLAT DRR to digitally captured Sim x-ray image
• Treatment (Weekly) – Same AP and LLAT portals taken with electronic portal imaging compared to DRRs. Use anatomy matching to generate couch shift data.

**We require agreement within 2 mm for brain and 3 mm for body sites**
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.
Organizational diagram of the various cooperative groups and their relationship to NCI and the QA resource centers.
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 Benchmark Package
  - Wedged fields
  - Irregularly shaped field
  - Central axis blocked field
  - Cranio-spinal irradiation technique
- 3D Treatment Planning Benchmark
- 3DCRT Facility Questionnaire
- IMRT Questionnaire and Benchmark (may also include phantom irradiation)
- Total Body Irradiation Benchmark
- Stereotactic Radiosurgery (SRS) Benchmark, including anthropomorphic phantom irradiation
  - SRS with Gamma Knife
  - SRS with Linear Accelerator
- Prostate Brachytherapy Credentialing
  - Some require “dry run” electronic data submission
Protocol Data Submission

• Timely and accurate data submission is essential to the success of the cooperative group process.
• Pre-treatment review or
• Rapid review – submit data 24-72 hours after start of RT.
• Some advanced tech trial require electronic data submission
A few of our former patients (and current friends)