Pediatric Radiation Therapy Planning, Treatment, and Late Effects

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Pediatric Treatment Planning I: Overview of Planning Strategies and Challenges

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Disclosure

No conflict of interest

Mention of certain product names do no constitute an endorsement.
Overview of this Presentation

• Normal tissue tolerance differences between children and adults
• Secondary cancer risk from radiotherapy
• Craniospinal irradiation techniques
• Total Body irradiation techniques
• General treatment planning issues
• Immobilization techniques
CHLA and St. Jude Patient Population

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

**Childhood Cancer Incidence (2% of all cancers)**

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

**Adult Cancer Incidence**

<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)

Histologies rare to not seen in adults.

Adult cancers are predominantly Carcinomas
Childhood Cancer Survival Rate

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

• Late Effects
• Secondary Malignant Neoplasms
Induction of Second Cancer for Pediatric Patients Treated with RT

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

- Multi-beam treatment by itself does not increase integral dose vs. conventional treatments.
- IMRT by itself does not increase integral or peripheral dose vs. conventional treatments.
- IMRT does give 3-4 times higher leakage dose and increases the volume receiving ultra low doses.
- SM *infrequently* occur where head leakage dose dominates, i.e. distant from the medium-high dose region.
- SM risk increases with increasing dose.
- Reducing the volume receiving moderate to high doses in trade for increasing the volume receiving <5 Gy should both reduce SM risk and better protect normal structures.
Q1: Which is **TRUE** about the risk of production of second malignancy from radiation therapy:

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

- Answer: b - Most secondary malignancies occur inside the medium-high dose region

Comparison of Critical Structure Dose for Children vs. Adults

<table>
<thead>
<tr>
<th>Structure</th>
<th>Children</th>
<th>Adult</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole Brain</td>
<td>18 Gy</td>
<td>35 Gy</td>
</tr>
<tr>
<td>Bones</td>
<td>18 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>
</tbody>
</table>

Cardiac toxicity may be higher for children, more years for problem to develop than in adults.
PENTEC
(Pediatric Normal Tissue Effects in the Clinic)

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

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

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

30% of pediatric brain tumors
¾ of all cases occur in children, median age 9 y.o.
Treatment of Medulloblastoma
Targets and Critical Structures

Brain (target and OAR)
Spinal cord (target and OAR)
Cochlea
Gut, throat, heart (PA spine exit doses)
Lenses
Skin (PA entrance dose)
Craniospinal Axis Treatment

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

CSI Planning issues:

• Prone vs. Supine

• Spine-brain junction dose (avoid cord overdose), junction level, and shifts

• Extended SSD vs. abutted PA spine fields
Conventional Craniospinal Irradiation Technique
(Supine is best)

- Immobilization Device
- PA Spine Field
- Lateral Opposed Whole Brain Fields
  (Collimator and couch rotation)
- Shield
Conventional Craniospinal Irradiation Technique

Right and left lateral whole brain fields

(Couch rotation)

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

Spine field
Split beam CSI technique
(No Couch Rotation for WB)

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

Medical Dosimetry, Vol. 28, No. 1, pp. 35–38, 2003
Need Abutted Spine Fields or Ext SSD for Bigger Kids
(can use 90 deg couch + gantry rotation to avoid divergence)
Spare lenses But Don’t Block the Cribiform Plate Region

Cribiform region of brain
Verification of Brain/Spine Junction for Supine Position as Seen From PA Spine Field

2-5 mm planned gap

Spine field outline

BB

BB
junction positions with shifts

No gap

Uniform dose

2 mm gap

-10%

5 mm gap

-20%
VMAT (Rapid Arc) for Cranial Spinal Irradiation
PA Spine and opposed Lateral whole Brain

CSI 36 Gy

Rapid Arc
PA Spine and opposed Lateral whole Brain

Rapid Arc
16 MeV PA Electron Beam Spine Field

***Requires Patient to be Prone, 2 spine flds***
Changing the Boost Treatment for Medulloblastoma

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

10 beam Conformal

6 Beam IMRT

Plan comparison for limited volume boost
Q2: Regarding CSI for Medulloblastoma, which is **TRUE**:

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

• Answer: c – not overdosing the spinal cord

Treatment of Acute Lymphoblastic Leukemia (A.L.L.)
also A.M.L. and some other diseases

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

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

- Beam spoiler typically used to bring full dose to skin surface
- Dose rate kept ≤ 10 cGy/min at patient midplane
- Goal is dose uniformity within 10%
- SSD > 3m needed
Total Body Irradiation for Leukemia
TBI stand

- Block tray holder
- Film holder
- Bicycle seat for patient to sit on

Not practical for children less than about 8 y.o. or for any sedated child
Physics Measurement for Commissioning and Calibration

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

Folgliata, IntJRadOncBiolPhys 2011
Q3: Acute Lymphoblastic Leukemia (ALL) is infrequently treated by radiation therapy but when it is, which is **NOT** a key consideration for total body irradiation:

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

10
The correct answer is:

- Answer: d - Extremity dose

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

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