Dosimetric Comparison of Whole-Lung Treatment Techniques in the Pediatric Population

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Introduction
Introduction

- Remarkable improvement in survival of Wilms’ tumor patients over last four decades
- Whole-lung irradiation (WLI) crucial component
  - Current multimodality methods → 90% survival outcome
  - Prior to this improvement, nearly all patients succumbed to their disease
- With more surviving, greater emphasis should be placed on potential for late toxicities
Introduction

- Late toxicities may be possible due to modern treatment approaches
  - Combination of radiotherapy and cardiac toxic chemotherapy
  - Several reports have shown that WLI with or without doxorubicin has led to higher prevalence of cardiac complications in these pediatric patients
  - Congestive heart failure, myocardial infarction, pericardial disease, and valvular heart disease
Introduction

With radiation therapy being a crucial component, information regarding the optimal treatment technique was sought

• Wanted to find a method which offered the best target coverage and best normal tissue sparing
• Of importance to the pediatric population, on-table time was a factor for this study
  • Wanted a method which could be delivered quickly and efficiently
Introduction

- Three treatment techniques tested:
  - Standard anteroposterior-posteroanterior (S-AP/PA) radiotherapy
  - Inverse-planned AP/PA (IP-AP/PA) radiotherapy
  - Volumetric-modulated arc radiotherapy (VMAT)

S-AP/PA  IP-AP/PA  VMAT
Introduction

- Techniques compared based on the following criteria:
  - Best target coverage
  - Best normal tissue sparing
  - Lowest body maximum dose
  - Evaluation of low dose regions
    - Percentage of body receiving 50% and 30% of prescription dose
Introduction

- A brief study of the use and non-use of tissue heterogeneity algorithms was conducted
  - Wanted to discover what was “thought” to be delivered versus what was actually delivered

1970s – 1990s: No tissue correction
1990s – 2000s: Pencil-beam
2000s - Present: AAA
Methods and Materials

Coffee...lots of coffee...and maybe a nap or two...
Methods and Materials

Eclipse Version 11
Methods and Materials

- Ten CT scans of pediatric patients (mean age 3.8 years, range 1-12 years) simulated between 2010 - 2014
- All scans included the neck superiorly and the reproductive organ region inferiorly
Methods and Materials

- Normal Tissue Contouring
  - Esophagus
  - Heart and Pericardium
    - Used RTOG contouring atlas
  - Spinal Canal
  - Spleen
  - Stomach
  - Reproductive Organ Region
    - Any tissue that fell within the volume of interest box with superior border between L5 and S1, inferior to include at least 1 cm beyond external genitalia, and laterally at outer edges of femoral heads
    - Cropped any contour that extended outside the body
O Superior border - between L5 and S1
O Inferior border - include at least 1 cm beyond external genitalia
O Lateral borders - outer edges of femoral heads
O Cropped any contour that extended outside the body
Methods and Materials

Contouring: Target Volumes

- GTV – both lungs in their entirety using acquisition window/level setting
- CTV – 1.5 cm expansion from GTV and cropped 0.3 cm within body
- PTV – an additional 0.3 cm expansion from the CTV
- PTV_DVH – cropped 3 mm beneath skin
PTV vs PTV_DVH

0.3 cm skin included

0.3 cm skin excluded

PTV

PTV_DVH
Methods and Materials

- **Treatment Planning**
  - 6-MV photons used for all plans
  - Prescription Dose = 1,500 cGy at 150 cGy/fraction

<table>
<thead>
<tr>
<th>Fractionation Id</th>
<th>Dose / Fraction [cGy]</th>
<th>Number of Fractions</th>
<th>Total Dose [cGy]</th>
<th>Target Volume</th>
<th>Primary Reference Point [Volume]</th>
<th>Total Dose at Primary [cGy]</th>
<th>Relative Dose at Primary [%]</th>
<th>Prescribed Percentage [%]</th>
<th>Plan Normalization Mode</th>
<th>Plan Normalization Value [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>150.0</td>
<td>10</td>
<td>1500.0</td>
<td>PTV Lungs</td>
<td>PTV Lungs DPV [PTV Lungs]</td>
<td>1500.0</td>
<td>100.0</td>
<td>100.0</td>
<td>No plan normalization</td>
<td>100.0</td>
</tr>
</tbody>
</table>
Methods and Materials

**Treatment Planning**

<table>
<thead>
<tr>
<th>Technique</th>
<th>Gantry Angle</th>
<th>Collimator Angle</th>
<th>MLC’s</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. S-AP/PA</td>
<td>0°/180°</td>
<td>90°</td>
<td>0.7 cm margin around PTV</td>
</tr>
<tr>
<td>2. IP-AP/PA</td>
<td>0°/180°</td>
<td>0°</td>
<td>Dynamic</td>
</tr>
<tr>
<td>3. VMAT</td>
<td>CW: 181° - 179°</td>
<td>30°</td>
<td>Dynamic</td>
</tr>
<tr>
<td>(9/10 patients)</td>
<td>CCW: 179° - 181°</td>
<td>330°</td>
<td></td>
</tr>
</tbody>
</table>
Methods and Materials

1. Treatment Planning: S-AP/PA
Methods and Materials

1. Treatment Planning: **S-AP/PA**
   - Gantry angles of 0° and 180° used
   - Collimator optimized to provide the best MLC conformation to the PTV (90° for all patients)
   - MLC’s: Static with a 0.7 cm margin around the PTV
Methods and Materials

2. Treatment Planning: IP-AP/PA

MLC Motion

95% Colorwash
2. Treatment Planning: **IP-AP/PA**
   - Gantry angles of 0° and 180° used
   - Collimator angle = 0°
   - Jaws: Not fixed in optimization page
   - MLC’s: Dynamic; Multiple Static Segments with Smoothing Levels = 13
   - Optimization: Highest priority given to targets with heart as most important critical structure
2. Treatment Planning: IP-AP/PA

- Gantry angles of 0° and 180° used
- Collimator angle = 0°
- Jaws: Not fixed in optimization page
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Methods and Materials

3. Treatment Planning: **VMAT**

- MLC/Gantry Motion
- 95% Colorwash
3. Treatment Planning: VMAT

- Two arcs used for 9/10 patients:
  - Clockwise: 181° - 179°
  - Counter-clockwise: 179° - 181°
- One patient required two isocenters and four half arcs (oldest patient and therefore the largest)
  - Clockwise: 0° - 179°
  - Counter-clockwise: 179° - 0°
  - Counter-clockwise: 0° - 181°
  - Clockwise: 181° - 0°
- Collimator angle:
  - Clockwise: 30°
  - Counter-clockwise: 330°
- Optimization: Highest priority given to targets with heart as most important critical structure
3. Treatment Planning: VMAT

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  - Clockwise: 181° - 0°

- Collimator angle:
  - Clockwise: 30°
  - Counter-clockwise: 330°

- Optimization: Highest priority given to targets with heart as most important critical structure
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- Collimator angle:
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  - Counter-clockwise: 330°

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Historic Portion:

- A brief study of the use and non-use of tissue heterogeneity algorithms was conducted
- Wanted to discover what was “thought” to be delivered versus what was actually delivered

- No tissue correction “S-NO” 1970s – 1990s
- Pencil-beam “S-PB” 1990s – 2000s
- AAA “S-AAA” 2000s - Present
Methods and Materials

1. Treatment Planning: S-NO
   - Indicative of plans created between 1970 - 1990
   - Created a S-AP/PA plan as described previously but turned off tissue heterogeneity correction
Methods and Materials

1. Treatment Planning: **S-NO**
   - Indicative of plans created between 1970 - 1990
   - Created a S-AP/PA plan as described previously but turned off tissue heterogeneity correction
2. Treatment Planning: S-PB

- Indicative of plans created between 1990 - 2000s
- Copy/pasted S-NO plan; changed calculation model to Pencil-Beam algorithm
- Monitor units from S-NO plan were noted and fixed for this new plan
2. Treatment Planning: S-PB

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<table>
<thead>
<tr>
<th>Particle Type</th>
<th>Calculation Type</th>
<th>Calculation Model</th>
<th>Algorithm</th>
<th>Calculation Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>Photon</td>
<td>Volume Dose</td>
<td>PBC_10020</td>
<td>Pencil Beam Convolution (Version 10.0.23)</td>
<td>Edit</td>
</tr>
<tr>
<td></td>
<td>Point Dose</td>
<td>PBC_10020</td>
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<tr>
<td></td>
<td>Stereotactic Dose</td>
<td>CTI_11031</td>
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<tr>
<td></td>
<td>Irregular Surface Compensator</td>
<td>DVC_CHP_311034</td>
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<td></td>
<td>Optimization</td>
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<tr>
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<td>Compensator</td>
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<td>PDIP_11031</td>
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<td>Electron Monte Carlo (Version 11.0.31)</td>
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</tbody>
</table>
Methods and Materials

2. Treatment Planning: S-PB

- Indicative of plans created between 1990 - 2000s
- Copy/pasted S-NO plan; changed calculation model to Pencil-Beam
- Monitor units from S-NO plan noted and fixed for this new plan
3. Treatment Planning: **S-AAA**
   - Modern Day
     - Copy/pasted S-NO plan; changed calculation model to Anisotropic Analytical Algorithm
     - Monitor units from S-NO plan were noted and fixed for this new plan
3. Treatment Planning: **S-AAA**

- Modern Day
- Copy/pasted S-NO plan; changed calculation model to Anisotropic Analytical Algorithm
- Monitor units from S-NO plan were noted and fixed for this new plan

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</tr>
</thead>
<tbody>
<tr>
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<td>Stereotactic Dose</td>
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<td>DVO_CHP_110031</td>
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<td>Edit</td>
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<td>Optimization</td>
<td>DVO_CHP_110031</td>
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<td>PGDIP_11031</td>
<td>Portal Dose Image Prediction (Version 11.0.31)</td>
<td>Edit</td>
</tr>
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<td>EMC_CHP_11031</td>
<td>Electron Monte Carlo (Version 11.0.31)</td>
<td>Edit</td>
</tr>
</tbody>
</table>
Methods and Materials

3. Treatment Planning: S-AAA

- Modern Day
- Copy/pasted S-NO plan; changed calculation model to Anisotropic Analytical Algorithm
- Monitor units from S-NO plan noted and fixed for this new plan

![Image of treatment planning software with S-NO and S-AAA plans compared]
3. Treatment Planning: S-AAA

- Using fixed MUs from S-NO plan and switching calculation model to AAA, this better illustrates what was actually delivered in the past.
Parameters used for comparison = (1) target coverage, (2) normal tissue sparing, (3) body maximum dose, and (4) doses in lower isodose regions (50% and 30%)

(1) Target comparison accomplished by evaluating the percent dose that 95% of the GTV, CTV, PTV, and PTV_DVH volumes received by calculating an average for each technique from the ten scans

(2) Average maximum dose to all normal tissue structures was calculated

(3) Average of body maximum doses calculated

(4) Evaluated by dividing the number of cc’s in the body that received 50% and 30% of prescription dose by the number of cc’s in the entire body structure. An average was determined for each set of plans and used for assessment.
Results

(1) Target Coverage

Best Coverage:
- 1. S-AP/PA for all target structures
- 2. VMAT
- 3. IP-AP/PA

<table>
<thead>
<tr>
<th>TARGET</th>
<th>S-AP/PA</th>
<th>IP-AP/PA</th>
<th>VMAT</th>
</tr>
</thead>
<tbody>
<tr>
<td>GTV</td>
<td>101.8%</td>
<td>92.3%</td>
<td>97.3%</td>
</tr>
<tr>
<td>CTV</td>
<td>98.1%</td>
<td>89.0%</td>
<td>93.0%</td>
</tr>
<tr>
<td>PTV</td>
<td>85.7%</td>
<td>78.6%</td>
<td>84.6%</td>
</tr>
<tr>
<td>PTV_DVH</td>
<td>97.1%</td>
<td>87.7%</td>
<td>91.9%</td>
</tr>
</tbody>
</table>

Values = percentage of prescription dose that 95% of the target volumes received
Results

(2) Normal Tissue Sparing

- Maximum doses to esophagus, heart and pericardium, spinal canal, spleen, stomach, and reproductive organs collected and mean calculated for each
- Additionally, mean dose to reproductive organs collected and averaged
- Findings:
  - VMAT best protected heart and pericardium, spinal canal, and stomach
  - IP-AP/PA best protected esophagus, stomach, and reproductive organs
  - S-AP/PA least effective for all normal tissues

<table>
<thead>
<tr>
<th>ORGAN</th>
<th>S-AP/PA</th>
<th>IP-AP/PA</th>
<th>VMAT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Esophagus</td>
<td>16.63 Gy</td>
<td>14.69 Gy</td>
<td>14.78 Gy</td>
</tr>
<tr>
<td>Heart and Pericardium</td>
<td>16.72 Gy</td>
<td>15.87 Gy</td>
<td>14.97 Gy</td>
</tr>
<tr>
<td>Spinal Canal</td>
<td>16.51 Gy</td>
<td>15.12 Gy</td>
<td>14.62 Gy</td>
</tr>
<tr>
<td>Spleen</td>
<td>16.4 Gy</td>
<td>16.12 Gy</td>
<td>15.96 Gy</td>
</tr>
<tr>
<td>Stomach</td>
<td>16.0 Gy</td>
<td>15.87 Gy</td>
<td>15.94 Gy</td>
</tr>
<tr>
<td>Reproductive Organ Max</td>
<td>23.6 Gy</td>
<td>19.6 Gy</td>
<td>34.0 Gy</td>
</tr>
<tr>
<td>Reproductive Organ Mean</td>
<td>0.66 Gy</td>
<td>0.53 Gy</td>
<td>2.9 Gy</td>
</tr>
</tbody>
</table>
Results

(3) Body Maximum Dose

- Average of body maximum doses calculated
- Best to worst:
  - 1. VMAT
  - 2. IP-AP/PA
  - 3. S-AP/PA

<table>
<thead>
<tr>
<th>PARAMETER</th>
<th>S-AP/PA</th>
<th>IP-AP/PA</th>
<th>VMAT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body Maximum</td>
<td>115.1%</td>
<td>113.0%</td>
<td>109.6%</td>
</tr>
</tbody>
</table>
Results

(4) Lower Isodose Regions – Think Integral Dose

- Evaluated by dividing the number of cc’s in the body that received 50% and 30% of prescription dose by number of cc’s in the entire body structure.
- Average was determined for each set of plans and used for assessment.

Example:
- 3342 cc’s receive 30% of Rx
- 8889 = # cc’s in body structure
- 3342/8889 = 37.6% of body receives 30% of Rx dose

* Process repeated for 50% dose
Results

(4) Lower Isodose Regions – Think Integral Dose

- **30% best to worst:**
  1. IP-AP/PA
  2. S-AP/PA
  3. VMAT

- **50% best to worst:**
  1. IP-AP/PA
  2. VMAT
  3. S-AP/PA

<table>
<thead>
<tr>
<th>PARAMETER</th>
<th>S-AP/PA</th>
<th>IP-AP/PA</th>
<th>VMAT</th>
</tr>
</thead>
<tbody>
<tr>
<td>% of Body Receiving 50% Rx</td>
<td>30.4%</td>
<td>29.0%</td>
<td>29.4%</td>
</tr>
<tr>
<td>% of Body Receiving 30% Rx</td>
<td>32.3%</td>
<td>31.1%</td>
<td>32.8%</td>
</tr>
<tr>
<td>% Variation from IP-AP/PA (50%/30%)</td>
<td>1.4% / 1.2%</td>
<td>0% / 0%</td>
<td>0.4% / 1.7%</td>
</tr>
</tbody>
</table>
Results

Historic Portion:

- No tissue correction “S-NO”
  - 1970s – 1990s

- Pencil-beam “S-PB”
  - 1990s – 2000s

- AAA “S-AAA”
  - 2000s - Present

- No Difference between S-AAA and S-NO (Real vs Presumed) plans for reproductive organ mean dose, 50% and 30% doses
- The Good:
  - Found that targets were actually covered slightly better than was presumed in the past
  - Body maximum, esophageal, and spinal canal doses were all lower than was thought in the past
- The Bad:
  - Maximum doses to heart, spleen, stomach, and reproductive doses were all higher than was supposed
- The Ugly:
  - See next slide...
Results

• The Ugly: Isodose Lines
  • Took time for physicians to get acquainted with the “new look” of these more accurate isodose lines

S-NO  S-PB  S-AAA
Results

- No Difference between S-AAA and S-NO (Real vs Presumed) plans for reproductive organ mean dose, 50% and 30% doses

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<td>93.2%</td>
<td>94.8%</td>
</tr>
<tr>
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<td>15.90 Gy</td>
<td>16.26 Gy</td>
</tr>
<tr>
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<td>15.83 Gy</td>
<td>16.08 Gy</td>
<td>16.33 Gy</td>
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<tr>
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<td>16.21 Gy</td>
<td>15.90 Gy</td>
<td>16.15 Gy</td>
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<td>16.04 Gy</td>
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<tr>
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<td>15.45 Gy</td>
<td>15.61 Gy</td>
</tr>
<tr>
<td>Reproductive Organ Max</td>
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<td>8.1 Gy</td>
<td>23.2 Gy</td>
</tr>
<tr>
<td>Reproductive Organ Mean</td>
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</tr>
<tr>
<td>% of Body Receiving 50% Rx</td>
<td>30.3%</td>
<td>30.9%</td>
<td>30.3%</td>
</tr>
<tr>
<td>% of Body Receiving 30% Rx</td>
<td>32.2%</td>
<td>32.4%</td>
<td>32.2%</td>
</tr>
<tr>
<td>% Variation from S-PB (50%/30%)</td>
<td>1.3% / 1.1%</td>
<td>1.9% / 1.3%</td>
<td>1.3% / 1.1%</td>
</tr>
</tbody>
</table>
Discussion

• Wilms’ Tumor is most common renal mass in children

• Radiotherapy remains a crucial therapeutic component
  • Statistics from National Wilms’ Tumor Study ➔ Children with favorable histology have relapse-free and overall survival rates of 72% and 78% respectively

• With cardiac toxic chemotherapy also being an important component, many more children are surviving these days with a greater emphasis being placed on possible late tissue effects
  • National Wilms’ Tumor Study ➔ 20-year congestive heart failure rate = 4.4% after initial treatment and 17.4% after first or successive relapse
Discussion

• Normal tissue sparing is one of the more essential principles in the management of pediatric radiotherapy

• As such, emphasis should be placed on normal tissue sparing when planning these patients
  • In this study, however, emphasis placed on target coverage so each technique could be compared side-by-side
  • If optimization was required (IP-AP/PA and VMAT), heart was given highest priority
Discussion

- Treatment of choice for normal tissue sparing = IP-AP/PA and VMAT

- Possible problems:
  - Motion interplay effect – both require dynamic MLCs
  - Potential for secondary malignancy production
    - This study found IP-AP/PA technique to be more effective in lower dose regions, however head leakage and scatter are a concern
    - Additionally, the IP-AP/PA technique required over twice the number of MUs as compared to VMAT and over 3.5 times number of MUs required for S-AP/PA technique

<table>
<thead>
<tr>
<th></th>
<th>S-AP/PA</th>
<th>IP-AP/PA</th>
<th>VMAT</th>
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</thead>
<tbody>
<tr>
<td>Avg # of MUs</td>
<td>130</td>
<td>462</td>
<td>219</td>
</tr>
</tbody>
</table>
Conclusion

- Treatment of choice for normal tissue sparing = IP-AP/PA and VMAT
  - VMAT excels at heart sparing
  - Both VMAT and IP-AP/PA provide more normal tissue sparing in high dose regions than more conventional S-AP/PA method
  - VMAT technique delivered a wider region of low dose throughout the patient
    - Raises risk potential for late effects and probability of second malignancies
Acknowledgements

- Marvene M. Ewing, B.S., C.M.D.
- Jeffrey Buchsbaum, M.D., Ph.D.
References


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