The Research Analysis Platform and IGRT Database (RAPID) software tool for the analysis of three dimensional conformal radiation therapy for node positive breast cancer

Phil Prior
Medical Physics Resident
Medical College of Wisconsin
Introduction

• Breast radiotherapy (RT) for node positive breast cancer (NPBC)
  – Traditionally used 2DRT
    • Wedged plan on single transverse contour
    • Matched to anterior field encompassing supraclavicular-axillary lymph nodes
• Improved therapeutic ratio at other sites using 3D conformal RT (3DCRT)
  – 2DRT delivery technique still common despite clinical trials showing a reduction in normal tissue toxicity
• NPBC dose-volume constraints
  – No standard exists
  – Concern about increase doses to normal tissues by using 3DCRT in NPBC treatment plan
    • Due to over emphasis in target coverage

• Within the setting of NPBC RT treatment planning, is target coverage compromised at the expense of normal tissue sparing?
  – Constraints were institutionally standardized in 2005
RAPID Database

• Retrospective dose-volume-response analysis of NPBC treated at our institution.
  – Development of software tools to facilitate the collection of dose-volume-response data
  • Research Analysis Platform and IGRT Database (RAPID)
  • MATLAB DVH calculator
RAPID cont’d

- Query anonymized data sets
- Export appropriate data for analysis using auxiliary tools (e.g., R, CERR, DREES, AutoEUD, etc)

Summary Patient Data

- Patient
  - Clinical
    - Demographics / Medical History
    - Histology / Pathology
    - Recurrence
    - Toxicity
    - MU/IA Scans
  - Dosimetry
    - Radiation Treatment Methods
    - Dose Data
    - Screen Captures

Export Data for Analysis Using Auxiliary Tools

- Query archives for existence of relevant cases
- Contact data custodians / investigators
- Obtain research approval and access to data
## Acute Toxicity, Follow-up, and Recurrence

### Acute Toxicity
- **Skin / Breast Edema**: None
- **Dermatitis**: Moderate to brisk erythema
- **Chest Wall / Breast Pain**: Moderate pain with radiation
- **Fatigue**: Mild fatigue over baseline
- **Nerve Dysfunction**: None

### Follow-up
- **Date Of Last Follow-up**: 3/11/2005
- **Type of F/U**: Surgeon
- **Last Rad Onc F/U**: 1/24/2005
- **Date Of Last Mammo**: 1/29/2005
- **Status at F/U**: 5
- **Date of Death**: 5
- **Cause of Death**: Anemia due to CA

### Recurrence
- **Local Recurrence**: Ipsilateral breast
- **Location of Recurrence in Spinal, Breast**: U1Q
- **Initial Date**: 11/7/2005
- **Contralateral Breast Cancer**: Yes
- **Breast Date**: 12/19/2006
- **Regional Recurrence**: No
- **Supraventricular Recurrence**: No
- **Date of SELV Recurr**: 11/7/2006
- **Operative Recurrence**: Yes
- **Breast Date**: 11/11/2005
- **Other Recurrence**: No
- **Date of Other Recurr**: 11/11/2005
- **Distant Metastasis**: Yes
- **Date of Distant Metastases**: 2/20/2004

### Treatment for Recurrence
- **Surgery for Recurrence**: Mastectomy
- **Treat Path, Control, Medications**: N/A
- **Radiation for Recurrence**: External Beam
- **Chemotherapy for Recurrence**: Yes
- **Alcoholics for Recurrence**: No
- **Anti-hormone for Recurrence**: No
- **Hermatop (Leukapheresis) for Recurrence**: No
- **Avastin (Erlotinib) for Recurrence**: No

### New Cancer Diagnosis
- **Secondary Cancer**: N/A
- **new_second_cancer**: N/A
### RAPID Dosimetry section

**Dosimetry Data**

<table>
<thead>
<tr>
<th>Case #</th>
<th>26660</th>
</tr>
</thead>
<tbody>
<tr>
<td>DOB</td>
<td>5/4/1933</td>
</tr>
<tr>
<td>gender</td>
<td>female</td>
</tr>
</tbody>
</table>

**Prescription Information**

- **CTV**
  - **prescription_crv**
    - **vol_crv**
      - Whole Breast: 6060 Gy
      -乳腺: 6060 Gy
    - **D95%_crv**
      - Whole Breast: 6150 Gy
      - 乳腺: 6150 Gy
    - **V100%_crv**
      - Whole Breast: 100%
      - 乳腺: 100%
    - **V15%_crv**
      - Whole Breast: 0%
      - 乳腺: 0%

- **pres_crv**
  - **vol_crv**
    - Whole Breast: 8880 cc
    - 乳腺: 8880 cc
  - **D95%_crv**
    - Whole Breast: 5560 cc
    - 乳腺: 5560 cc
  - **V100%_crv**
    - Whole Breast: 35%
    - 乳腺: 35%
  - **V15%_crv**
    - Whole Breast: 0%
    - 乳腺: 0%

**Axilla nodes**

- **pres_snx**
  - **vol_snx**
    - Whole Breast: 4860 cc
    - 乳腺: 4860 cc
  - **D95%_snx**
    - Whole Breast: 5370 cc
    - 乳腺: 5370 cc
  - **V100%_snx**
    - Whole Breast: 33%
    - 乳腺: 33%
  - **V15%_snx**
    - Whole Breast: 0%
    - 乳腺: 0%

**Isolateral Lung**

- **vol_lspL**
  - **D95%_lspL**
    - Whole Breast: 1119.6 cc
    - 乳腺: 1119.6 cc
  - **V30Gy_lspL**
    - Whole Breast: 59.9 cc
    - 乳腺: 59.9 cc
  - **V10Gy_lspL**
    - Whole Breast: 36.7 cc
    - 乳腺: 36.7 cc

- **vol_lspR**
  - **D95%_lspR**
    - Whole Breast: 39.3 cc
    - 乳腺: 39.3 cc
  - **V30Gy_lspR**
    - Whole Breast: 49.4 cc
    - 乳腺: 49.4 cc
  - **V10Gy_lspR**
    - Whole Breast: 30.1 cc
    - 乳腺: 30.1 cc

- **vol_contL**
  - **D95%_contL**
    - Whole Breast: 0 cc
    - 乳腺: 0 cc
  - **V30Gy_contL**
    - Whole Breast: 0 cc
    - 乳腺: 0 cc
  - **V10Gy_contL**
    - Whole Breast: 0 cc
    - 乳腺: 0 cc

**Isolateral Lung**

- **vol_R**
  - **D95%_R**
    - Whole Breast: 0 cc
    - 乳腺: 0 cc
  - **V30Gy_R**
    - Whole Breast: 0 cc
    - 乳腺: 0 cc
  - **V10Gy_R**
    - Whole Breast: 0 cc
    - 乳腺: 0 cc

**Spinal Cord**

- **vol_S**
  - **D95%_S**
    - Whole Breast: 12.3 cc
    - 乳腺: 12.3 cc
  - **V30Gy_S**
    - Whole Breast: 0 cc
    - 乳腺: 0 cc

**Esophagus**

- **vol_E**
  - **V30Gy_E**
    - Whole Breast: 0 cc
    - 乳腺: 0 cc

**Ipsilateral Thymus**

- **vol_T**
  - **V30Gy_T**
    - Whole Breast: 0 cc
    - 乳腺: 0 cc

**Contralateral Breast**

- **vol_FB**
  - **V30Gy_FB**
    - Whole Breast: 0 cc
    - 乳腺: 0 cc
Methods

• Dosimetry Data Collection
  – NPBC patients receiving regional nodal and whole breast / chestwall irradiation from 2000-2009
  – Targets and organs at risk (OAR) volumes delineated on free breathing axial CT scans
  – Treatment planning using XiO treatment planning system (TPS) (Elekta, inc.)
    • Dose calculations used inhomogeneity corrections
    • Dose-volume-histograms (DVHs) used to assess plan quality
Methods cont’d

• **Plan Quality**

  – Assess target coverage and organs at risk (OAR) sparing using DVHs from TPS.

  • Ideal – 95% of target volume covered by 95% of prescription dose

  • Acceptable – 90% volume covered by 90% of prescription dose

<table>
<thead>
<tr>
<th>Definition of Constraints</th>
<th>Site / OAR</th>
<th>Ideal dose-volume constraints</th>
<th>Acceptable dose-volume constraints</th>
</tr>
</thead>
<tbody>
<tr>
<td>Targets</td>
<td>Whole Breast/Chestwall (WB/CW)</td>
<td>$D_{95%} \geq 47.5 \text{ Gy}$</td>
<td>$D_{90%} \geq 45 \text{ Gy}$</td>
</tr>
<tr>
<td></td>
<td>Axillary Lymph Node (AX)</td>
<td>$D_{95%} \geq 45.6 \text{ Gy}$</td>
<td>$D_{90%} \geq 43.0 \text{ Gy}$</td>
</tr>
<tr>
<td></td>
<td>Supraclavicular Lymph Node (SCLV)</td>
<td>$D_{95%} \geq 45.6 \text{ Gy}$</td>
<td>$D_{90%} \geq 43.0 \text{ Gy}$</td>
</tr>
<tr>
<td></td>
<td>Internal Mammary Lymph Nodes (IMC)</td>
<td>$D_{90%} \geq 42 \text{ Gy}$</td>
<td>$D_{90%} \geq 38 \text{ Gy}$</td>
</tr>
<tr>
<td>Organs at Risk</td>
<td>Ipsilateral Lung</td>
<td>$V_{20} \leq 25%$</td>
<td>$V_{20} \leq 30%$</td>
</tr>
<tr>
<td></td>
<td>Heart</td>
<td>$V_{25} \leq 5%$</td>
<td>$V_{25} \leq 9%$</td>
</tr>
</tbody>
</table>
Methods cont’d

• Statistical Analysis
  – Compare dose-volume analysis of plans from two time periods
    • 2000-2004 vs. 2005-2009
  – Hypothesis
    • Use of Acceptable “Institutional constraints” will lead to significant different in target coverage between the two time period
    • However; this will not lead to significant increase in the OAR doses.
  – Two-tailed $t$-tests used to test significance.
    • P-value and 95% CI for difference in means
Results

• 262 patient’s RT treatment plans restored from 2000-2009
  – Proportion of cases meeting acceptable “institutional constraints”
    • 72.1% - WB/CW
    • 83.5% - SCLV
    • 72.0% - AX
    • 71.9% - IMC
    • 83.2% - lung
    • 92.7% - heart
  – Total number of cases for 2000-2004 & 2005-2009, respectively
    • 130, 132 - WB/CW
    • 130, 132 - SCLV
    • 130, 132 - AX
    • 100, 110 - IMC
    • 130, 132 - lung
    • 81, 77 - heart
Results

- Mean values of $D_{90\%}$ for targets, $V_{10}$ & $V_{20}$ for lung, and $V_{25}$ & $V_{45}$ for heart.

<table>
<thead>
<tr>
<th>Time Span</th>
<th>WB/CW $D_{90%}$ (Gy)</th>
<th>SCLV $D_{90%}$ (Gy)</th>
<th>AX $D_{90%}$ (Gy)</th>
<th>IMC $D_{90%}$ (Gy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000-2004</td>
<td>44.3 ± 5.8</td>
<td>42.2 ± 11.3</td>
<td>38.6 ± 11.4</td>
<td>33.5 ± 18.3</td>
</tr>
<tr>
<td>2005-2009</td>
<td>47.4 ± 5.5</td>
<td>47.6 ± 6.8</td>
<td>47.3 ± 5.0</td>
<td>41.4 ± 14.4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Time Span</th>
<th>Lung $V_{10}$ (%)</th>
<th>Heart $V_{20}$ (%)</th>
<th>Heart $V_{25}$ (%)</th>
<th>Heart $V_{45}$ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000-2004</td>
<td>30.9 ± 14.4</td>
<td>25.5 ± 13.5</td>
<td>4.7 ± 4.7</td>
<td>1.4 ± 2.3</td>
</tr>
<tr>
<td>2005-2009</td>
<td>34.3 ± 7.4</td>
<td>26.0 ± 5.0</td>
<td>4.4 ± 3.6</td>
<td>1.0 ± 1.4</td>
</tr>
</tbody>
</table>
Results

- Target Coverage and OAR doses by time period

<table>
<thead>
<tr>
<th>Time Span</th>
<th>WB/GW</th>
<th>SCLV</th>
<th>AX</th>
<th>IMC</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000-2004</td>
<td>58.5%</td>
<td>71.5%</td>
<td>46.2%</td>
<td>62.0%</td>
</tr>
<tr>
<td>2005-2009</td>
<td>85.6%</td>
<td>93.9%</td>
<td>94.7%</td>
<td>80.9%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Time Span</th>
<th>Lung</th>
<th>Heart</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000-2004</td>
<td>87.7%</td>
<td>89.2%</td>
</tr>
<tr>
<td>2005-2009</td>
<td>78.8%</td>
<td>96.2%</td>
</tr>
</tbody>
</table>

\[ p < 0.0001 \ [0.376,0.581] \]

\[ p = 0.817 \ [-0.090,0.113] \]
Results

• The number of cases from 2005-2009 meeting acceptable target dose-volume constraints broken down by which OAR constraint was met/not met.

<table>
<thead>
<tr>
<th>Organs at Risk Constraints</th>
<th>Met</th>
<th>Not Met</th>
</tr>
</thead>
<tbody>
<tr>
<td>Met Lung &amp; Heart</td>
<td>86</td>
<td>16</td>
</tr>
<tr>
<td>Only Lung</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Only Heart</td>
<td>25</td>
<td>0</td>
</tr>
<tr>
<td>Neither Met</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>115</strong></td>
<td><strong>17</strong></td>
</tr>
</tbody>
</table>
Conclusions

• “Institutional” dose-volume constraints in 3DCRT for NPBC patients
  – Improves target coverage without increasing OAR doses
  – Cautionary Evidence
    • Compromise had been made in some circumstances where the clinician met OAR constraints by accepting lower target coverage
Conclusions

• RAPID database
  – Used by Sparks et al. and Bradley et al. concerning our clinical dose-response experience with 3DCRT of NPBC patients
    • Acute dermatitis Grade 1 & 2 was 83.0% and 13.4%, respectively
    • Telangiectasia Grade 1 and 2-3 were 9% and 3.2%, respectively
    • only 1 reported case of pneumonitis and pericarditis
    • Furthermore, achieved a local control rate of 94.7% and regional lymph node control of 99.4% at a median follow-up of 7 years

• Those studies suggest the constraints provide high level of control with acceptable toxicity
  – Future clinical trials will demonstrate validate
Studies Utilizing Rapid Database

- **Manuscripts**

- **Conference Abstracts**
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