Imaging/Imagine Needs for Proton Therapy: Treatment Planning

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Disclosure

- Software licensing agreement with Varian Medical Systems through MD Anderson Cancer Center
Goals

- Evaluating imaging needs for treatment planning
- Comparison of the use of images in planning between photons and protons
- Uncertainties in CT imaging to stopping power conversion
- A wish list
Growth of Proton Treatments

100,000th patient in 2012

Number of Patients Treated

Year

'50 '60 '70 '80 '90 2000

USA
Europe
Japan
Russia
S. Africa
Proton Therapy Centers in US

- Operating
- Under construction/development
Why protons?

- Depth
- Dose
- Photons
- Protons
- Bragg peak
The Goal of Treatment Planning

Goal: To design a treatment plan based on an anticipated patient treatment

- Requirements
  - Delineate target and normal structures
  - Accurate modeling for the patient
  - Accurate dose calculation
  - Evaluating simulation results
The Goal of Treatment Planning

- Imaging Needs
  - Target and normal structure delineation
  - Accurate modeling for the patient
    - Imaging the patient in treatment position
  - Accurate dose calculation
    - Simulate deliverable dose distributions
  - Evaluating simulation results
    - Present DVHs, Isodose lines, PTV or other plan robustness parameters etc.
Imaging for Target Delineation

- No difference from photon therapy
Imaging Patient in Treatment Condition

Organ Motion
Impact of motion to proton dose distribution

Gated treated on exhale

Tsunashima/Dong
Protons are more sensitive to motion than IMRT

(Proton-ITV)  (IMRT-ITV)

10 Gy  20 Gy  35 Gy  50 Gy  70 Gy
Every Proton Plan is a 4D Plan

Treatment planned based on single Free-breathing (FB) CT image (conventional approach)

The same treatment plan calculated on 4D CT images

Impact of Organ Motion on Proton Dose Distribution

Treatment planned based on single Free-breathing (FB) CT image (conventional approach)

Final composite dose distribution after deformable image registration

Imagine Patient in Treatment Condition

Treatment Couch and Immobilization Devices
Setup Error and Positional Variation of Immobilization Device
Mitigation

- Avoiding sharp edges in immobilization devices
- Avoiding beam passing through the immobilization device
Couch Edge or Dense Immobilization Device

H. Yu et al.
Modeling the treatment couch

- 520HU (1.3g/cm³)
- -235HU (0.8g/cm³)

Measured physically at 0.95cm uniform across
CT Imaging Artifacts

CT artifacts:
- 0.42 g/cm³
- 0.38 g/cm³
- 0.26 g/cm³
- 1.38 g/cm³
The digital template of the couch support

- Water-Equivalent-Thickness (WET) was measured experimentally from the change in the distal edge position of a proton beam.
- HU numbers were assigned to the geometry template obtained in previous CT scans.
Replacing CT couch with a treatment couch in CT images

Before

After
Repeat Imaging During Treatment

Original Proton Plan

Dose recalculated on the new anatomy

Bucci/Dong et al. ASTRO Abstract, 2007
Metal Artifacts
Figure 2. An axial and coronal MVCT slice of a prostate cancer patient (a) and an axial slice of a head and neck patient (b). Bony anatomy and some soft tissue anatomy are visible. The prostate and rectum can be identified in the pelvic anatomy. Structures with less density contrast, e.g., the parotid glands, are harder to distinguish.
Fig. 5
Use of Orthovoltage CT Imaging

Accurate Dose Calculation

CT number to proton stopping power conversion
Uncertainties in a Proton Plan

- CT imaging to measure stopping power of human tissue
- Dose calculation algorithm
- Setup errors and motion
- Couch or immobilization device in the beam path
- Anatomical changes
CT calibration to generate proton stopping power ratio
SPR uncertainties have a significant impact on proton dose distributions

Commonly it’s not visible on proton plans

-3.5%  +3.5%

0% uncertainty
What does the Bragg Peak brag about?

- Uncertainty in SPR estimation
  - Estimated to be 3.5% (Moyers et al, 2001, 2009)
- Proton SPR calculated by the Bethe-Bloch equation:

\[ SPR = EDR \times \frac{\ln[2m_e c^2 \beta^2 / I_m (1 - \beta^2)] - \beta^2}{\ln[2m_e c^2 \beta^2 / I_{water} (1 - \beta^2)] - \beta^2} \]

- SPR: proton stopping power ratio (relative to water)
- EDR: relative electron density
- Im: mean excitation energy of the element
Conventional CT-based SPR Estimation

- Degeneracy problem
  - $\text{HU} (\rho_1, Z_1) = \text{HU} (\rho_2, Z_2)$
  - $\text{SPR}(\rho_1, Z_1) \neq \text{SPR}(\rho_2, Z_2)$
Phantom Composition is Different from Human Tissue!
Stoichiometric Calibration Method

- Measured CT#s of Human Tissue Substitutes
- CT Modeled by a Parameter Set \( (K_{ph}, K_{coh}, K^{KN}) \)
- Predicted CT#s
- Calculated SPRs
- Elemental Composition of Human Body Tissues
- Bethe-Bloch Equation
- ICRU Standard Human Tissues

Examples of ICRU Report #44
Standard Human Tissue Composition

<table>
<thead>
<tr>
<th>Rod Material</th>
<th>H</th>
<th>C</th>
<th>N</th>
<th>O</th>
<th>Cl</th>
<th>F</th>
<th>Ca</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adipose (AP6)</td>
<td>8.36%</td>
<td>69.14%</td>
<td>2.36%</td>
<td>16.93%</td>
<td>0.14%</td>
<td>3.07%</td>
<td>0.00%</td>
</tr>
<tr>
<td>Breast</td>
<td>8.68%</td>
<td>69.95%</td>
<td>2.37%</td>
<td>17.91%</td>
<td>0.14%</td>
<td>0.00%</td>
<td>0.95%</td>
</tr>
<tr>
<td>True Water</td>
<td>11.20%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>88.80%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
</tr>
<tr>
<td>Liver (LV1)</td>
<td>11.00%</td>
<td>4.10%</td>
<td>1.20%</td>
<td>82.50%</td>
<td>1.20%</td>
<td>0.00%</td>
<td>0.00%</td>
</tr>
<tr>
<td>Inner Bone</td>
<td>7.90%</td>
<td>63.79%</td>
<td>4.23%</td>
<td>9.88%</td>
<td>14.20%</td>
<td>0.00%</td>
<td>0.00%</td>
</tr>
<tr>
<td>Bone (CB2-50%)</td>
<td>4.77%</td>
<td>41.63%</td>
<td>1.52%</td>
<td>31.99%</td>
<td>0.08%</td>
<td>0.00%</td>
<td>20.03%</td>
</tr>
<tr>
<td>Cortical Bone (SB3)</td>
<td>3.10%</td>
<td>31.26%</td>
<td>0.99%</td>
<td>37.57%</td>
<td>0.05%</td>
<td>0.00%</td>
<td>27.03%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Atomic Number (Z)</th>
<th>1</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>17</th>
<th>9</th>
<th>20</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atomic Weight (A)</td>
<td>1.0079</td>
<td>12.011</td>
<td>14.006</td>
<td>15.999</td>
<td>35.45</td>
<td>18.998</td>
<td>40.08</td>
</tr>
</tbody>
</table>

During treatment planning, the anthropomorphic phantom is constructed of tissue-equivalent materials. These materials can be made by mixing materials of known atomic number and atomic weight so that the properties of the tissue are approximated. The densities of the materials are carefully chosen so that the mass of each material is equal to the mass of the equivalent volume of tissue. The materials can be designed to be either rod or disk shaped, which allows the ratio of density to local dose rate to be determined.
Stoichiometric Calibration Method

Relative electron density

\[ HU_{sc} = HU + 1000 = \rho_e (AZ + BZ + C) \]

- Linear regression determine A, B & C.
- HU can be calculated for any tissue with known density and composition.
Relative Stopping Power &
Calibration Curve

\[ S_p = \rho_e K \]

\[ K = \frac{L_{\text{tissue}}}{L_{\text{water}}} \]

\[ L = \log \left( \frac{2m_e c^2 \beta^2}{I(1 - \beta^2)} \right) - \beta^2 \]

- $m_e$ – mass of electron
- $c$ – speed of light
- $\beta$ – $v/c$
- $v$ – speed of the proton
- $I$ – excitation energy

ICRP tissues
<table>
<thead>
<tr>
<th>Uncertainty Category</th>
<th>Uncertainty Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT imaging uncertainties</td>
<td>The deviation of HU value from its calibrated value when imaging a patient.</td>
</tr>
<tr>
<td>Uncertainties in predicting theoretical CT numbers using tissue substitute phantoms</td>
<td>This includes the uncertainties in the definition and measurement using CT imaging for a tissue substitute phantom, including the parameterization of equation</td>
</tr>
<tr>
<td>Uncertainties to calculate SPRs of human tissues</td>
<td>The uncertainties caused by modeling SPR and variations of tissue composition in patient population.</td>
</tr>
<tr>
<td>Uncertainties in mean excitation energies</td>
<td>The value of mean excitation energy is critical in calculating SPR</td>
</tr>
<tr>
<td>Uncertainties caused by an assumption used in a dose calculation algorithm</td>
<td>For simplicity, some treatment planning systems ignored the SPR dependency on proton energy.</td>
</tr>
</tbody>
</table>
### Uncertainties for Tissue Specific SPR

<table>
<thead>
<tr>
<th>Uncertainty Source</th>
<th>Uncertainties in SPR Estimation (1σ)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Lung</td>
</tr>
<tr>
<td>CT imaging uncertainties</td>
<td>3.3%</td>
</tr>
<tr>
<td>Uncertainties in predicting theoretical CT numbers using tissue substitute phantoms</td>
<td>3.8%</td>
</tr>
<tr>
<td>Uncertainties to calculate SPR of human tissues</td>
<td>0.2%</td>
</tr>
<tr>
<td>Uncertainties in mean excitation energies</td>
<td>0.2%</td>
</tr>
<tr>
<td>Uncertainties caused by an assumption used in a dose calculation algorithm</td>
<td>0.2%</td>
</tr>
<tr>
<td>Total (root-sum-square)</td>
<td>5.0%</td>
</tr>
</tbody>
</table>

Comprehensive analysis of the stoichiometric calibration. Yang M. et al.
## Composite Uncertainties in Typical Cases

<table>
<thead>
<tr>
<th>Tumor Site</th>
<th>Composite Range Uncertainty</th>
<th>Percentile when Range Uncertainty = 3.5%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median</td>
<td>90th Percentile</td>
</tr>
<tr>
<td>Prostate</td>
<td>1.3%</td>
<td>2.5%</td>
</tr>
<tr>
<td>Lung</td>
<td>1.5%</td>
<td>2.9%</td>
</tr>
<tr>
<td>Head &amp; neck</td>
<td>1.3%</td>
<td>2.6%</td>
</tr>
</tbody>
</table>

Yang M. et al.
Summary of Uncertainties

Moyers, et al. *Ion stopping powers and CT numbers*. Medical Dosimetry, 35:179-194, 2010

### Table 7. Summary of estimated uncertainties in treatment planning due to CT numbers and stopping powers

<table>
<thead>
<tr>
<th>Cause</th>
<th>Uncertainty Before Mitigation</th>
<th>Mitigation</th>
<th>Uncertainty After Mitigation</th>
<th>Possible Future Uncertainty</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scanner calibration for standard conditions</td>
<td>±0.3% day-to-day</td>
<td>Patient-specific scaling</td>
<td>±0.0%</td>
<td>±0.0%</td>
</tr>
<tr>
<td>kVp, filter, and FOV selection</td>
<td>±2.0% PMMA, PC</td>
<td>Use only calibrated conditions</td>
<td>±0.0%</td>
<td>±0.0%</td>
</tr>
<tr>
<td>&gt; ± 2.0% bone</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Volume and configuration scanned</td>
<td>±2.5%</td>
<td>Patient-specific scaling</td>
<td>±0.0%</td>
<td>±0.0%</td>
</tr>
<tr>
<td>Position in scan</td>
<td>±1.5% water</td>
<td>—</td>
<td>±1.5% water*</td>
<td>±0.5% water&lt;sup&gt;DE*&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>±2.5% tissue</td>
<td></td>
<td>±2.5% tissue</td>
<td>±0.8% tissue&lt;sup&gt;DE&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>&gt; ± 3.0% bone</td>
<td></td>
<td>&gt; ± 3.0% bone*</td>
<td>&gt; ± 1.0% bone&lt;sup&gt;DE*&lt;/sup&gt;</td>
</tr>
<tr>
<td>Metal implants</td>
<td>100%</td>
<td>$z \leq 22$ - MVXCT</td>
<td>±5.0% metal*</td>
<td>±5.0% metal*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>$z &gt; 22$ - substitution</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stopping power of water</td>
<td>±1.0%</td>
<td>—</td>
<td>±1.0%</td>
<td>±0.5%</td>
</tr>
<tr>
<td>RLSP of tissues and devices</td>
<td>±0.0 to 3.0%</td>
<td>Contour and substitute</td>
<td>±1.0%</td>
<td>±1.0%</td>
</tr>
<tr>
<td>WEQ vs. RLSP (soft tissues only)</td>
<td>±1.6%</td>
<td>—</td>
<td>±1.6</td>
<td>±1.6</td>
</tr>
<tr>
<td>Energy dependence of RLSP for low Z</td>
<td>±1.2%</td>
<td>—</td>
<td>±1.2</td>
<td>±0.5&lt;sup&gt;MC&lt;/sup&gt;</td>
</tr>
<tr>
<td>Total (soft tissues only)</td>
<td>—</td>
<td>—</td>
<td><strong>±3.5</strong></td>
<td>±2.2</td>
</tr>
</tbody>
</table>

Abbreviations: DE, dual-energy CT; MC, Monte Carlo calculations.
*Not considered in total.
Summary of CT# Variation

- Patient size is the dominating factor
- Uncertainty is a function of tissue types

<table>
<thead>
<tr>
<th>Tissue Groups</th>
<th>Time and Scanner</th>
<th>Size</th>
<th>Position</th>
<th>Couch Position</th>
<th>Root-Sum-Square (RSS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT# Lung</td>
<td>1.0%</td>
<td>4.4%</td>
<td>2.2%</td>
<td>1.8%</td>
<td>5.3%</td>
</tr>
<tr>
<td></td>
<td>0.3%</td>
<td>0.5%</td>
<td>0.1%</td>
<td>0.4%</td>
<td>0.7%</td>
</tr>
<tr>
<td></td>
<td>0.6%</td>
<td>2.4%</td>
<td>1.3%</td>
<td>0.7%</td>
<td>2.9%</td>
</tr>
<tr>
<td>SPR Lung</td>
<td>1.0%</td>
<td>4.5%</td>
<td>2.2%</td>
<td>1.8%</td>
<td>5.4%</td>
</tr>
<tr>
<td></td>
<td>0.3%</td>
<td>0.3%</td>
<td>0.1%</td>
<td>0.3%</td>
<td>0.5%</td>
</tr>
<tr>
<td></td>
<td>0.4%</td>
<td>1.6%</td>
<td>0.9%</td>
<td>0.5%</td>
<td>1.9%</td>
</tr>
</tbody>
</table>

Yang M. et al.
CT Number Uncertainties: Phantom Size

Small

Large
Mitigation of CT imaging uncertainties

- Distal and proximal margins
- Site-specific CT calibration (small phantom vs. large phantom)
- In patient calibration of CT numbers for known anatomy (Moyer et al. 2010)
- Avoiding couch or immobilization device outside CT scanner’s FOV
A wish list

- A proton CT to measure SPR in patient
- A MV CT for SPR measurement
- A dual-energy CT to minimize the effect of atomic number
- In-room (4D) CT
## kV-MV Dual Energy CT

<table>
<thead>
<tr>
<th></th>
<th>SPR Uncertainty (1-SD)</th>
<th>Range Uncertainty (2-SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung</td>
<td>3.7%</td>
<td>1.9%</td>
</tr>
<tr>
<td>Soft</td>
<td>0.99%</td>
<td>2.3%</td>
</tr>
<tr>
<td>Bone</td>
<td>1.4%</td>
<td>1.9%</td>
</tr>
</tbody>
</table>

**kV-MV DECT**
A Proton CT Scanner

Proton beam

Fiber scintillator tracking detectors:
Record paths of individual protons with high precision

Stacks of thin scintillator plates:
Determine energy loss of protons with high precision
Uncertainties in Proton Therapy

- CT imaging to measure stopping power of human tissue
- Dose calculation algorithm
- Setup errors and motion
- Couch or immobilization device in the beam path
- Anatomical changes
Summary

The imaging needs for proton therapy are to minimize range uncertainties