Promises and Perils of Proton Therapy

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Disclosure

• Member, ASTRO Proton Therapy Task Force
• Physics Consultant Faithful and Gould
  – Proton Therapy project management company
• Bankhead Coley Research Awards
  – Medical informatics research
Promises of Proton Therapy

Compared to external beam photon therapy, proton therapy:

- Decreases the integral dose due to the “finite range” of protons
- Reduces the volume of normal tissue exposed to low doses, potentially lowering the risk of second malignancies. This risk is notably higher for young patients, as they are more at risk to future radiation induced cancers.
- Has demonstrated advantage for treating small tumor volumes at shallow depths (eye tumors and CNS such as chordomas and chondrosarcomas)
- Has demonstrated advantage for treating a few select cases in almost all disease site
The objective of this presentation is to give this audience a "feel" for what it really takes to make good on this promise
Physical characteristics that make Protons clinically attractive

- Protons have a finite depth of penetration into material, the magnitude of which depends on their energy and on the stopping power of irradiated material.
- Protons exhibit a Bragg peak with negligible dose at the end of their range.
- The dose from a proton beam falls off sharply, both laterally and distally.
Factors that contribute to range uncertainties

• Inherent uncertainties in linear stopping power
• Uncertainties in the formation of broad clinical proton beams (laterally and in-depth)
• Uncertainties in the determination of radiological thicknesses of bolus/compensator materials and accessories
Impact of inherent uncertainty in Linear Stopping Power

122 MeV Protons on water: $I_w$ - dependence

$P_{122 I_w} = 67\text{eV}$
$P_{122 I_w} = 75\text{eV}$
$P_{122 I_w} = 80\text{eV}$

$dE/dz$ (MeV/g cm$^2$) per incident particle
depth in water (g/cm$^2$)

Peak spread is .7 g/cm$^2$ for 230 MeV protons

Andreo, PMB, 54(1), 2009
122 MeV Protons on water: \( I_w \) - dependence

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\( \pm 1.5\% - 2.0\% \) Uncertainty in Range Calculation

Impact of inherent uncertainty in Linear Stopping Power
Uncertainties in the formation of Broad clinical beam

Uncertainties in the formation of Broad clinical beam


± 1.0 mm Uncertainty in Range Reproducibility
Uncertainties in the thickness of bolus/compensator materials
Uncertainties in the thickness of bolus/compensator materials

Range modulator wheel

Scatterer

Aperture

Compensator

Target

Patient

± 1.0 mm Systematic Uncertainty in Range
CT Numbers to Relative Stopping Power Conversion Uncertainties

![Graph showing the relationship between CT numbers and relative stopping power for different phantom sizes. The x-axis represents HU (Hounsfield Units) ranging from -1000 to 2000, and the y-axis represents relative stopping power ranging from 0.0 to 1.8. The graph includes data points for large, small, and medium phantoms.](image-url)
2-4% ($1.0 \sigma$) error in CT numbers to relative stopping powers
Impact of CT Hounsfield number uncertainties on dose distributions

Individualized patient determination of tissue composition along the complete beam path, rather than CT Hounsfield numbers alone, would probably be required even to reach “sub-centimeter precision”
“It is imperative that body-tissue compositions are not given the standing of physical constants and their reported variability is always taken into account” (ICRU-44, 1989).
Figure 14.6: Range uncertainties computed for a small pediatric and a large prostate patient. The discrepancies in the proton range varied .4-.7% and .6-1.2% for prostate and pediatric patient respectively. Please note that these uncertainties are only due to the phantom size. Other uncertainties such as position within the phantom, FOV, filtration, and tissue composition are not included. However, those uncertainties are much smaller in magnitude compared to the phantom size.
Range degradation in patients

- patient alignment and setup in the treatment beam
- relative motion of internal structures with respect to the target volume
- misalignment of the apertures and compensator (if present) with the target volume and critical organs
Misalignment of the compensator with target volume

Correct alignment of the compensator and target volume

Patient is shifted left

Patient is rotated clockwise

ICRU Report 78
Edge-scattering effect in proton beam is not as significant as in electron beam.
Proton Range Uncertainty in the Presence of heterogeneities

Lomax : AAPM SS 2003
Impact of complexly structured heterogeneities in proton beam

Sawaguchi et al. PMB, 53(17), 2008
Anatomic Variations During Course of Radiotherapy

Impact of Tumor Shrinkage on Proton Dose Distribution

Original Proton Plan

Dose recalculated on the new anatomy

Bucci et al. ASTRO Abstract, 2007
Impact of Organ Motion on Proton Dose Distributions
In Silico Comparison of Proton Therapy with IMRT

It is incontrovertible that dose distributions of protons can be **theoretically** superior to those of high energy photons.
Plan DVH Evaluation (PTV)

What you see is not what you always get....

Volume

Dose
Plan DVH Evaluation (PRV)

What you see is not what you always get..

![Graph showing dose-volume histogram for proton and photon DVHs](graph.png)
Rectal DVH from multiple post treatment PET/CT

Uncertainties in Rectal $V_{74}$ and $V_{39}$

<table>
<thead>
<tr>
<th></th>
<th>Mean ± Dev.</th>
<th>Rel. Dev. ± Dev.</th>
</tr>
</thead>
<tbody>
<tr>
<td>$V_{74}$</td>
<td>9.6%±7.2%</td>
<td>73.9%±20.5%</td>
</tr>
<tr>
<td>$V_{39}$</td>
<td>25.2%±11.4%</td>
<td>42.1%±15.3%</td>
</tr>
</tbody>
</table>

Yin: UFPTI, 2008
Improving Proton Therapy

• Anatomy variations
  – IGRT/adaptive radiotherapy
  – Robust optimization

• Intra-fractional motion
  – Gating, coaching, tracking...

• Accurate stopping power ratios (CT number conversion)

• Scanning pencil beams (IMPT) with beam angle optimization.
Summary

- Proton beams stop - no exit dose
  - Although we don’t know exactly where they stop
- Proton beams are more sensitive to
  - CT Hounsfield number/Stopping Power accuracy
  - Organ motion
  - Anatomy changes
- Proton plans are difficult to evaluate
  - “What you see is not what is delivered”
- Protons demonstrate excellent low dose sparing
Summary

- IMPT shows additional benefits both in low dose sparing and high dose conformality
- IGRT and Adaptive RT will play an important role
- Inter/Intra-fractional variations have far more significant consequences in patients treated with proton therapy
  - Approaches and data to deal with this issue is still lacking
    - Minimize it and develop strategies to deal with the residual motion
<table>
<thead>
<tr>
<th>Source of Uncertainty</th>
<th>Uncertainty Before Mitigation</th>
<th>Mitigation Strategy</th>
<th>Uncertainty After Mitigation</th>
</tr>
</thead>
<tbody>
<tr>
<td>*Inherent range uncertainty</td>
<td>±1-3 mm</td>
<td>None</td>
<td>±1-3 mm</td>
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<tr>
<td>(pristine Bragg peak)</td>
<td></td>
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<tr>
<td>*Inherent range uncertainty</td>
<td>±.6-1.0mm</td>
<td>None</td>
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<tr>
<td>(spread out Bragg peak)</td>
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<tr>
<td>Range reproducibility</td>
<td>±1.0mm</td>
<td>Rigorous QA</td>
<td>±.5mm</td>
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<tr>
<td>Compensator</td>
<td>±1.0mm</td>
<td>Rigorous QA of</td>
<td>±.5mm</td>
</tr>
<tr>
<td>compensator material</td>
<td></td>
<td></td>
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<tr>
<td>Accessories (table top, immobilization jig, etc.)</td>
<td>±1.0mm</td>
<td>Rigorous QA of all accessories</td>
<td>±.5mm</td>
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<tr>
<td>CT</td>
<td>± 3.5% of range</td>
<td>Site specific imaging protocols</td>
<td>± 1-2.0% of range</td>
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<tr>
<td>Patient setup</td>
<td>± 1.5mm</td>
<td>Rigorous patient selection criteria</td>
<td>± 1.0mm</td>
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<tr>
<td>Intrafractional patient motion</td>
<td>Variable</td>
<td>Rigorous patient selection criteria</td>
<td>± 1.0mm</td>
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<tr>
<td>Compensator position relative to patient</td>
<td>Variable</td>
<td>Rigorous patient selection criteria</td>
<td>± 1.0mm</td>
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<tr>
<td>Range uncertainty (straggling) due to complex heterogeneities</td>
<td>± 1mm</td>
<td>Rigorous patient selection criteria</td>
<td>±.5mm</td>
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<tr>
<td>CT artifacts</td>
<td>Variable</td>
<td>Rigorous patient selection criteria</td>
<td>± 1.0mm</td>
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<tr>
<td>Range computation in water in a TPS</td>
<td>Variable</td>
<td>Rigorous patient selection criteria and image edits</td>
<td>± 0.5mm</td>
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<td>Range computation in tissue of known composition and density in a TPS</td>
<td>± 0.5mm</td>
<td>None</td>
<td>± 0.5mm</td>
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<td>Multi-modality image registration</td>
<td>±1mm</td>
<td>Better dose computation algorithms</td>
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<td>Treatment delivery (target coverage uncertainty)</td>
<td>±1-3mm</td>
<td>Site specific image registration protocols</td>
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<tr>
<td>Treatment delivery (dosimetric uncertainty)</td>
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<td>Rigorous site specific delivery technique selection</td>
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<tr>
<td>Treatment delivery (dosimetric uncertainty)</td>
<td>±1-3.0%</td>
<td>Rigorous QA</td>
<td>±1.0%</td>
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