Range Uncertainties in Proton Therapy

Harald Paganetti PhD
Professor of Radiation Oncology, Harvard Medical School
Director of Physics Research, Massachusetts General Hospital, Department of Radiation Oncology
Proton Beam Range

Protons

Photons

Copyright © MGH/NPTC 2003
Proton Beam Range Uncertainty

The difference compared to photon therapy: range uncertainties
In proton therapy, generic homogeneous PTV margin recipes are typically not sufficient!
Proton Beam Range Uncertainty

Applied range uncertainty margins for non-moving targets

Range uncertainties sometimes limit our ability to exploit the end of range

Example: Prostate treatments
Proton Beam Range Uncertainty

Protons and Prostate Treatments

Current technique: Lateral fields
Use lateral penumbra (10 mm, 50-95%) to spare rectum (penumbra not better than 15 MV photon fields)

Why not AP fields?
Use much sharper distal penumbra (~ 4 mm, 50-95%)
Proton Beam Range Uncertainty

Range uncertainty margins for non-moving targets

<table>
<thead>
<tr>
<th>Source of range uncertainty in the patient</th>
<th>Range uncertainty</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Independent of dose calculation:</strong></td>
<td></td>
</tr>
<tr>
<td>Measurement uncertainty in water for commissioning</td>
<td>± 0.3 mm</td>
</tr>
<tr>
<td>Compensator design</td>
<td>± 0.2 mm</td>
</tr>
<tr>
<td>Beam reproducibility</td>
<td>± 0.2 mm</td>
</tr>
<tr>
<td>Patient setup</td>
<td>± 0.7 mm</td>
</tr>
<tr>
<td><strong>Dose calculation:</strong></td>
<td></td>
</tr>
<tr>
<td>Biology (always positive)</td>
<td>+ 0.8 %</td>
</tr>
<tr>
<td>CT imaging and calibration</td>
<td>± 0.5 %</td>
</tr>
<tr>
<td>CT conversion to tissue (excluding I-values)</td>
<td>± 0.5 %</td>
</tr>
<tr>
<td>CT grid size</td>
<td>± 0.3 %</td>
</tr>
<tr>
<td>Mean excitation energies (I-values) in tissue</td>
<td>± 1.5 %</td>
</tr>
<tr>
<td>Range degradation; complex inhomogeneities</td>
<td>- 0.7 %</td>
</tr>
<tr>
<td>Range degradation; local lateral inhomogeneities *</td>
<td>± 2.5 %</td>
</tr>
<tr>
<td>*<em>Total (excluding <em>)</em></em></td>
<td>2.7% + 1.2 mm</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>4.6% + 1.2 mm</td>
</tr>
</tbody>
</table>

Proton Beam Range Uncertainty

Range degradation Type I

(Sawakuchi et al., 2008)
Proton Beam Range Uncertainty

Range degradation Type II

analytical    Monte Carlo

(Paganetti et al., 2008)
Proton Beam Range Uncertainty

Range uncertainty margins for non-moving targets

Heterogeneity Index based on patient geometry relative to pencil kernel

Range and Heterogeneities

Avoiding density heterogeneities

<table>
<thead>
<tr>
<th>Field</th>
<th>Applied plan</th>
<th>‘Standard’ plan</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Gantry angle</td>
<td>Table angle</td>
</tr>
<tr>
<td>1</td>
<td>-45</td>
<td>-90</td>
</tr>
<tr>
<td>2</td>
<td>-10</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>-120</td>
<td>-120</td>
</tr>
</tbody>
</table>

© T. Lomax (PSI)
In addition(!): patient geometry changes

Example: Intra-fractional geometry changes

Before RT

After RT

• Parotid glands

• Subm.glands

• Tumor

E. M. Vasques Osorio et al.
IJROBP 70: 875-82
In addition(!): patient geometry changes

- Patient weight gain / loss
- Filling up of sinuses
- (Sub-clinical) pneumonia
- Wet hair / gel / hairspray
Proton Beam Range Uncertainty

Lung

• Dose fall-off often in lung tissue (density ~0.25-0.3)
  -> range differences magnified by factor 3-4

Pencil Beam  Monte Carlo  Difference
Motion

Photons

Protons

Isodose levels

20 50 80 95 100

© Engelsman, MGH
Motion

Transversal  Coronal  Sagittal

dose delivered over time

cumulative dose
### Source of range uncertainty in the patient

<table>
<thead>
<tr>
<th>Source of range uncertainty in the patient</th>
<th>Range uncertainty</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Independent of dose calculation:</strong></td>
<td></td>
</tr>
<tr>
<td>Measurement uncertainty in water for commissioning</td>
<td>± 0.3 mm</td>
</tr>
<tr>
<td>Compensator design</td>
<td>± 0.2 mm</td>
</tr>
<tr>
<td>Beam reproducibility</td>
<td>± 0.2 mm</td>
</tr>
<tr>
<td>Patient setup</td>
<td>± 0.7 mm</td>
</tr>
<tr>
<td><strong>Dose calculation:</strong></td>
<td></td>
</tr>
<tr>
<td>Biology (always positive)</td>
<td>+ 0.8 %</td>
</tr>
<tr>
<td>CT imaging and calibration</td>
<td>± 0.5 %</td>
</tr>
<tr>
<td>CT conversion to tissue (excluding I-values)</td>
<td>± 0.5 %</td>
</tr>
<tr>
<td>CT grid size</td>
<td>± 0.3 %</td>
</tr>
<tr>
<td>Mean excitation energies (I-values) in tissue</td>
<td>± 1.5 %</td>
</tr>
<tr>
<td>Range degradation; complex inhomogeneities</td>
<td>- 0.7 %</td>
</tr>
<tr>
<td>Range degradation; local lateral inhomogeneities *</td>
<td>± 2.5 %</td>
</tr>
<tr>
<td>*<em>Total (excluding <em>)</em></em></td>
<td>2.7% + 1.2 mm</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>4.6% + 1.2 mm</td>
</tr>
</tbody>
</table>

**Monte Carlo dose calculation**

- ± 0.2 %
- ± 0.1 %

H. Paganetti: Range uncertainties in proton beam therapy and the impact of Monte Carlo simulations  
Addressing range uncertainties

H. Paganetti: Range uncertainties in proton beam therapy and the impact of Monte Carlo simulations

4 mm gain!
Addressing range uncertainties

Proton therapy works on similar principles. Wilson first suggested in 1946 that the energetic protons produced at the Harvard Cyclotron Laboratory might be an effective cancer treatment. The very first treatments were performed at particle accelerators originally built for physics research: Berkeley Radiation Laboratory in 1954, and Uppsala in Sweden in 1951.

So proton therapy has been around for about 50 years, generally reserved for the most complicated cancers, such as tumors in the head, eyes, or neck that have not yet spread to distant areas of the body – locations where collateral damage to surrounding tissue could have serious consequences.

That’s because proton therapy offers fewer side effects. In conventional x-ray therapy, the x-rays travel through the body and deliver radiation to all the tissues along the way to the actual tumor. To cut down on the damage to healthy tissue, doctors usually limit the dose delivered to the tumor.
Addressing range uncertainties

Head & Neck Patient

Proton Dose XiO

Proton Dose TOPAS

Dose_Difference

Avg. diff.: [-5mm ; 3mm]

RMSD: 3mm - 7mm
Addressing range uncertainties

1. Balloon with detector array embedded on the surface
2. Deliver dose (< 1 cGy) for 500 ms using a few cm of extra beam range to cover dosimeters
3. Measure dose rate functions by a multi-channel electrometer
4. Match data (pattern matching) to determine WEPL at dosimeters and adjust beam range
5. Commence treatment
Addressing range uncertainties

Mitigating range uncertainties using robust planning in IMPT

Beam 1

Beam 2

Beam 3

Total dose:

© Unkelbach, MGH
Addressing range uncertainties

Mitigating range uncertainties using robust planning in IMPT

Beam 1

Beam 2

Beam 3

Total dose:

© Unkelbach, MGH
Conclusion

• Range uncertainties in proton therapy can be substantial (i.e. several mm)
• Advanced dose calculation only solves part of the problem
• Robust planning can mitigate the impact of range uncertainties
• Proton treatment planning needs to be done by experienced planners who understand the impact of range uncertainties
• For some sites (e.g. prostate) range uncertainties prevent us from exploiting the full potential of proton therapy
• In vivo range verification is highly desirable