Do uncertainties in proton therapy limit its clinical potential?

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Disclaimer

I work for an institution (MGH) which does have a proton therapy facility

Doing research, I do not consider this a conflict of interest ☺

Introduction

Protons vs. IMRT vs. Photons

Proton advantage and challenge: The end of range

Proton advantage: The 'integral dose' difference : 2-3

Proton advantage and challenge: The end of range
Integral dose

**IMRT plan**
(7 coplanar photon beams)

Integral dose

**IMPT plan**
(4 coplanar proton beams)

Clear advantage of protons due to lower integral dose

**Rhabdomyosarcoma of Paranasal Sinus (7 y old boy)**

6 MV Photons
(3 field)

Photon IMRT
(9 field)

160 MeV Protons
(2 field)

Proton IMPT
(9 field)

Clear advantage of protons due to lower integral dose
Is a small volume of high dose ‘better’ compared to a large volume of low dose?

Second cancer induction

Cognitive development in children (!)

Integral dose

Is the integral dose the decisive parameter?

Note:

• To use the ‘integral dose’ to conclude superiority of protons might be too simplistic. We need to consider the distribution of dose and the distribution of organs at risk!

This affects also the comparison of protons vs. protons!

Integral dose

In beam scanning, spot size matters!

\[ \sigma = 12 \text{mm} \]

\[ \sigma = 12 \text{mm} + \text{aperture} \]

\[ \sigma = 3 \text{mm} \]

Depending on the beam characteristics, there are considerable differences between different proton beams (potentially showing inferiority compared to photon treatments)
Rhabdomyosarcoma
Total dose = 50.4 Gy
Number of proton fields = 2
Number of IMRT fields = 5

Note:
- NTCP considerations in treatment planning are based on photon dose distributions
- Organ doses in proton therapy are more heterogeneous. There are no proton specific normal tissue constraints
Conclusion I:

The total energy deposited in a patient ("integral dose") is always lower when treating with protons. This, theoretically, should always result in an advantage for proton treatments. However,

• the dose distribution matters
• this may not always result in a significant clinical gain (site dependent; clinical trials?)
• the delivery system matters

Finite range

Medulloblastoma

Protons

Photons

Clear advantage of protons due to finite range

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Uncertainties when predicting dose

The difference compared to photon therapy: range uncertainties

symmetric margin expansion does not make sense!
Uncertainties when predicting dose

Applied range uncertainty margins for non-moving targets

- **Patient setup**: ± 0.7 mm
- **Beam reproducibility**: ± 0.2 mm
- **Compensator design**: ± 0.2 mm
- **Measurement uncertainty in water for commissioning**: ± 0.3 mm
- **Biology (always positive)**: ± 0.8 %
- **CT imaging and calibration**: ± 0.5 %
- **CT grid size**: ± 0.3 %
- **Mean excitation energies (I-values) in tissue**: ± 1.5 %
- **Range degradation; complex inhomogeneities**: ± 2.5 %
- **Range degradation; complex inhomogeneities**: ± 0.7 %

**Total**: ± 4.6 % + 1.2 mm

Uncertainties when predicting dose


better dose calculation might reduce uncertainties:
Symposium on Thursday 10:30-12:30; Room 213CD

In addition(!): patient geometry changes
Example: Intra-fractional geometry changes

- Parotid glands
- Subm. glands
- Tumor

E. M. Vasques Osorio et al. IJROBP 70: 875-882

Comment
Uncertainties when predicting dose

In addition(!): patient geometry changes

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

Uncertainties when predicting dose

Note:

In proton therapy, generic margin recipes are not sufficient!

Treatment planners need to understand the origin and magnitude of range uncertainties!

Uncertainties when predicting dose

Mitigating range uncertainties using robust planning in IMPT

Total dose:
Uncertainties when predicting dose

Mitigating range uncertainties using robust planning in IMPT

Beam 1  Beam 2  Beam 3

Total dose:

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

Example: Prostate treatments

Uncertainties when predicting dose

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%)

LAT  AP
Conclusion II:

- 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.

Will Proton Therapy Gradually Replace Photon Therapy?

From a pure physics perspective (putting economic constraints aside and assuming well-trained personnel):

For some sites (e.g. pediatrics), YES (because clear advantages can be expected)

For other sites, POTENTIALLY (we are not there yet), if:
  - We can reduce planning and delivery uncertainties (e.g. beam range)
  - We understand the impact of ‘better’ dose distributions (i.e. their clinical significance)
  - We use ‘optimized’ proton delivery systems (e.g. small beam spots in proton beam scanning)
What do you consider the **main** obstacle in physics before proton therapy can become mainstream?

<table>
<thead>
<tr>
<th>Percentage</th>
<th>Obstacle</th>
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<tbody>
<tr>
<td>21%</td>
<td>Treatment planning is too complex (need more training)</td>
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<tr>
<td>20%</td>
<td>Current range uncertainties are unacceptable and need to be reduced</td>
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<tr>
<td>21%</td>
<td>Unproven clinical advantage of a lower integral dose</td>
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<tr>
<td>19%</td>
<td>Biological consequences of different dose distributions compared to photons</td>
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<tr>
<td>19%</td>
<td>Proton therapy will never be a mainstream treatment option</td>
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