Understanding the Uncertainties in Proton Therapy

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Is there an issue with these illustrations?

YES……

Proton spot scanning (from PSI home page, Pedroni et al)
The issue is to accurately deliver proton therapy to a real dynamic patient.
Uncertainties in Proton Therapy Delivery

• **Common to conventional photon radiotherapy:**
  – Target definition
  – Target motion
  – Tumor regression/growth during treatment course

• **Range Uncertainties**
  – CT Hounsfield number to stopping power conversion uncertainties
    • HU uncertainties as function of
    – patient size
    – scanning techniques
    – reconstruction algorithms
  – CT artifacts
  – Stopping power measurement/calculation uncertainties

• **Normal organ motion and changes**
  – Bladder filling
  – Rectum gas
  – Amount of lung in beam path for thorax
<table>
<thead>
<tr>
<th>Factors</th>
<th>Protons</th>
<th>Photons</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT # and stopping powers accuracy</td>
<td>Sensitive - affect range, distal target coverage or distal normal tissue sparing</td>
<td>Not sensitive</td>
</tr>
<tr>
<td>Target motion normal to beam</td>
<td>Affects margin, may affect dose distribution distal to target</td>
<td>Affects margin</td>
</tr>
<tr>
<td>Normal structure motion orthogonal to beam</td>
<td>Affects range, dose distribution distal to structure</td>
<td>Minimal effect</td>
</tr>
<tr>
<td>Target motion along beam direction</td>
<td>No effect</td>
<td>Affects margin</td>
</tr>
<tr>
<td>Normal structure motion along beam direction</td>
<td>No effect</td>
<td>Minimal effect</td>
</tr>
<tr>
<td>Complex inhomogeneities</td>
<td>Not well characterized, perturb dose distributions, degrade distal edge</td>
<td>Well understood, effect not strong</td>
</tr>
<tr>
<td>Anatomy changes over course of RT</td>
<td>Affect dose distribution</td>
<td>Minimal effect</td>
</tr>
<tr>
<td>Plan Evaluation</td>
<td>Impact of uncertainties significant, PTV concept not valid, validity of initial nominal plan questionable</td>
<td>PTV concept valid, dose distributions relatively invariant to uncertainties, initial plan acceptable approximations</td>
</tr>
</tbody>
</table>
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
Intrinsic basic physics uncertainty (I-values)

Protons on water $I_w$ dependence

The peak spread increases with energy

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

P Andreo, Phys Med Biol, 2009

P122 $I_w$67
P122 $I_w$75
P122 $I_w$80
P183 $I_w$67
P183 $I_w$75
P183 $I_w$80
P230 $I_w$67
P230 $I_w$75
P230 $I_w$80
average I-values of various soft tissues

P Andreo, Phys Med Biol, 2009
164 MeV protons on various tissues
(+/- 10% change in I-values)

Peak spread assuming 10% uncertainty in I-values

P Andreo, Phys Med Biol, 2009
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 0.7 g/cm$^2$ for 230 MeV protons

\[ \pm 1.5\% - 2.0\% \text{ Uncertainty in Range Calculation} \]

Andreo, PMB, 54(1), 2009
Uncertainties in the formation of Broad clinical beam


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

± 1.0 mm Systematic Uncertainty in Range
2-4% (1.0 6) error in CT numbers to relative stopping powers
HU-Stopping Power Conversion Uncertainties
Results in Range Uncertainties

Large prostate patient, Right lateral field

Small prostate patient, Right lateral field

Pediatric spine patient, Anterior field

Head patient, Left lateral field
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.

Flampouri, UFPTI
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).
Improving CT number accuracy and reducing metal artifacts with Orthovoltage CT imaging

Megavoltage CT for Proton Dose Calculation
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.
Impact of complexly structured heterogeneities in proton beam

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

Planning CT

Three Weeks into RT

Impact of Tumor Shrinkage on Proton Dose Distribution

Original Proton Plan

Dose recalculated on the new anatomy
Impact of Organ Motion on Proton Dose Distributions

Tsunashima/MDACC
Free breathing Treatment

Gated treated on exhale

L Dong: MDAH
Comparing Proton Therapy with IMRT

It is incontrovertible that dose distributions of protons can be theoretically superior to those of high energy photons.

Protons Therapy

Ca Oropharynx

Photon IMRT

Yeung UFPTI
Inter-Fraction Motion in H &N

- Setup uncertainty
- Anatomic volume changes
  - Tumor shrinks
  - Parotid glands shrink
Plan DVH Evaluation (PTV)
What you see is not what you always get....
Plan DVH Evaluation (PRV)

What you see is not what you always get..
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
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)
Research Driven Patient Care

Current Photon Therapy

Current Proton Therapy

Future Image-Guided Adaptive Proton Therapy

L Dong: ASTRO 2010
The three 'orders' of proton therapy compared

Intensity Modulated Proton Therapy (IMPT)

Passive scattering

Spot scanning

IMPT

1 field

1 field

1 field

3 fields

3 fields

3 fields

Lomax/PSI
Summary

- Uncertainties in predicting the proton beam range in patients are in the order of ~3-5%
  - (Advanced dose calculation methods might reduce this to ~2.5%)
  - Uncertainties can be minimized in (robust) IMPT optimization

- 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”
Summary

• Reduction in radiation “dose bath,” (by up to ~60% vs. photons) expected to be the principal basis for clinical advantage for protons
  – IMRT is more conformal in the high dose region immediately around the target than 3D conformal protons
  – IMPT may deliver comparable dose distribution but more research is necessary to ensure optimization and delivery of IMPT

➢ 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>
</tr>
<tr>
<td>(pristine Bragg peak)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>*Inherent range uncertainty (spread</td>
<td>±.6-1.0mm</td>
<td>None</td>
<td>±.6-1.0mm</td>
</tr>
<tr>
<td>out Bragg peak)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range reproducibility</td>
<td>±1.0mm</td>
<td>Rigorous QA</td>
<td>±.5mm</td>
</tr>
<tr>
<td>Compensator</td>
<td>±1.0mm</td>
<td>Rigorous QA of</td>
<td>±.5mm</td>
</tr>
<tr>
<td></td>
<td></td>
<td>compensator material</td>
<td></td>
</tr>
<tr>
<td>Accessories (table top,</td>
<td>±1.0mm</td>
<td>Rigorous QA of all</td>
<td>±.5mm</td>
</tr>
<tr>
<td>immobilization jig, etc.)</td>
<td></td>
<td>accessories</td>
<td></td>
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<td>-----------------------------------------------</td>
<td>-------------------------------</td>
<td>--------------------------------------------</td>
<td>------------------------------</td>
</tr>
<tr>
<td>CT</td>
<td>± 3.5% of range</td>
<td>Site specific imaging protocols</td>
<td>± 1-2.0% of range</td>
</tr>
<tr>
<td>Patient setup</td>
<td>± 1.5mm</td>
<td>Rigorous patient selection criteria</td>
<td>± 1.0mm</td>
</tr>
<tr>
<td>Intrafractional patient motion</td>
<td>Variable</td>
<td>Rigorous patient selection criteria</td>
<td>± 1.0mm</td>
</tr>
<tr>
<td>Compensator position relative to patient</td>
<td>Variable</td>
<td>Rigorous patient selection criteria</td>
<td>± 1.0mm</td>
</tr>
<tr>
<td>Range uncertainty (straggling) due to complex heterogeneities</td>
<td>± 1mm</td>
<td>Rigorous patient selection criteria</td>
<td>± 0.5mm</td>
</tr>
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<td>Mitigation Strategy</td>
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<td>-----------------------</td>
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<tr>
<td>CT artifacts</td>
<td>Variable</td>
<td>Rigorous patient selection criteria</td>
<td>± 1.0mm</td>
</tr>
<tr>
<td>Range computation in water in a TPS</td>
<td>Variable</td>
<td>Rigorous patient selection criteria and image edits</td>
<td>± .5mm</td>
</tr>
<tr>
<td>Range computation in tissue of known composition and density in a TPS</td>
<td>± .5mm</td>
<td>None</td>
<td>± .5mm</td>
</tr>
<tr>
<td>Source of Uncertainty</td>
<td>Uncertainty Before Mitigation</td>
<td>Mitigation Strategy</td>
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<td>------------------------------------------------------------</td>
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<tr>
<td>Multi-modality image registration</td>
<td>±1 mm</td>
<td>Better dose computation algorithms</td>
<td>±0.5 mm</td>
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<tr>
<td>Treatment delivery (target coverage uncertainty)</td>
<td>±1-3 mm</td>
<td>Site specific image registration protocols</td>
<td>±1-2 mm</td>
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<tr>
<td>Treatment delivery (dosimetric uncertainty)</td>
<td>±1-3 mm</td>
<td>Rigorous site specific delivery technique selection</td>
<td>±1 mm</td>
</tr>
<tr>
<td>Treatment delivery (dosimetric uncertainty)</td>
<td>±1-3.0%</td>
<td>Rigorous QA</td>
<td>±1.0%</td>
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