Proton Treatment Planning
SAM Educational Session

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Northwestern Medicine Chicago Proton Center
Today’s objectives

– Discuss the general planning tools used in proton planning
  • Aperture / Compensator based delivery
  • Pencil Beam delivery

– Review the unique handling of CTV / ITV / PTV when treating with protons

– Understanding the benefits of PBS and some additional concerns

– PBS patient specific QA
Aperture / Compensator based Planning Strategies

• Cover the target with appropriate margins

• Spare the critical structures

• Plan with fields that deliver the most “robust” plan
Tools to do our job

- Protons
  - Range: The depth of the Bragg peak (D90%)
  - Modulation: The spread of the Bragg peak
  - Apertures: Shaping the beam perpendicular to the path
  - Compensators: Distal Shaping
  - Patch Fields: Distal Edge to Lateral Edge Matching
The Physics of Protons

Spread Out Bragg Peak (SOBP)

Healthy Tissue
Tumor
Healthy Tissue

Depth in Tissue (cm)
Relative Dose

Northwestern Medicine
Chicago Proton Center
Range and Modulation
Spreading the beam across the field
Patient Specific Devices

Aperture
Aperture Design

Graph showing 95% Penumbra with different air gaps (5, 10, 15, 20, 25, 30 cm) and their corresponding range in centimeters.
Brass Aperture mounted in Treatment Snout
Penumbra at Various Air Gaps
Penumbra as Mid SOBP at various ranges
Compensators for Distal Shaping
No Compensator

Target Area

Inhomogeneity (Air Pocket)

Proton Beam

Aperture
Design of the compensator
Design of the compensator
With Discrete Compensator

Compensator

Aperture

Target Area

Inhomogeneity (Air Pocket)
Smearing Radius * = \sqrt{(Set \ up \ Margin)^2 + (Int \ Motion)^2 + (0.03 \cdot \ Depth)^2}
With Discrete Compensator

Compensator

Aperture

Inhomogeneity (Air Pocket)

Target Area
Smearing

- Sacrificing distal conformity to ensure you have enough range (and modulation) to cover the target

- Accounts for the fact that treatment path lengths may be different than planned path lengths due to set-up errors and internal motion.

- Can easily be built into compensator design

- Not directly accounted for in PBS
Question 1
Which statement is true regarding the smearing radius in compensator based proton therapy?:

A. Smearing helps to increase dose conformity to the target.

B. Smearing decreases range uncertainty

C. Smearing is not necessary in inhomogeneous regions

D. The magnitude of the smearing radius is related to the expected set-up errors, the internal motion and the range of the proton beam

E. Smearing is directly applicable to photon treatments as well
Question 1

Which statement is true regarding the smearing radius in compensator based proton therapy?:

a) Smearing helps to increase dose conformity to the target.
b) Smearing decreases range uncertainty
c) Smearing is not necessary in inhomogeneous regions
d) The magnitude of the smearing radius is related to the expected set-up errors, the internal motion and the range of the proton beam
e) Smearing is directly applicable to photon treatments as well

Correct Answer (d) : The magnitude of the smearing radius is related to the expected set-up errors, the internal motion and the range of the proton beam

ICRU 78
Patch Field Technique

Patch Field

Patch Line

Through Beam

Tumor

OAR
Patch Field Technique: Match Line Change

Through Beam

Tumor

OAR

Patch Line

Patch Field
RC ID: CompBeam1
Isovalue (cGy)
60.0
47.5
35.0
22.5
10.0

ref pnt X(cm): -2.79
Y(cm): -6.20
Z(cm): 0.97
dose (cGy): 48.3
global max (cGy): 71.9
local max (cGy): 59.0

Maximized T: -5.20 (cm) Scale=1:1.41
Match Technique

Through Beam

Match Field

Tumor

OAR

Match Line
ICRU Definitions

$\text{PTV} = \text{ITV} + \text{SM}$
ICRU Definitions

**ITV**

**Patient**

**PTV = ITV + SM**
Protons need no distal Set-up margin?

But.... What about Range Uncertainties
Where do range uncertainties come from??

• Depends

Figure 12. Dotted lines: typically applied range uncertainty margins in proton therapy treatment planning as currently typically applied at the MGH (3.5% + 1 mm), the MD Anderson Proton Therapy Center in Houston (3.5% + 3 mm), the Loma Linda University Medical Center (3.5% + 3 mm), the Roberts Proton Therapy Center at the University of Pennsylvania (3.5% + 3 mm) and the University of Florida Proton Therapy Institute (2.5% + 1.5 mm). Note that these centers may apply bigger margins in specific treatment scenarios. Dashed line: estimated uncertainty without the use of Monte Carlo dose calculation. Solid line: estimated uncertainty for complex geometries without the use of Monte Carlo dose calculation. Dashed-dotted line: estimated uncertainty with the use of Monte Carlo dose calculation.

Paganetti, Phys. Med Biol (57), 2012
### 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&lt;sup&gt;DE&lt;/sup&gt;</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&lt;sup&gt;DE&lt;/sup&gt;</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&lt;sup&gt;DE&lt;/sup&gt;</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 ≤ 22 – MVXCT</td>
<td>±5.0% metal&lt;sup&gt;*&lt;/sup&gt;</td>
<td>±5.0% metal&lt;sup&gt;*&lt;/sup&gt;</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>RLSF 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. RLSF (soft tissues only)</td>
<td>±1.6%</td>
<td></td>
<td>±1.6</td>
<td>±1.6</td>
</tr>
<tr>
<td>Energy dependence of RLSF 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>±3.6</td>
<td>±2.2</td>
</tr>
</tbody>
</table>

Abbreviations: DE, dual-energy CT; MC, Monte Carlo calculations.
*Not considered in total.
Yang: Comprehensive analysis of proton range uncertainties related to patient stopping power ratio estimation using the stoichiometric calibration

Table 8. Estimates of uncertainties (1σ) in patient SPR estimation in current clinical practice.

<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>Uncertainties in patient CT imaging</td>
<td>3.3</td>
</tr>
<tr>
<td>Uncertainties in the parameterized stoichiometric formula to calculate theoretical CT numbers</td>
<td>3.8</td>
</tr>
<tr>
<td>Uncertainties due to deviation of actual human body tissue from ICRU standard tissue</td>
<td>0.2</td>
</tr>
<tr>
<td>Uncertainties in mean excitation energies</td>
<td>0.2</td>
</tr>
<tr>
<td>Uncertainties due to energy dependence of SPR not accounted by dose algorithm</td>
<td>0.2</td>
</tr>
<tr>
<td>Total (root-sum-square)</td>
<td>5.0</td>
</tr>
</tbody>
</table>

Table 9. Median, 90th percentile and 95th percentile of composite range uncertainties and the corresponding percentile when the range uncertainty is 3.5% at different clinical sites.

<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 and neck</td>
<td>1.3</td>
<td>2.6</td>
</tr>
</tbody>
</table>
Paganetti: Range uncertainties in proton therapy and the role of Monte Carlo simulations

<table>
<thead>
<tr>
<th>Source of range uncertainty in the patient</th>
<th>Range uncertainty without Monte Carlo</th>
<th>Range uncertainty with Monte Carlo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Independent of dose calculation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Measurement uncertainty in water for commissioning</td>
<td>± 0.3 mm</td>
<td>± 0.3 mm</td>
</tr>
<tr>
<td>Compensator design</td>
<td>± 0.2 mm</td>
<td>± 0.2 mm</td>
</tr>
<tr>
<td>Beam reproducibility</td>
<td>± 0.2 mm</td>
<td>± 0.2 mm</td>
</tr>
<tr>
<td>Patient setup</td>
<td>± 0.7 mm</td>
<td>± 0.7 mm</td>
</tr>
<tr>
<td>Dose calculation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biology (always positive) ^</td>
<td>+ ~ 0.8%</td>
<td>+ ~ 0.8%</td>
</tr>
<tr>
<td>CT imaging and calibration</td>
<td>± 0.5%&lt;sup&gt;a&lt;/sup&gt;</td>
<td>± 0.5%&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>CT conversion to tissue (excluding I-values)</td>
<td>± 0.5%&lt;sup&gt;b&lt;/sup&gt;</td>
<td>± 0.2%&lt;sup&gt;g&lt;/sup&gt;</td>
</tr>
<tr>
<td>CT grid size</td>
<td>± 0.3%&lt;sup&gt;c&lt;/sup&gt;</td>
<td>± 0.3%&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Mean excitation energy (I-values) in tissues</td>
<td>± 1.5%&lt;sup&gt;d&lt;/sup&gt;</td>
<td>± 1.5%&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>Range degradation; complex inhomogeneities</td>
<td>−0.7%&lt;sup&gt;e&lt;/sup&gt;</td>
<td>± 0.1%</td>
</tr>
<tr>
<td>Range degradation; local lateral inhomogeneities *</td>
<td>± 2.5%&lt;sup&gt;f&lt;/sup&gt;</td>
<td>± 0.1%</td>
</tr>
<tr>
<td>Total (excluding *, ^)</td>
<td>2.7% + 1.2 mm</td>
<td>2.4% + 1.2 mm</td>
</tr>
<tr>
<td>Total (excluding ^)</td>
<td>4.6% + 1.2 mm</td>
<td>2.4% + 1.2 mm</td>
</tr>
</tbody>
</table>
Adding Setup and Range Uncertainty with Protons

- Perpendicular Expansion
  - Physical Distance (cm)

- Parallel Expansion
  - Radiobiological Depth (WET)
Graphics Measure
Point Location 1:
X(cm): -7.56
Y(cm): -15.90
Z(cm): -0.52
CT: -531  Relative Electron Density: 0.447

Point Location 2:
X(cm): -8.02
Y(cm): -15.90
Z(cm): -0.71
CT: -740  Relative Electron Density: 0.229

Distance Between Points(cm): 0.50
Radiological Distance (cm): 0.12

Mouse buttons in SPV's
LEFT : Place point 1
MIDDLE : Place point 2
CANCEL
Graphics Measure

Point Location 1:
X(cm): -1.73  
Y(cm): -15.90 
Z(cm): -0.42
CT: 266 Relative Electron Density: 1.140

Point Location 2:
X(cm): -1.38  
Y(cm): -15.90 
Z(cm): -0.78
CT: 189 Relative Electron Density: 1.104

Distance Between Points(cm): 0.50
Radiological Distance (cm) 0.57

Mouse buttons in SPV's
LEFT : Place point 1
MIDDLE : Place point 2
Question 2

Which statement is true about range uncertainty of a proton beam?

A. Range Uncertainty can not be quantified.
B. Range Uncertainty Is very poorly understood
C. Range Uncertainty can be accounted for by adding a beam specific distal and proximal margins
D. Range Uncertainty will completely eliminate the benefits of decreased integral dose given to the patient by a proton treatment
E. Range Uncertainty will lead to lower tumor control rates for proton patients
Question 2

Which statement is true about range uncertainty of a proton beam?

a) Range Uncertainty can not be quantified.
b) Range Uncertainty is very poorly understood
c) Range Uncertainty can be accounted for by adding a beam specific distal and proximal margins
d) Range Uncertainty will completely eliminate the benefits of decreased integral dose given to the patient by a proton treatment
e) Range Uncertainty will lead to lower tumor control rates for proton patients

Correct Answer (c) : Range Uncertainty can be accounted for by adding a beam specific distal and proximal margins

HU Unit conversions

• Conversion from HU to RSP has inherent problems
  – Noise
  – Beam hardening

• Trying to make our CT scanner a spectrometer
  – Two tissues can have same HU but different RSP

• Anything not natural can have large errors.
  – Contrast
  – Fillings
  – Implants
Chestwall Expander
Breast Prosthesis

Fig. 3: Treatment plan for patient with silicone breast prosthesis. (a) Planned dose distribution without RLSP reassignment. (b) Delivered dose distribution if planned without proper pRLSP assignment.
Is there any hope for improvements?

• Dual Energy CT (kV / MVCT)

• Proton activation (PET/SPECT) Tomography

• Prompt Gamma verification

• Proton Radiography

• Proton Tomography
Importance of Image Guidance (IGRT)

- Image Guidance critical to avoid a geometric miss if the target

- For protons, verification of proton path length equivalence is essential.
Effect of Path Length Variances: Photons

From ICRU 78
Effect of Path Length Variances
Protons

From ICRU78
Pencil Beam Delivery / Planning

• Layers of spot patterns delivered over the target volume

• Variable Intensity Control
  • Dose uniformity
  • Simultaneous Intergraded Boost

• Distal AND Proximal conformity

• The ability to perform Multi-Field Optimizations
Spot Intensity for SFUD plan

BEV of the Intensity patterns
Spot Positions and Intensity

- Impossible to manually define spot positions and intensities and hope they relate to each other.
- Inverse planning is required
- Objective function is defined
- An iterative process is used to minimize the objective function
Aperture/Compensator vs. PBS

Norm:Dose(1000.0 cGy = 100%)

Isovalues(%)
100.0
95.0
90.0
70.0
50.0
Advantage of a Compensator

No Compensator vs. With Compensator

No Compensator

With Compensator
Advantage of a Compensator
PBS Planning is lacking critical tools that are easily available in Aperture /Compensator delivery:

How do we account for?

• **Smearing**
  – Set-up errors
  – Internal motion and inconsistent anatomy
  – No physical device (compensator)

• **Range Uncertainties**
Single Field Unif. Dose: Single Field Optimized: IMPT $XX$
Multi-Field Uniform Dose: \((\text{IMPT}_{\text{FULL}})\)
SFUD with range error

OAR

< 100% of Dose

100% of Dose
Multi Field Optimized with a range error

OAR

< 100% of Dose

100% of Dose
Delivery timing of your PBS delivery system and method need to be understood

• PBS Beam delivery method
  – Delivery speed perpendicular to incident beam
  – Delivery speed parallel to incident beam
Delivery perpendicular to incident beam

~ 1 second
Delivery parallel to incident beam

Not Quick ~ 2-5 second
With PBS we need to consider Robustness:

- Quantify the sensitivity of the PBS plan to:
  - Set-up errors
  - Internal Motion
  - Range Uncertainties

- Two methods to do this:
  - Prospectively: Robustness Optimization
  - Retrospectively: Robustness Evaluation
• Evaluation of beam angle prior to optimization
  - Evaluate path lengths
  - Concept can be expanded to 4-D evaluations
• Adding robustness penalties into the objective function of the PBS optimizer
  - Calculate several possible scenarios of setup errors and range uncertainties and iteratively optimize the worst case dose distribution (Unkelbach J et al, Phys Med Biol. 2007 May 21;52(10), MGH)
  - A probabilistic approach: the dose distribution depends on a set of random variables which parameterize the uncertainty, and therefore the objective function used to optimize the treatment plan. (Unkelbach J et al Med Phys. 2009 Jan;36(1):149–63, MGH)
  - The result: optimizer will give lower weights to spots lacking robustness
Robustness Analysis

Process of evaluating several potential scenarios to understand potential “worse case” results

• Translate and/or rotate individual fields and recalculate
  – Mimic Set-up errors

• Re-assign shifted HU conversion curves and recalculate
  – Mimic HU conversion errors

• Move Target structures and recalculate
  – Mimic Internal Motion
Question 3

Which statement/s true about robustness evaluations?

A. Robustness evaluation quantity potential differences in dose distributions of PBS plans caused by set-up and/or range uncertainties.

B. Robustness evaluation compare proton and photon plans

C. Robustness evaluation are not necessary for Multi Field Optimized proton plans

D. Robustness evaluation should be different to the nominal treatment plan

E. Robustness evaluation will speed up the planning process
Which statement is true about robustness evaluations?

a) Robustness evaluation quantity potential differences in dose distributions of PBS plans caused by set-up and/or range uncertainties.
b) Robustness evaluation compare proton and photon plans
c) Robustness evaluation are not necessary for Multi Field Optimized proton plans
d) Robustness evaluation should be different to the nominal treatment plan
e) Robustness evaluation will speed up the planning process

Correct Answer (a) : Robustness evaluation quantity the differences in dose distributions of PBS plans caused by set-up and/or range uncertainties.

A few cases where PBS was beneficial:
40 y/o Male History of Brain irradiation at age 2 for acute lymphoblastic leukemia.

50.4Gy(RBE)

Boost to 59.4Gy(RBE)
Pineal Blastoma

13 y/o Male
Germinoma : Pineal Region

$54.0\text{Gy}_{(\text{RBE})}$
PBS Patient Specific QA

• Secondary independent measurement of planned fluence onto a uniform phantom
  – With protons:
    • 3-dimensional dose distribution
    • A profiles at one depth does not predict the profile at other depths

• Profile Measurements: Must obtained at various depths
  – How many is enough?
    • Initially obtained at least 4 depths
    • Distal portion of CTV
    • Center portion of CTV
    • Proximal portion of CTV
    • Depth = 10cm or less: Plateau region
Patient Specific PBS QA S/U

Zero at front of water buildup

Meas. depth at notch on MatriXX

Isocenter depth remains constant
PBS Patient Specific QA Process

Norm: Abs

Isovalues (cGy)
- 2750.0
- 2500.0
- 2250.0
- 2000.0
- 1500.0
- 1000.0

Ref pnt X(cm): 0.00
Y(cm): 0.00
Z(cm): 3.00

Dose (cGy): 2748.5
Global max (cGy): 2880.8
Local max (cGy): 2840.8

QA PLAN

Scale=1: 2.98
Obtain expected planned dose planes
Profile evaluation of calculated vs. measured profiles
Obtain expected planned dose planes

Mid Distal Proximal Plateau
Distal Edge Evaluation
Distal Edge Evaluation
Distal Edge Evaluation
In Conclusion: Is it too hard?? Should we give up??

No way!!

The true benefit of proton is in the difference in integral dose. Make the best of this!!
Thank You for listening!