A Cliff's Notes Version of Proton Therapy
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AAPM Annual Meeting, 2016

Things You Wanted to Know About Proton Therapy, but Didn't Know to Ask
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• Chris Beltran, Ph.D.
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Cliff’s Notes for Proton Therapy

- Basic description of proton therapy
  - The Bragg Peak
  - Delivery systems
  - Treatment process
- Interesting differences between protons and photons
  - CT number to relative stopping power
  - Dealing with range uncertainties
  - Patient specific QA
  - Relative biological effectiveness

Bragg Peak Depth Dose

Nuclear Interactions

Proton Launcher
Nuclear Interactions

Proton Launcher

Proton Counter

Absorber Thickness [cm]

Protons Counted

Lose 1%/cm water
Interactions with Electrons: Bethe-Bloch

\[
\frac{dE}{dx} = 4 \pi z^2 \epsilon \epsilon_0 N_{A Z} \left( \ln(2mV/(1-\beta^2)) - \beta^2 - S(C/Z) \right) \]

Bragg Peak Depth Dose

Cyclotrons

Ernest Lawrence Cyclotron
80 keV protons (and a Nobel Prize)

Modern Cyclotron
250 MeV protons Superconducting Magnet
Cyclotrons
Energy Selection System

Flanz et al., NIMB (1995) p. 830

Synchrotrons

Beam Transport to Multiple Treatment Rooms

Single Room System
Mevion Gantry Mounted Superconducting Cyclotron

Delivery Techniques: Scattered Protons

250 MeV Proton Beam

Patient

Tumor
Delivery Techniques: Scattered Protons

250 MeV Proton Beam

Add Double Scatterer

Add Field Aperture
Delivery Techniques: Scattered Protons

SOBP with Mod Wheel

Patient

Tumor

Where Can I Improve?

Scatterer: Lose Field Size And Depth

Patient

Tumor
Where Can I Improve?

**Modulator: Constant Width of SOBP**

- Patient
- Tumor

Where Can I Improve?

**Compensator: Custom machined and changed by hand for each field**

Where Can I Improve?

**Aperture: Custom machined for each field and changed by hand**

And brass is heavy and expensive. And a potential source of neutrons.
Delivery Techniques: Spot Scanned Protons

Variable Energy Proton Beam

Y-Scanning Magnets

X-Scanning Magnets

Patient

Tumor

Delivery Techniques: Scattered vs Scanned Protons

Scattered Protons

Scanned Protons

Scanning Nozzle Design

Hitachi Spot Scanning Nozzle at Mayo
Delivery Techniques: Scattered vs Scanned Protons

Scattered Protons
- Beam treats entire volume continuously
- ITV approach for moving tumors

Scanned Protons
- Better conformity
- No field specific hardware
- Cheaper
- Faster
- No aperture to produce neutrons
- Bigger field size at max depth
- Individual fields don’t have to deliver uniform dose
- IMPT
- Moving tumor/scanning beam interplay

Proton Treatment Process

Anesthesia Suite

Imaging Rooms

Beam Matched Tx Rooms

Anesthesia Induction Room
Proton vs Photon Treatment Plan

Things You Wanted to Know About Proton Therapy, but Didn’t Know to Ask
Photon Planning: Relative Electron Density

• Scan commercial phantom with known RED
• Measure HU in scan
• Enter HU-RED curve in photon planning system

Proton Planning: Stopping Power

• Proton stopping power comes from Bethe-Bloch equation:
  \[ S = \frac{4\pi}{\sqrt{2}} \frac{n z^2}{\beta E} \bigg( \frac{Z}{A} \bigg)^2 \cdot \ln \bigg( \frac{2m_e c^2 \beta^2}{\alpha^2 \bigg( 1 - (1 - \beta^2) \bigg)} \bigg) - \beta^2 \bigg] \]
• n is electron density of the medium
• I is excitation energy of the medium
• HU-SP degeneracy
• Phantom materials are not like human tissues
• Stoichiometric Calibration Process
Stoichiometric Calibration

1. Measure HU of materials with known RED
   - Plugs have well known RED values
   - Elemental composition not tissue equivalent
   - Typically scan one plug at a time in center of phantom
   - Use fixed, clinical CT protocol

Schneider et al., PMB 1996

Stoichiometric Calibration

2. Parameterize CT Scanner by Fitting HUs
   - \( \hat{Z} \) and \( \hat{\mathcal{Z}} \) are material properties for photoelectric and Compton
   - Scanner parameters:
     - A: photoelectric
     - B: Compton
     - C: Klein-Nishina

\[ HU_{\text{meas}} = \rho_0^{\text{RED}} (A \cdot \hat{Z} + B \cdot \hat{\mathcal{Z}} + C) \]

Schneider et al., PMB 1996

Stoichiometric Calibration

3. Calculate Predicted HU for ICRU Tissues
   - \( \hat{Z} \) and \( \hat{\mathcal{Z}} \) can be calculated for tissues with physical properties published by ICRU
   - Scanner parameters:
     - A: photoelectric
     - B: Compton
     - C: Klein-Nishina

\[ HU_{\text{pre}} = \rho_0^{\text{RED}} (A \cdot \hat{Z} + B \cdot \hat{\mathcal{Z}} + C) \]

Schneider et al., PMB 1996
Stoichiometric Calibration

4. Calculate Relative Stopping Power for Reference Tissues

\[ S_p = \mu_{p_0} \frac{\ln \left[ \frac{\mu_{e_0}}{\mu_{e_{water}}} \right]}{\ln \left[ \frac{\mu_{p_0}}{\mu_{p_{water}}} \right]} - \beta \]

- \( I \) is ionization potential for material
- \( I \) is assumed to be ~ 75 eV for water
- More uncertainty in \( I \) for other materials

Schneider et al., PMB 1996

5. Plot Relative Stopping Power vs. Calc. CT

- Nominally fit to bi-linear curve
- More segments used in soft tissue region to cover tissues with differing H composition

Schneider et al., PMB 1996

Uncertainties in HU to SP

- Degeneracy in SP values for tissues with same HU
- HU value uncertainty
  - Technique
  - Position in scanner
  - Artifact
- Uncertainties in mean excitation value
- Variations in human tissue composition
- Expected Range Uncertainty: ~3.5% + 1 mm
Every chef and every proton physicist should be friends with their butcher.

Bone
Liver
Kidney
Fat
Brain
Setup and Volume Variations

- In both photon and proton therapy, CTV is the volume within the patient that needs to receive Rx dose.
- Patient’s body has a minimal effect on photon dose distribution: irradiating a portion of the room around the CTV (PTV) reliably treats CTV.
- Proton dose distributions are heavily affected by the patient; PTV not a viable concept in proton therapy.
Geometric Uncertainties in Proton Therapy

Nominal Plan 3% Error in rSP

Geometric Uncertainties in Proton Therapy

Nominal Plan Internal Target Motion

PTVs in Proton Therapy

CTV GTV
ICRU Report 78

“It is required that the dose distribution within the PTV be recorded and reported. This would be unworkable if there were a separate PTV for each beam employed, and impossible if separate lateral and depth margins were built into the computer’s beam-design algorithm. It is therefore proposed that, in proton therapy, the PTV be defined relative to the CTV on the basis of lateral uncertainties alone.”

Robust Treatment Planning

- A single PTV cannot account for all geometric uncertainties in a multi-field proton plan
- Geometric uncertainties are incorporated into the optimization process
- Optimized treatment plans are recalculated with each of these errors incorporated
- A robust plan provides CTV coverage and critical organ sparing in presence of errors
- Physicians review coverage of CTV in light of expected variations
Robust Optimization

Proton Plan Robustness Evaluation

Nominal Plan  Robust Proton Plan

Proton Treatment Process
Proton Plan Robustness Evaluation

- Nominal Plan
- +/- 3 mm x
- +/- 3 mm y
- +/- 3 mm z
- +/- 3% range

- Nominal Plan
- +/- 3 mm x
- +/- 3 mm y
- +/- 3 mm z
- +/- 3% range

Verification of Plan Robustness

- Positional setup variations
  - These are random occurrences. Therapists receive patient-specific instructions for alignment tolerance
- Relative Stopping Power errors
  - Systematic and can only be controlled through careful commissioning and QA
- Volumetric changes
  - Monitored through regular re-scans and calculations

Patient Specific Matching Instructions

Anatomical matching instructions reflect the robustness built into the plan
Scheduled rescan shows significant change in external contour and rectum/bladder filling.

Increased bladder filling does not significantly impact nodal coverage.
Patient Specific IMRT QA: Phantom Measurements

Photon IMRT QA
- Transmission and scattering of x-rays in patient is trivial and well modeled by planning systems
  - Phantom measurements do not reflect these conditions
- Modeling fluence output from moving MLC is very challenging
  - Some phantom measurements can verify the quality of this modeling

Proton IMRT QA
- Transmission and scattering of protons in patient is very difficult to model analytically
  - Phantom measurements do not reflect these conditions
- Modeling spot scanning fluence is trivial
  - Phantom measurements are not necessary to verify fluence

Patient Specific Quality Assurance: Photon vs Proton

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Proton IMPT QA
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GPU-based Monte Carlo Second Check
Analytical TPS Usually Does Fine

Analytical TPS Sometimes Fails

Verify That Monte Carlo Plan is Delivered by Machine

- DICOM plan sent from TPS to a file, and to Monte Carlo
- Treatment plan delivered to water jugs
- Delivery log records MU and location for each beam spot
- Beam spot list compared to DICOM file from TPS
- Verify that the two plans are identical
Verify That Monte Carlo Plan is Delivered by Machine

• DICOM plan sent from TPS to a file, and to Monte Carlo
• Treatment plan delivered to water jugs
• Delivery log records MU and location for each beam spot
• Beam spot list compared to DICOM file from TPS
• Verify that the two plans are identical
What We ‘Know’ About RBE

- RBE average is 1.1 for middle of SOBP
  - Built into planning software
  - 1.2 +/- 0.2 in vitro
  - 1.12 +/- 0.1 in vivo
- RBE is higher at end of range
  - 1.35 distal edge
  - 1.7 at distal fall-off
- RBE is higher for low α/β tissues (20%)
- RBE is higher for lower doses


RBE Variation for Similar Physical Dose
Variable RBE Modeling

• Quantitative data for RBE modeling are not available yet
• To ignore variation of RBE within a proton plan is dangerous
• Conservative models can indicate potential problematic regions
• Spot scanning proton plans are degenerate – there are many ways to achieve the same physical dose distribution.
• LET/RBE will someday be incorporated into the optimization process

Summary

• Proton therapy is an exciting modality with lots of promise, also lots of things still to learn
• Many of the challenges associated with proton therapy are unique to protons, and not present in x-ray therapy
• Anything else you want to ask? Thanks!