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A Cliff's Notes Version of Proton Therapy

Jon J. Kruse
Mayo Clinic, Rochester MN
AAPM Annual Meeting, 2016

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Things You Wanted to Know About Proton Therapy, but Didn't Know to Ask

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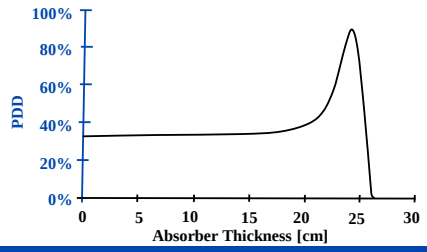
Acknowledgements

- Chris Beltran, Ph.D.
- Nadia Laack, M.D.

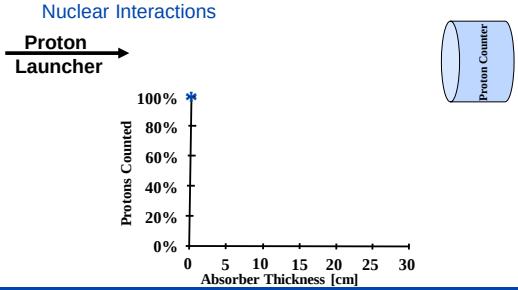
Cliff's Notes for Proton Therapy

- 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



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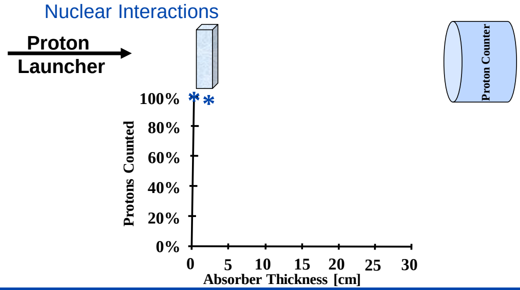

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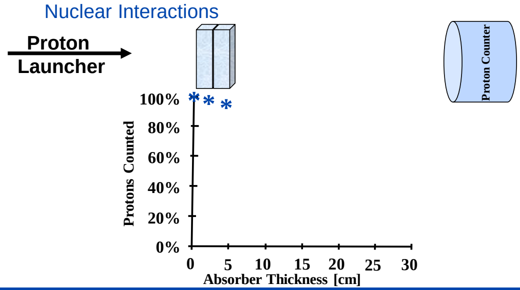

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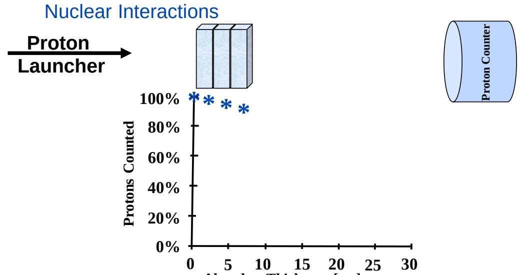
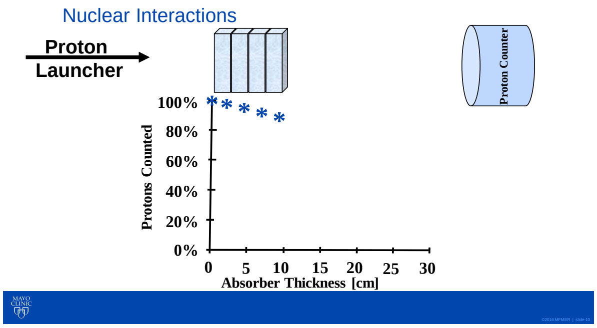
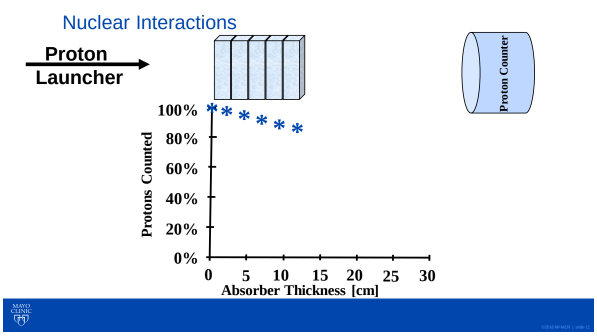



Nuclear Interactions
Proton
Launcher
Proton Counter
100%
80%
60%
40%
20%
0%
Protons Counted
0
5
10
15
20
25
30
Absorber Thickness [cm]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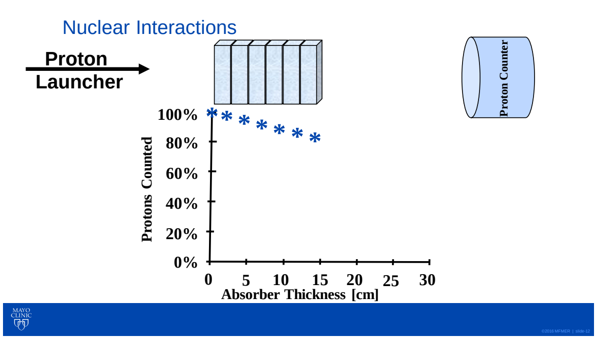
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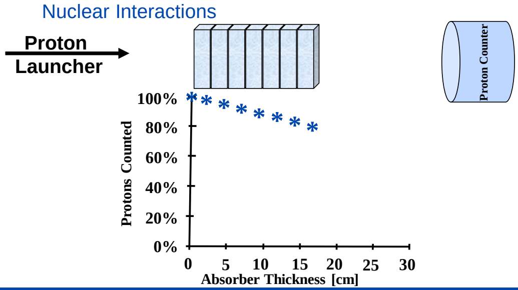

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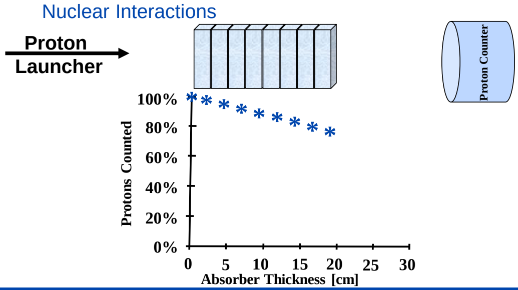

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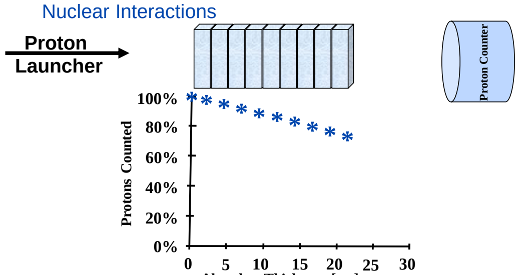

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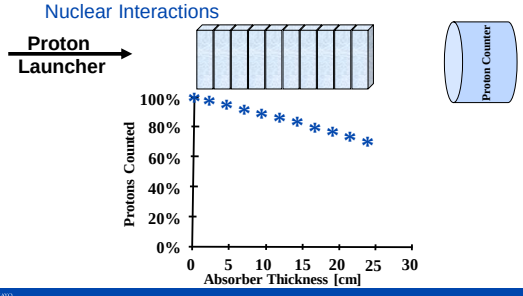

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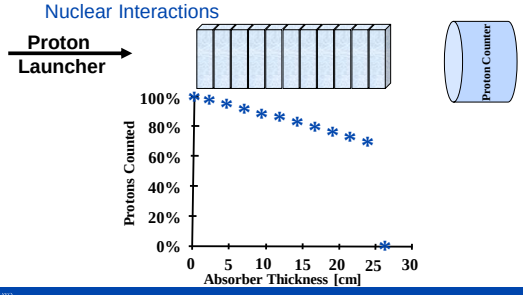

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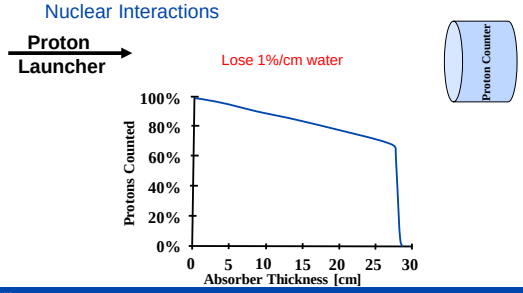
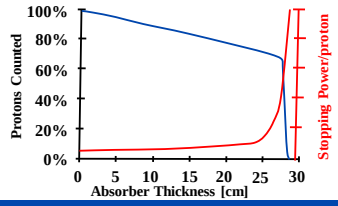
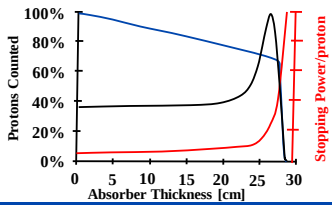


Interactions with Electrons: Bethe-Bloch

$$(dE/dx) = \frac{4\pi z_{eff}^2 e^4 (N_A Z)\{\ln(2mv^2/I(1-\beta^2)) - \beta^2 - \Sigma(Ci/Z)\}}{A\, m_e v^2}$$



Bragg Peak Depth Dose



Cyclotrons

Ernest Lawrence Cyclotron

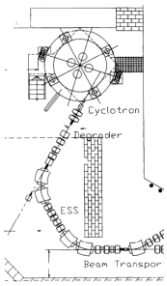
80 keV protons
(and a Nobel Prize)

Modern Cyclotron

250 MeV protons
Superconducting Magnet

Cyclotrons

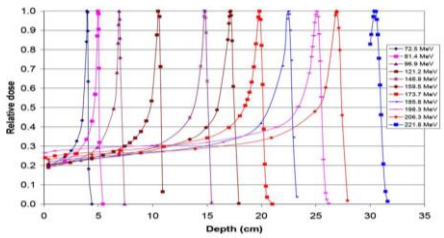
Energy Selection System



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

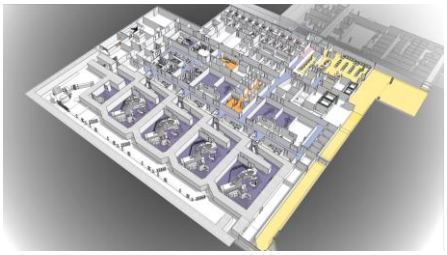
Synchrotrons

Synchrotron Bragg Peaks



Gillin et al., Med Phys 37 (2010) p. 154

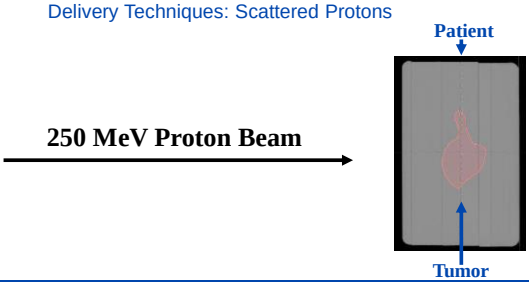
Beam Transport to Multiple Treatment Rooms



Single Room System

Mevion Gantry Mounted Superconducting Cyclotron

Delivery Techniques: Scattered Protons



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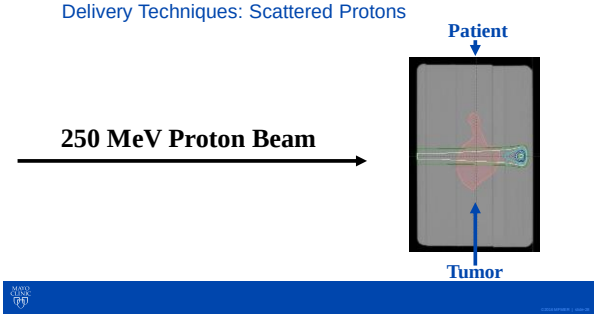

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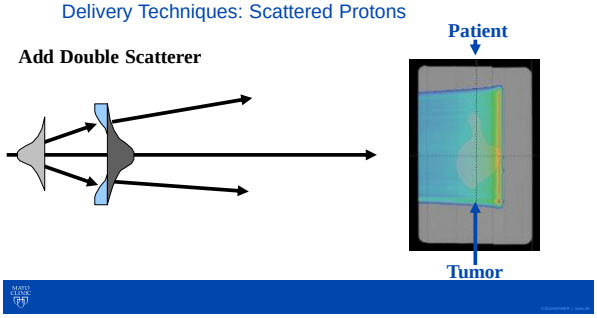

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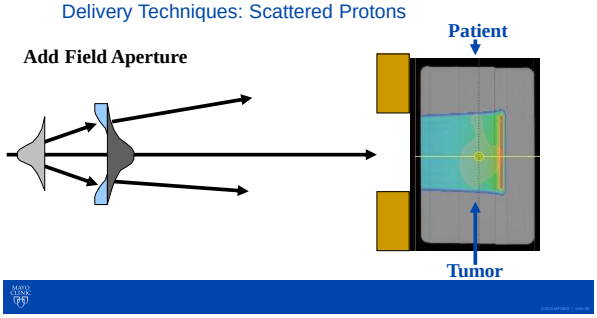
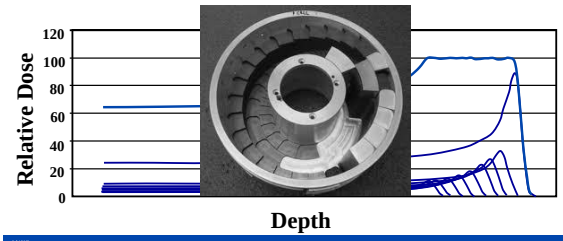


Spread out Bragg Peak



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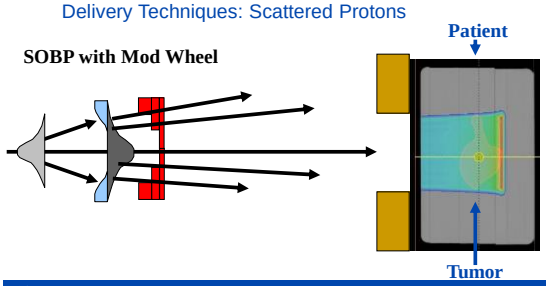

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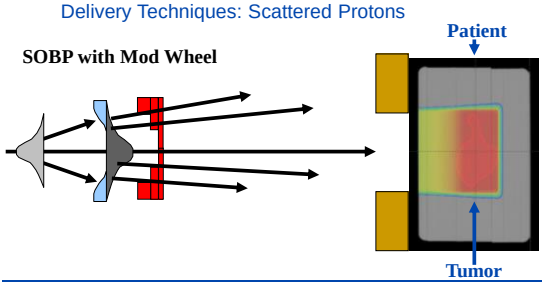
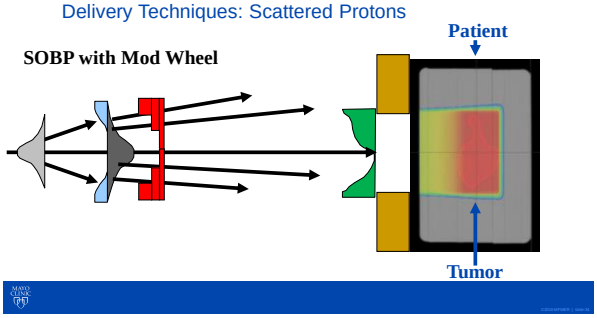


Delivery Techniques: Scattered Protons



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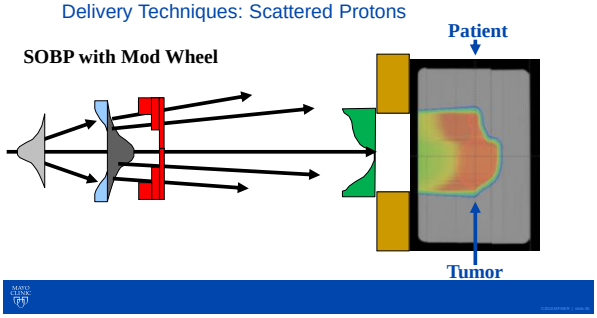
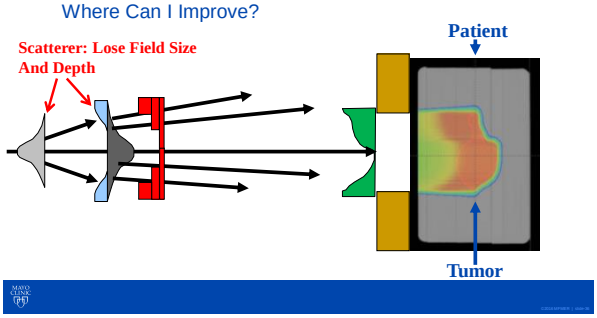


Where Can I Improve?



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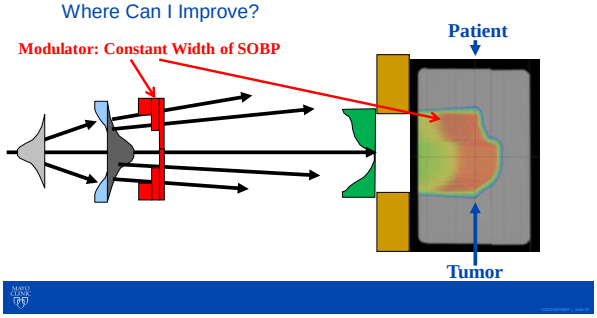

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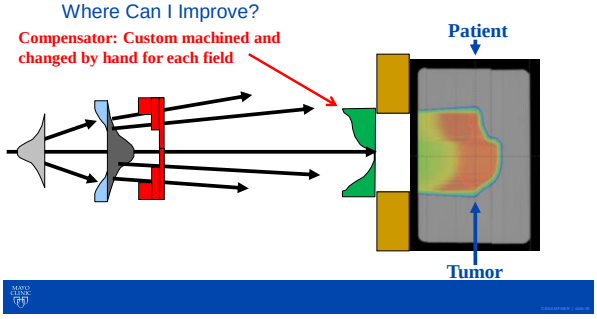

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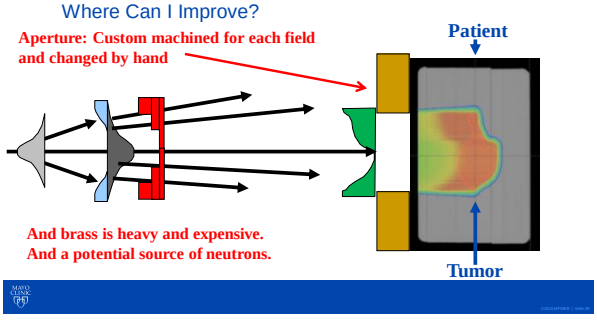
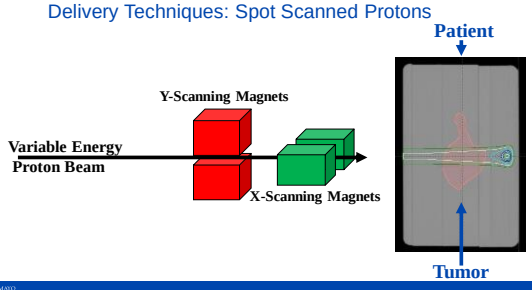
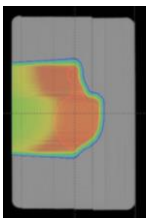


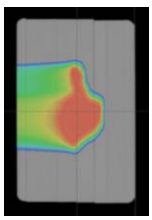
Delivery Techniques: Spot Scanned Protons



Delivery Techniques: Scattered vs Scanned Protons



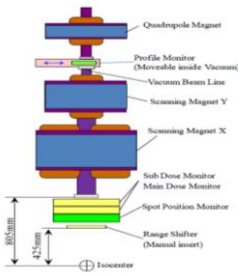
Scattered Protons



Scanned Protons

Scanning Nozzle Design

Hitachi Spot Scanning Nozzle at Mayo



Delivery Techniques: Scattered vs Scanned Protons

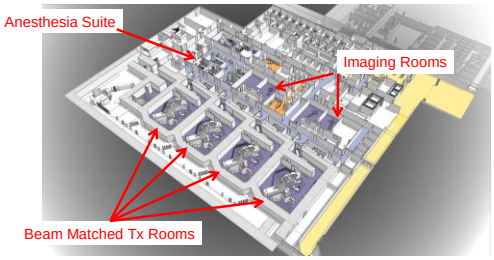
Scattered Protons

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

Scanned Protons

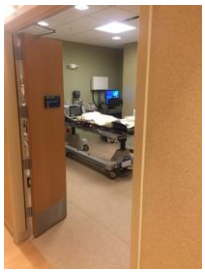
- Better conformality
- No field specific hardware
  - Cheaper
  - Faster
- No aperture to produce neutrons
- Bigger field size at max depth
- Individual fields don't have to delivery uniform dose
  - IMPT
- Moving tumor/scanning beam interplay

Proton Treatment Process



Proton Treatment Process

Anesthesia Induction Room



Proton Treatment Process

Setup/Imaging Room

Proton Treatment Process

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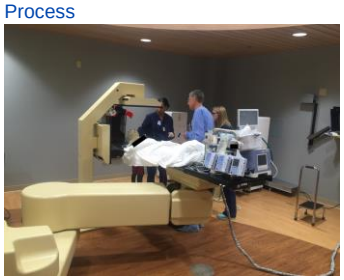
Proton Treatment Process

Setup/Imaging Room



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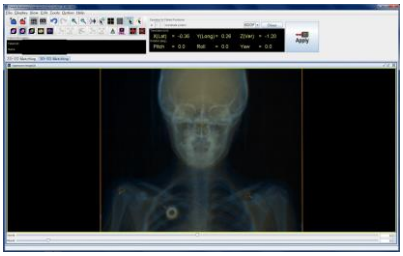

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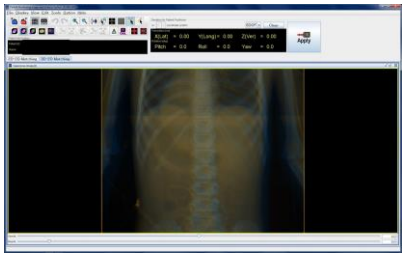

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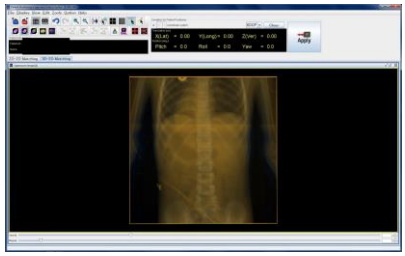
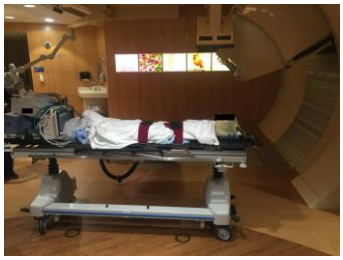


Proton Treatment Process

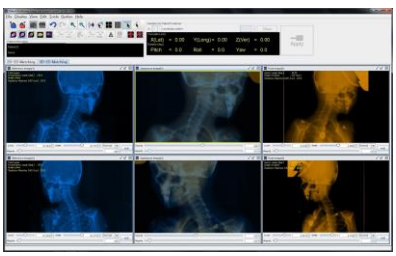
Treatment Room



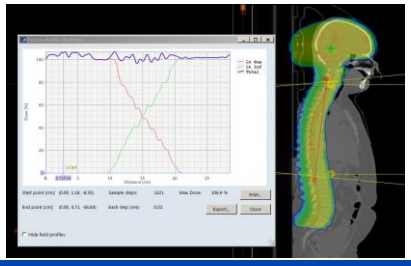
Proton Treatment Process

Treatment Room

Proton Treatment Process

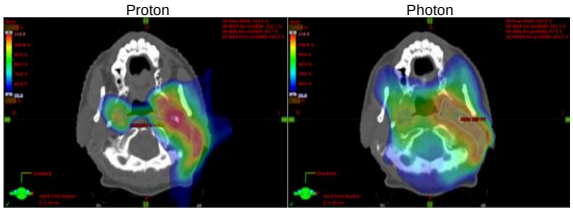


Proton Treatment Process



Proton vs Photon Treatment Plan

Proton Photon



Proton vs Photon Treatment Plan

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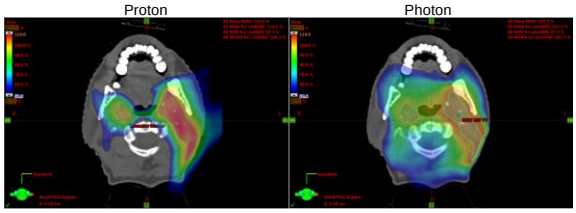
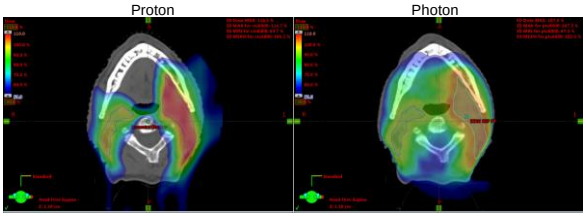
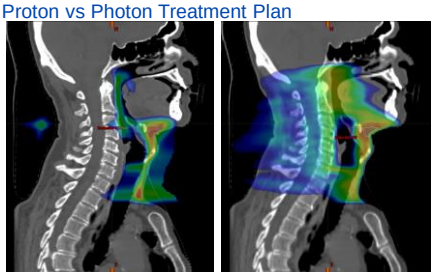


Proton vs Photon Treatment Plan

Proton | Photon



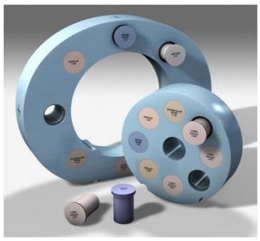
Proton vs Photon Treatment Plan



MAYO CLINIC

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

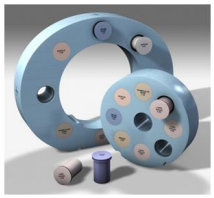
- Proton stopping power comes from Bethe-Bloch equation:

$$S = \frac{4\pi}{m_e c^2} \cdot \frac{nz^2}{\beta^2} \cdot \left(\frac{e^2}{4\pi\epsilon_0}\right)^2 \cdot \left[\ln\left(\frac{2m_e c^2 \beta^2}{\langle I \rangle \cdot (1-\beta^2)}\right) - \beta^2\right]$$

- 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

$$\mathrm{HU}_{sc} = \rho_{e^-}^{\mathrm{rel}}(A \cdot \tilde{Z} + B \cdot \hat{Z} + C)$$

- $\tilde{Z}$ and $\hat{Z}$ are material properties for photoelectric and Compton
- Scanner parameters:
  - A: photoelectric
  - B: Compton
  - C: Klein-Nishina

Schneider et al., PMB 1996

Stoichiometric Calibration

3. Calculate Predicted HU for ICRU Tissues

$$\mathrm{HU}_{sc} = \rho_{e^-}^{\mathrm{rel}}(A \cdot \tilde{Z} + B \cdot \hat{Z} + C)$$

- $\tilde{Z}$ and $\hat{Z}$ can be calculated for tissues with physical properties published by ICRU
- Scanner parameters:
  - A: photoelectric
  - B: Compton
  - C: Klein-Nishina

Schneider et al., PMB 1996

Stoichiometric Calibration

4. Calculate Relative Stopping Power for Reference Tissues

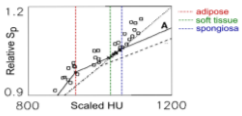
$$S_p = \rho_{e^-}^{rel} \cdot \frac{\left\{\ln\left[\frac{2m_e c^2 \beta^2}{\langle I_{mat}\rangle(1-\beta^2)}\right] - \beta^2\right\}}{\left\{\ln\left[\frac{2m_e c^2 \beta^2}{\langle I_{water}\rangle(1-\beta^2)}\right] - \beta^2\right\}}$$

- 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

Stoichiometric Calibration

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

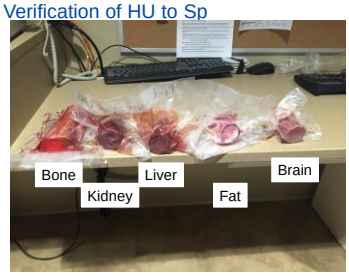
Schneider et al., PMB 1996

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

Experimental Verification of HU to Sp

Every chef and every proton physicist should be friends with their butcher



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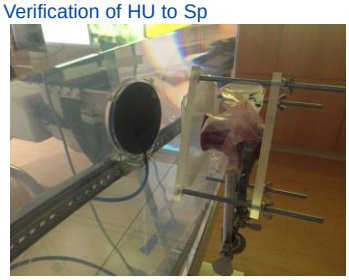

Experimental Verification of HU to Sp

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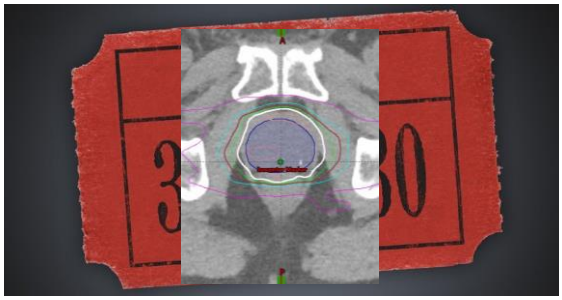
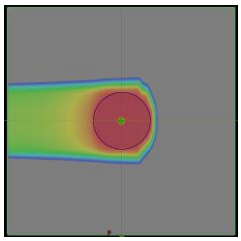


Setup and Volume Variations

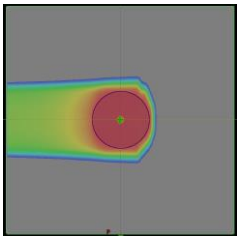
- In both photon and proton therapy, CTV is the volume within the patient that needs to receive Rx dose
- Patient's body has a minimal effect on photon dose distribution: irradiating a portion of the room around the CTV (PTV) reliably treats CTV
- Proton dose distributions are heavily affected by the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

Geometric Uncertainties in Proton Therapy

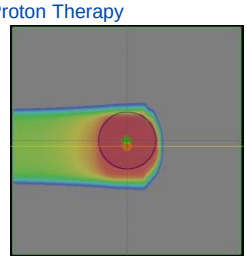


Nominal Plan

Geometric Uncertainties in Proton Therapy

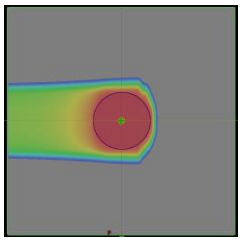


Nominal Plan



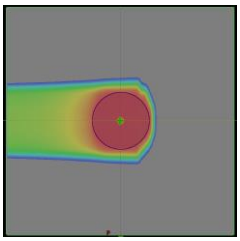
Lateral Shift in BEV

Geometric Uncertainties in Proton Therapy

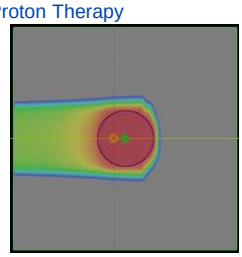


Nominal Plan

Geometric Uncertainties in Proton Therapy

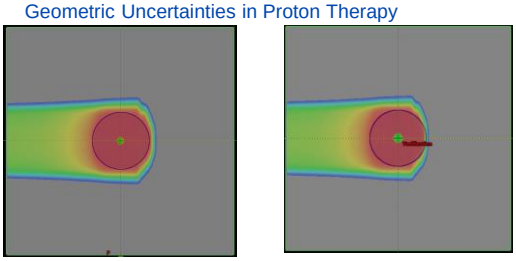


Nominal Plan



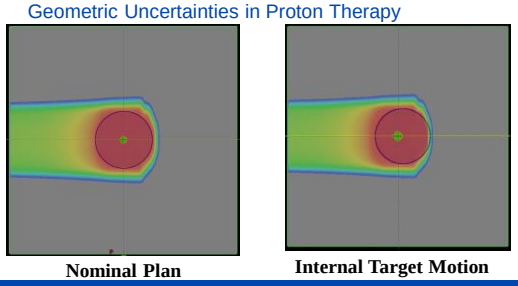
Long Shift in BEV

Geometric Uncertainties in Proton Therapy



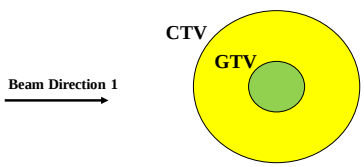
Nominal Plan | 3% Error in rSP

Geometric Uncertainties in Proton Therapy

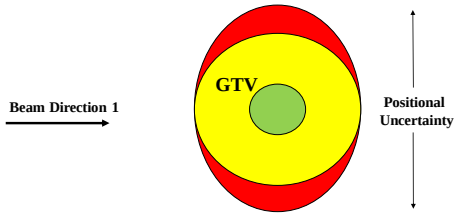


Nominal Plan | Internal Target Motion

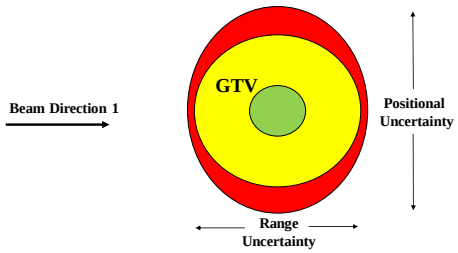
PTVs in Proton Therapy



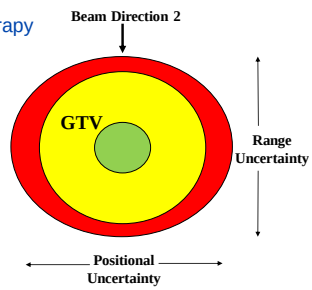
PTVs in Proton Therapy



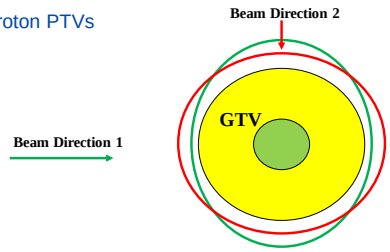
PTVs in Proton Therapy



PTVs in Proton Therapy



Proton PTVs



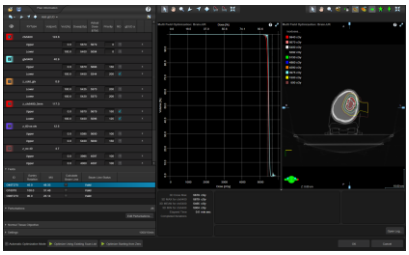
ICRU Report 78

"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."

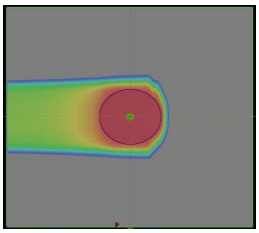
Robust Treatment Planning

- 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

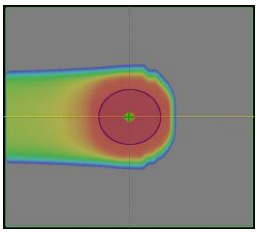
Robust Optimization



Proton Plan Robustness Evaluation

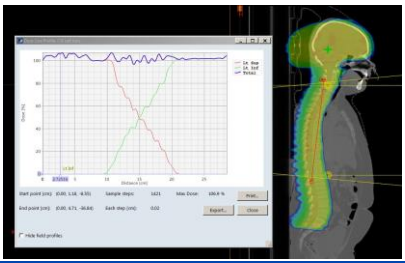


Nominal Plan

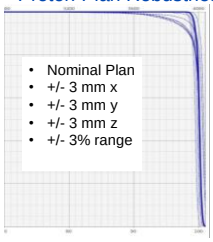


Robust Proton Plan

Proton Treatment Process



Proton Plan Robustness Evaluation



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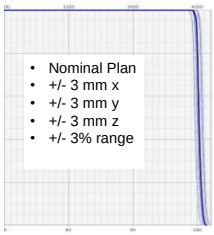


Robust Proton Plan

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

Field Sequencing: Treat R1 side one day L1 side the next

Fields G140T0deg / G140T0inf Treat Day 1

Fields G140T180deg / G140T180 inf Treat Day 2

Dry Run completed

Alert Note **R3/4*** See field note for shift information

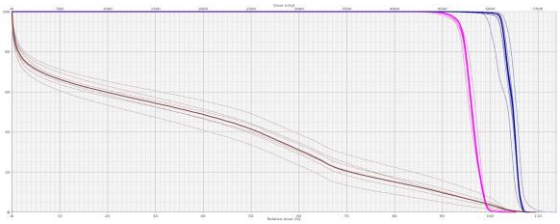
G3	Couch Coordinates	G4	Couch Coordinates	SG2	Couch Coordinates
X		X	1.1	X	1.3
Y		Y	-24.3	Y	-22.4 (-6shift)= -28.4
Z		Z	1.28	Z	8.8

Field Order:

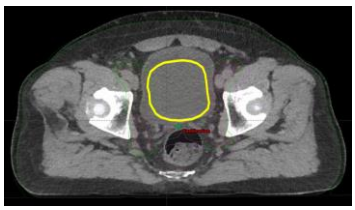
Each Day:	Day 1	Day 2

Matching Tolerance: Match to 2mm on Cribriform Plate and match Spine to 3mm Ant and 5mm R/L/Post

Robust Proton Planning

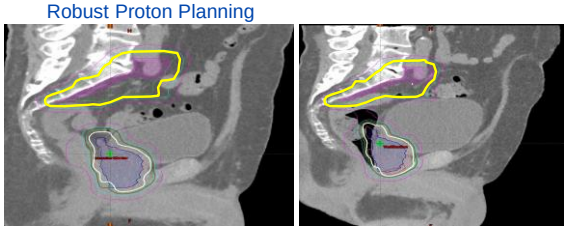


Robust Proton Planning



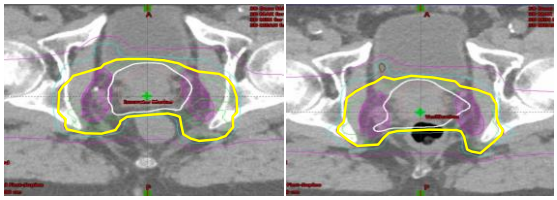
Scheduled rescan shows significant change in external contour and rectum/bladder filling.

Robust Proton Planning



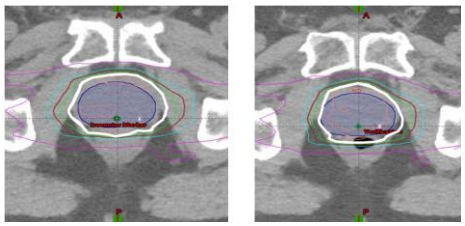
Increased bladder filling does not significantly impact nodal coverage

Robust Proton Planning



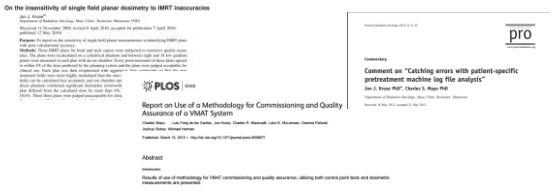
Original Plan **Recalc**

Robust Proton Planning



Original Plan **Recalc**

Patient Specific IMRT QA: Phantom Measurements


On the insensitivity of single field planar dosimetry to IMRT inaccuracies

PLOS ONE

Report on Use of a Methodology for Commissioning and Quality Assurance of a VMAT System

Abstract

pro

Commentary

Comment on "Catching errors with patient-specific pretreatment machine log file analysis"

Patient Specific Quality Assurance: Photon vs Proton

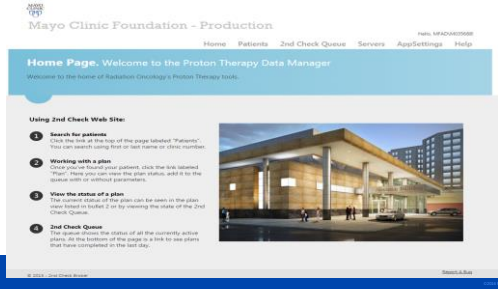
Photon IMRT QA

- 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

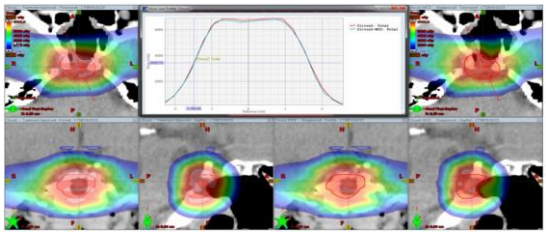
Proton IMPT QA

- 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

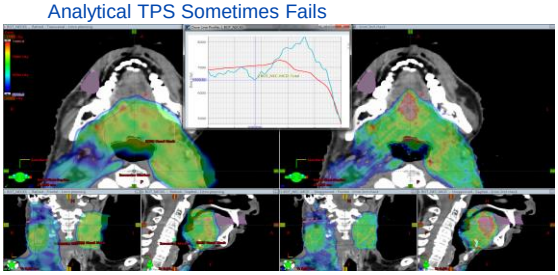
GPU-based Monte Carlo Second Check



Analytical TPS Usually Does Fine



Analytical TPS Sometimes Fails



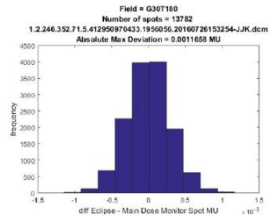
Analytical TPS

Monte Carlo

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



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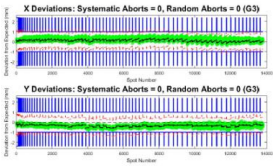

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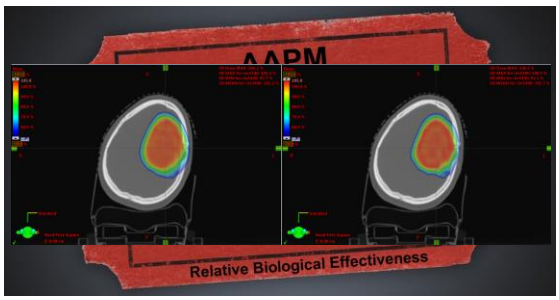
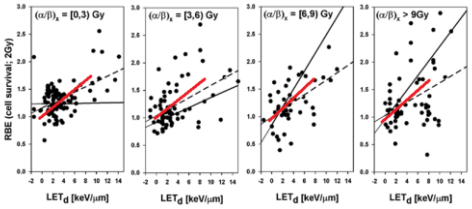


What We 'Know' About RBE

- 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

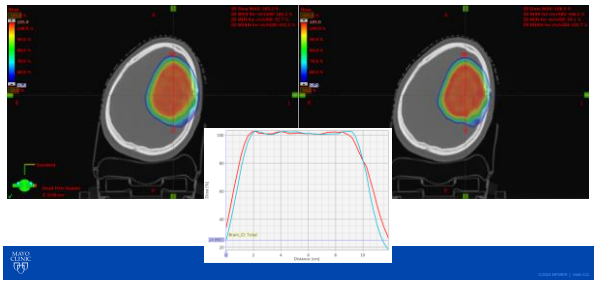
H. Paganetti, et al. Int J Radiat Oncol Biol Phys, 2002

What We 'Know' About RBE



Black data points and curves from Paganetti et al.
Red lines are Mayo model by Beltran, used in our Monte Carlo calculation

RBE Variation for Similar Physical Dose



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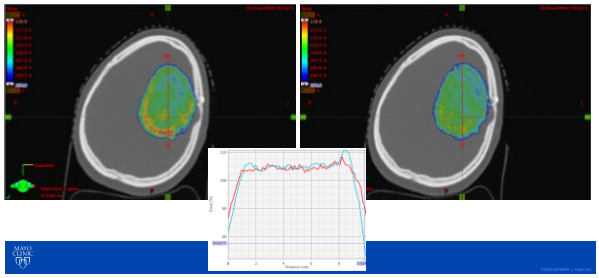

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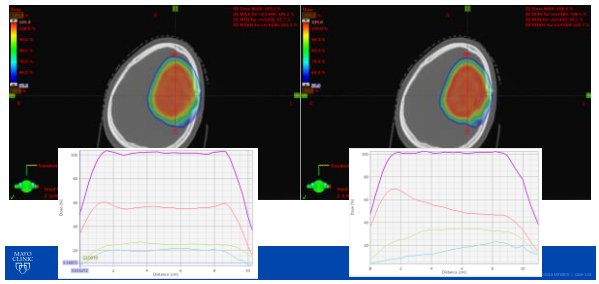
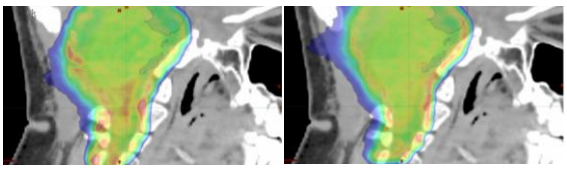


RBE Variation for Similar Physical Dose



BioDose 1 BioDose 2

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!