Proton beam therapy treatment planning

Short introduction

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Outline

- Dose calculation in TPS
- Physics of proton therapy
  - Interactions
  - Features of single beam dose distribution (PDD, lateral spread)
- Proton beam delivery
- Proton dose calculation in TPS

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Why protons?

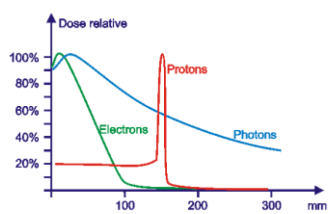

Image http://www.oncoprof.net/Generale2000/g08_Radiotherapie/gb08_rt25.html

- No dose past Bragg peak (no exit dose)
  - Potentially 1 beam treatments
- Protons demonstrate excellent low dose sparing

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Components of treatment planning

- Patient/target/Rx/OAR model:
  - Patient represented by a CT scan, information in Hounsfield units
  - Targets/prescriptions are defined by physician, relevant OAR are contoured
- Beam model
  - TPS software takes measured phantom data as input, creates custom parameter set, look-up tables, etc.
- Dose computation algorithm
  - Accuracy vs speed of calculations

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Dose calculation in computerized treatment planning

- Based on physical interaction of radiation or radiation transport (photons vs charged particles)
- Aim of dose calculation algorithm is to mimic this process in heterogeneous patient material
- Dose computation algorithms:
  - Correction based (TAR, pencil beam and similar)
  - Model-based (Convolution/superposition, Monte Carlo, Boltzmann equations)

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Physics of proton transport

- Primarily Coulomb interactions with the orbital electrons of the target atoms
  - Direct excitation and ionizations of atoms → dose deposition
  - Energy loss per interaction is small → CSDA up until the very end of track (Bragg peak)
  - Max energy transferred W_m ~4 $(m_e c^2/m_p c^2)$ T = 0.35 MeV at T=160 MeV; secondary electron range <1mm → local dose deposition
  - No deflections of protons (p/e mass ratio is ~2000)
- Elastic scattering with nuclei → slight deflection
- Head-on collisions with nuclei are rare, result in nuclear reactions (in soft tissue ^{11}C, ^{13}N, ^{15}O – positron emitters with short half-life)

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Proton range straggling

- Each interaction with the orbital electron results in small discrete energy loss, subject to statistical fluctuations
- Protons passing through medium will lose slightly different amounts of energy, i.e. monoenergetic protons will not all stop at exactly the same depth resulting in 'range straggling'
  - Bragg peak will have some minimum width even if the incident beam has zero energy spread

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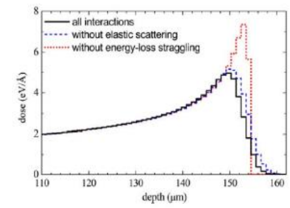
Proton range straggling



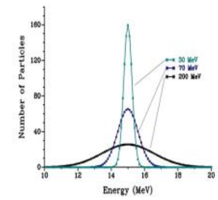


Image from: http://medicalphysicsweb.org/cws/article/research/47448 Image from: http://iaea.org

- Simulation of depth-dose distribution corresponding to a 3MeV proton beam in liquid water (Left)
- The effect increases with energy (Right), depends on media

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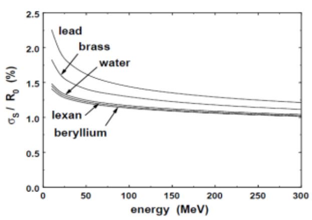
Proton range straggling



Range straggling in several materials, tabulated as standard deviation σ_S per range R_0

Data from J.F. Janni, 'Proton Range-Energy Tables, 1KeV - 10 GeV,' Atomic Data and Nuclear Data Tables 27 parts (Academic Press, 1982)

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Physics of proton transport – cont.

- Elastic scattering through Coulomb interactions with nuclei produce proton deflections (2% of the range in the Bragg peak region)
- About 20% of the incident protons have inelastic nuclear interactions with the target nuclei, produce secondary particles (p, n, heavy fragments)
  - Secondary protons contribute up to 10% of dose
  - Secondary neutrons may deposit dose anywhere in the patient (long range effect), but are typically only accounted in shielding calculations

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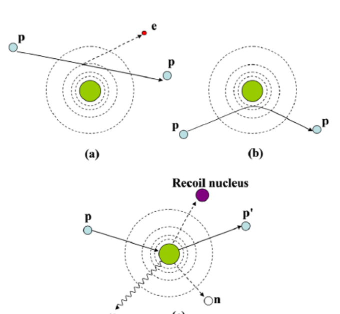

Wayne D Newhauser and Rui Zhang 2015 *Phys. Med. Biol.* **60** R155

Figure 1. Schematic illustration of proton interaction mechanisms: (*a*) energy loss via inelastic Coulombic interactions, (*b*) deflection of proton trajectory by repulsive Coulomb elastic scattering with nucleus, (*c*) removal of primary proton and creation of secondary particles via non-elastic nuclear interaction (p: proton, e: electron, n: neutron, γ: gamma rays)

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Dose calculation for protons

- Energy transfer rate to the medium is quantitatively characterized by stopping power $S\sim 1/v^2$ (recall – no radiative stopping power, $S_r\sim 1/m^2$, proton mass is too high)
- Stopping power corrected for density (mass stopping power S/ρ) is lower for high Z materials
- Scattering in high Z materials is significantly higher than in those with low Z
- For proton beam fluence Φ, in Gp/cm^2 and S/ρ in MeV/(g/cm2) dose is calculated as

$$D = 0.1602 \cdot \Phi \cdot \frac{S}{\rho}\ [\mathrm{Gy}]$$

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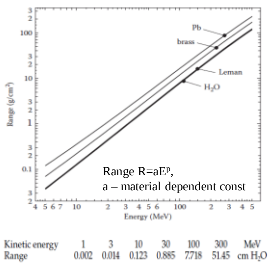
Dose calculation for protons



- Accurate stopping power or range determination is crucial
- Proton range–energy relation around the clinical regime for four useful materials (not straight lines)
- For heterogeneity calculations, scale range relative to that of water (water-equivalent thickness)

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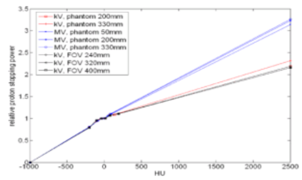
Dose calculation for protons

- Stopping power is determined based on HU (may differ kV vs MV), error ~3% has to be accounted for in TPS



Calibration of CT Hounsfield units for proton therapy treatment planning: use of kilovoltage and megavoltage images and comparison of parameterized methods, L De Marzi, C Lesven, et al., PMB 58, 2013

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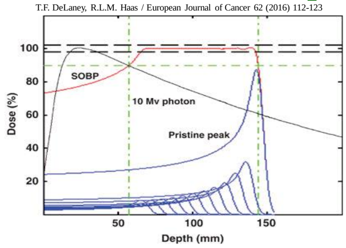
Relative dose vs depth

T.F. DeLaney, R.L.M. Haas / European Journal of Cancer 62 (2016) 112-123



- SOBP – spread out Bragg peak for coverage of extended target
- Range straggling
- No skin sparing in proton therapy (electron build-up region is <<1mm)

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Relative dose vs depth

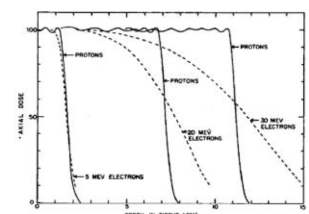

Figure 12. Comparison of depth-dose curves from proton SOBPs and from electron beams. Because the proton mass is nearly 2000 times that of an electron, proton scattering interactions (individual angular deflections and variations in collisional energy losses) are much smaller, leading to sharper lateral and distal falloff distances (reproduced with permission from Koehler and Preston 1972).

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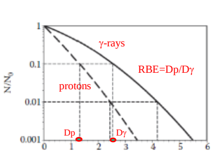
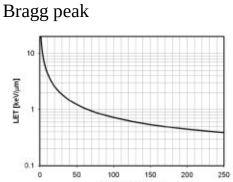
Radiobiology of proton beams

- Characterized by RBE (relative biological effectiveness), dose-level dependent
- RBE depends on LET: for protons depends on their energy – higher in the vicinity of the Bragg peak





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Radiobiology of proton beams

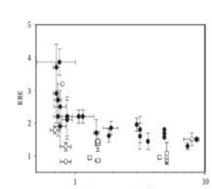

FIGURE 19.7
Experimental RBE values (relative to ^{60}Co; various dose levels) as a function of proton energy for cell inactivation measured in vitro for near mono-energetic protons. Open circles refer to human tumor cell lines at 2 Gy. (From Paganetti et al., Int J Radiat. Oncol. Biol Phys., 53, 407, 2003. With permission.)

- Measured in-vivo and in-vitro, different cell lines show different sensitivity
- Due to typical use of multiple proton energies (SOBP), an average RBE =1.1 is assigned to the overall treatment field
- May under-estimate OAR dose near the target

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Dose distribution

- Dose vs depth: to cover a target of certain width need to “spread” Bragg peak, or modulate range of protons before they enter patient – use energy degrader
- Lateral dose spreading: the typical 1-cm size of a proton beam is much smaller than typical tumor dimensions; commonly use passive scattering
- Prescriptions are adjusted for proton RBE=1.1 compared to Co-60

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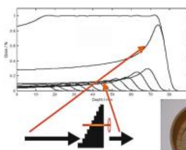
Dose distribution with depth



- Spread-out Bragg peak composed of a number of weighted pristine Bragg curves modulated in depth by a set of absorbers of different thickness
- The lower right image shows a wheel with three different tracks used for different modulation widths

A range compensator made of plastic (stopping power is greater for low Z materials). It is used to conform the proton dose distribution to the distal shape of a target.

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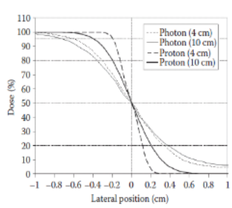
Dose distribution: lateral spread



Lateral beam profiles in the penumbra region for scattered beam with range of 14 cm and modulation width of 10 cm at both 4- and 10-cm depths in water. The profiles of a 6-MV photon beam at the two depths are also shown for comparison

- At shallower depths, proton penumbra (both 20%–80% and 50%–95%) is smaller than that of photon beams
- It increases rapidly with depth and becomes larger than the 15-MV photon beam for depths greater than 17 cm for 20%–80% and 22 cm for 50%–95%

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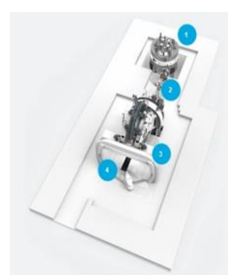
Proton beam delivery



Varian cyclotron facility outline

- **Cyclotrons** (compact size) and synchrotrons
- Cyclotrons structure: D’s with accelerating E-field, requires energy degradation
- Hard to keep the particle inside as it slows down when its mass increases close to relativistic velocities

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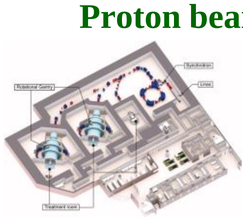
Proton beam delivery



- **Synchrotrons** are circular accelerator ring with a set of bending magnets, requires larger space
- Multiple energies are available
- As with electron beam, minimizing the air gap to the patient reduces the lateral penumbra of the dose distribution

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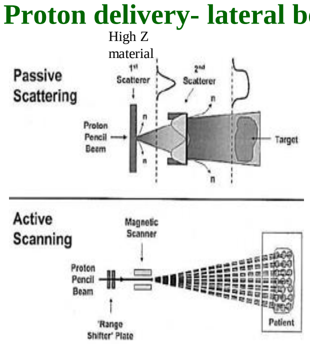
Proton delivery- lateral beam spreading



- Proton beam spot size ~1cm, requires spreading to cover the whole target
- Two principal approaches:
  - Passive scattering (most common)
  - Beam scanning

Image from http://www.dattoli.com/non-surgical-prostate-treatment/what-about-protons/

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Proton beam treatment design

- As a single proton field can deliver a homogeneous dose to the target, it is possible to deliver the entire prescribed dose with only a single field (e.g., lacrimal gland tumors)
- More frequently multiple beams are patched to spread out the dose to normal tissues, just as in photon radiotherapy
- Beams should be positioned as perpendicular to the patient skin as possible (with minimal gap)
- High density materials (e.g., titanium rods) in patient should be avoided if possible due to range uncertainties and dose shadowing effects

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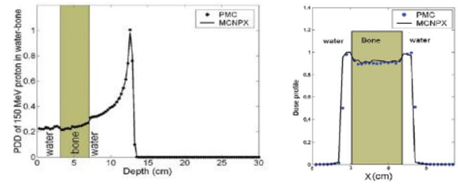
Proton beam treatment design



Jabbari, Keyvan & Seuntjens, Jan. (2014). A fast Monte Carlo code for proton transport in radiation therapy based on MCNPX. Journal of med. physics / Association of Med. Physicists of India. 39. 156-63.

- PDD of 150 MeV protons in the water phantom with embedded 4 cm slab of bone
- Dose lateral profile at the middle of the bone slab for 6×6cm^2 field size (same energy, at depth of 2 cm)

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Proton beam treatments

- Treatment of **ocular tumors** is one of the success stories of proton radiotherapy (typical Rx is 10-14 Gy x 5 fractions, daily)
  - The main OARs: lens, the macula, and the optic nerve
  - Local control rate of well over 95% after 5 years
- Treatment planning is typically based on a recreated geometry rather than on CT-imaging
  - a model of the eye and tumor is created in the TPS based on ultrasound measurements and orthogonal x-rays

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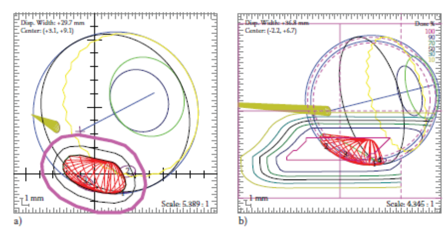
Proton beam treatments



(a) BEV: magenta line indicates the aperture outline; the optic nerve (yellow cone), the lens (green and blue circles), the optic axis (blue line), the macula (magenta cross), and some of the clips (magenta ellipses, 1–4)

(b) Dose distribution in the vertical beam plane in a slice through the center of the tumor

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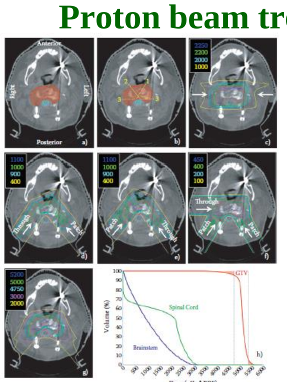
Proton beam treatments



Treatment planning of a **C-spine tumor** (Rx= 50 Gy, 2Gy/fr)

(a) target (red) and dose-limiting (<30Gy) spinal cord (blue)

(b) Multiple patch lines (yellow) for multiple patch combinations

(c) Dose delivered by a left- and a right lat. fields (white arrows)

(d-f) Dose distribution of the 1st, 2nd and 3rd patch combinations

(g) Cumulative dose distribution for all treatment fields

(h) DVH with the vertical dashed lines indicating 95% and 107% of the Rx dose. The solid red areas indicate underdosing and overdosing of the CTV

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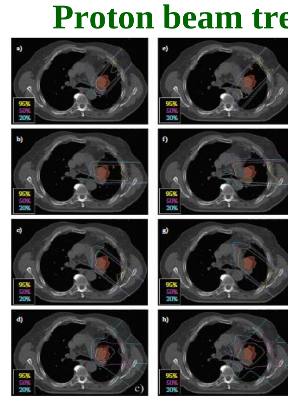
Proton beam treatments



Treatment planning of a **lung tumor** (Rx= 70 Gy, 2Gy/fr)

(a–c) Relative dose distribution for each of 3 individual fields when conforming the high-dose region tightly to the target volume (indicated in red)

(d) Cumulative dose distribution for all three fields

The right-hand panels (e–h) show the same information but now for the planning stage when taking into account range uncertainties, breathing motion, and setup errors.

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Proton dose TPS summary

- Proton beams stop - no exit dose
  - Although we don't know exactly where they stop
- Proton beams are more sensitive to
  - CT Hounsfield number/Stopping Power accuracy
  - Complex inhomogeneities
  - Organ motion and anatomy changes
- Proton plans are difficult to evaluate due to uncertainties
- Protons demonstrate excellent low dose sparing

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References

- Proton therapy physics, ed. H. Paganetti, Taylor & Francis 2012
- H. Paganetti and T. Bortfeld, Proton Therapy, in 'New Technologies in Radiation Oncology', ed. Schegel et al., Springer 2006
- Wayne D Newhauser and Rui Zhang 2015 *Phys. Med. Biol.* **60** R155
- Tony Lomax, State-of-the-art proton therapy: The physicist's perspective, PTCOG47, Jacksonville, 2008
- T.F. DeLaney, R.L.M. Haas / European J.of Cancer 62 (2016) 112-123
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- JR Palta et al., Proton Therapy Treatment Planning: Challenges and Solutions

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