PHYSICS OF PROTON THERAPY

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Protons are charged particles and directly interact with electrons.

Their mass ($M_p$) is $938\text{ MeV}/c^2$ in comparison $M_e = 0.511\text{ MeV}/c^2$

Knock-out electrons easily.

Impart their energy to electrons thus to the medium.

This energy imparted gives rise to the idea of DOSE.
Dose is a measure of the amount of energy deposited in a small volume as a result of the radiation - be that energy deposited locally, or brought to the point of interest by secondary radiation generated at some distance from the primary interaction.

Dose is defined as the energy deposited in a volume divided by its mass.

Dose is expressed in units of Gray (Gy) $\sim 1\text{Gy} = \text{Joule/kg}$

To understand this energy deposition, need to understand charge particle interaction with matter.
BASIC INTERACTIONS

• Energy Loss - Coulomb interactions with electrons. Defines the range and shape of dose profile along the beam line.

• Scattering - Coulomb interactions with target nuclei. Defines the shape of lateral profile.

• Nuclear Interactions - Inelastic nuclear interaction with target nuclei. Modifies the depth dose and lateral dose distribution.
Heavy charged particle therapy can reduce the dose load “integral dose” to normal tissues surrounding the tumor target volume by a factor of 2-3 (reduced “dose bath”)
Why Heavy Charged Particles?

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WHY HEAVY CHARGED PARTICLES?

Increased dose conformality - dose gradient between tumor target volume and surrounding normal tissue.

Physics: ionization of atoms and possible direct breakage of one or both DNA strands.

Chemistry: creation of free radicals and other chemical changes.

Biology: damage to DNA and other intracellular targets - cell kill
ENERGY LOSS

- Protons predominantly lose energy via coulomb interactions with the outer shell electrons of the target.
  - excitation and ionization of atoms
- Loss per interaction is small - “continuously slowing down approximation” (CSDA) is valid.
- Range of secondary e+ is < 1mm - locally absorbed dose.
- Protons are ~2000 times heavier than electrons - no significant deflection.
- Energy loss is given by Bethe-Bloch equation.
ENERGY LOSS: BETHE-BLOCH EQUATION

\[
-\frac{dE}{dx} = 4\pi N_A r_e^2 m_e c^2 Z_A \frac{Z_2}{A} \frac{\beta}{\beta^2} \left[ \frac{1}{2} \ln \frac{2m_e c^2 y^2 \beta^2 T_{max}}{1} - \beta^2 - \frac{\delta(\beta)}{2} - \frac{C(\beta)}{Z_2} \right]
\]

http://physics.nist.gov/PhysRefData/Star/Text/PSTAR.html
ENERGY LOSS: BETHE-BLOCH EQUATION

\[ -\frac{dE}{dx} = 4\pi N A e^2 Z_2^2 \frac{1}{A \beta^2} \left[ \frac{1}{2} \ln \frac{2Z_e^2\gamma^2\beta^2 T_{\text{max}}}{1} - \beta^2 - \frac{\delta(\beta)}{2} - \frac{C(\beta)}{Z_2} \right] \]

- \( \delta \) is density correction - Screening of outer electrons from inner shell electrons. Effect is larger in dense medium.
- \( C \) is shell correction - Important for low energies where the particle velocity is similar to velocity of atomic electrons.
- \( Z, A \) - Atomic number, atomic mass of absorber.
- \( T_{\text{max}} \) - Max energy transfer to free electrons
- \( I \) - Mean excitation energy

Stopping power = \(-dE/dx\)

- To first order \(-dE/dx \sim 1/\beta^2 = 1/v^2\)
- \( T_{\text{max}} = 4T_m e^2/m_p c^2 \)
- \( T = 200\text{MeV} \Rightarrow T_{\text{max}} = 0.4\text{MeV} \) corresponds to electron range of 1.4mm.
- For most electrons KE is much lower energy

http://physics.nist.gov/PhysRefData/Star/Text/PSTAR.html
Energy Loss: Bragg Peak

- Protons go almost straight in water - no significant deflection.
- High energy protons - small energy losses
- Low energy protons - large energy losses
- Not all protons lose the same energy - give rise to range straggling.

Fraction of particles surviving

Energetic protons with minimal energy loss

dE/dx

Most of the energy deposited at end of track

Width of the peak dependent on range straggling and initial energy spectrum

Depth in material

Averange range R

100 %
Range Straggling:
Protons lose their energy in individual collisions with electrons.
Some protons lose more energy earlier in their journey they do not get to travel that far.
Some protons suffer less collisions and get to travel farther.
Protons with the same energy $E_0$ have slightly different ranges.
- Range straggling is Gaussian and is $1\%$ of $R_0$. 

Convolution for range straggling
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Convolution for range straggling
ENERGY LOSS: RANGE

Energy-range relationship, protons in water

- 200 MeV, 26.0 cm
- 150 MeV, 15.6 cm
- 100 MeV, 7.6 cm
- 50 MeV, 2.2 cm
ENERGY LOSS: RANGE

Energy-range relationship, protons in water

ICRU 49
Analytical fit: $R_0 = 0.0022E_0^{1.77}$

200 MeV, 26.0 cm
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50 MeV, 2.2 cm
SPREAD OUT BRAGG PEAK
RANGE & SOBP (MODULATION)
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Dose vs. depth graph showing the range and modulation with various dose levels at different depths.

- **Range**: 90%
- **Modulation**: 90%
- **Dose Levels**:
  - 75%
  - 50%
- **Depth Markers**:
  - 3 cm
  - 8 cm
- **End Points**:
  - Distal end
  - Proximal end
COULOMB SCATTERING

- Protons predominantly scatter due to elastic coulomb interaction with target nuclei.
- Many small angle deflections.
- For radiotherapy a pure Gaussian approximation gives excellent result.
- Full description is given by Moliere scattering and later by Highland approximation.

\[ \theta_0 = \frac{14.1 \text{ MeV}}{pv} \ z \sqrt{\frac{L}{L_R}} \left[ 1 + \frac{1}{9} \log_{10} \left( \frac{L}{L_R} \right) \right] \]

- \( p \) proton momentum
- \( v \) proton speed
- \( L \) target thickness
- \( L_R \) target radiation length

\( \theta_0 \propto 1/pv = 1/(2T) = 1/\text{K.E} \) for \( T \ll 938 \text{ MeV} \); \( T=1/2pv \)

\( \theta_0 \propto 1/L_R^{0.5} \)

- 1.0 g/cm\(^2\) of water (\( L_R=36.1 \text{ g/cm}^2 \)) \( \theta_0 \sim 5 \text{ mrad} \) for 200MeV protons
- 1.0 g/cm\(^2\) of lead (\( L_R=6.37 \text{ g/cm}^2 \)) \( \theta_0 \sim 14 \text{ mrad} \) for 200MeV protons

- Large angle scattering in high Z materials.
Coulomb Scattering

Radial spread in water

- $E_0 = 100\text{MeV} \ (R=7.7\text{g/cm}^2)$
- $E_0 = 150\text{MeV} \ (R=15.8\text{g/cm}^2)$
- $E_0 = 200\text{MeV} \ (R=26.0\text{g/cm}^2)$
- $E_0 = 250\text{MeV} \ (R=37.9\text{g/cm}^2)$

Approximation:

$\sigma \approx 0.02 \times \text{range}$

Calculation using Highland's equation.
About 20% of incident protons have inelastic nuclear interactions with the target nuclei.

Reduction of primary proton fluence with depth.

Secondaries
- charged \((p,d,\alpha,\text{recoil target nuclie})\) \(\sim 60\% \) of energy - absorbed locally.
- neutral \((n,\gamma)\) \(\sim 40\% \) of energy - absorbed in surrounding tissues.

Production of unstable recoil particles (activation)
NUCLEAR INTERACTION

Nuclear interactions take away the dose from the peak

secondary protons generated in nuclear interaction
A certain fraction of protons have nuclear interactions with the absorbing matter (tissue), mainly with \(^{16}\text{O}\).

These protons are lost from the beam.

Janni data suggests 1% loss per cm.
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ANATOMY OF PENCIL BEAM

Along the beam direction

- $1/r^2$ and transverse size set peak to entrance ratio
- Width from range straggling and beam energy spread
- Overall shape from increase of dE/dx as proton slows
- Nuclear reactions take away from the peak and add to this region

Transverse to the beam direction

The lateral distribution: Multiple Coulomb scattering

- Dose
- Multiple Coulomb scattering
- Plural/single Coulomb scattering
- Proton halo from inelastic scattering

Graphical representation of beam characteristics and lateral distribution.
Dividing the problem into two parts:

The Lateral Problem:
How to spread the beam laterally to reach a uniform field up to 24 cm or more in diameter?

The Longitudinal Problem:
How to modulate the beam energy to reach a uniform field from a given range down to skin?
BROAD MODULATED BEAM

- Lateral scattering use thick scatterer or beam scanning (scanning magnets) makes the beam laterally uniform
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**BROAD MODULATED BEAM**

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- Pristine Bragg peaks with shifted ranges are superimposed with correct weights and is achieved by pulling back the range - stepped wheel spinning at high speed.
DOUBLE SCATTERING (DS)

Range Modulator revolves at 600 RPMs

Pristine Bragg peak

lateral profile

depth profile

Nozzle

Second Scatterer

Block and Range compensator

All layers in a SOBPs are delivered at the same time.
UNIFORM SCANNING (US)

Pristine Bragg peak

Beam is delivered layer by layer. At any given time beam is a pristine Bragg peak of certain range.
LATERAL PROFILE

Nozzle Entrance
After FS & RM
After SS
After block & RC

Nozzle Entrance
After FS & RM
After Scanning Magnets
After block and RC

LATERAL PROFILE
These protons are stopped in the nozzle, snout, and aperture and generate neutrons.
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Lateral profile becomes important in clinical beam - is a function of depth.
Small fields
~20% of the beam treats
~80% of the beam produces neutrons

Large fields
~60% of the beam treats
~40% of the beam produces neutrons
What contributes to lateral penumbra
What contributes to lateral penumbra
What contributes to lateral penumbra

\[ \text{width}_{80-20} \sim \sigma_{\text{tot}} \]

\[ \sigma_{\text{tot}} = \sqrt{\sigma_{\text{source}}^2 \left( \frac{z_p - z_{\text{ap}}}{z_{\text{ap}}} \right)^2 + \sigma_{\text{rc}}^2 + \sigma_{\text{pat}}^2} \]

(Virtual) Source

Aperture

geometric contribution
At shallow depth lateral penumbra is dominated by the source size.

As depth in the patient increases patient scatter starts to increase.

Beyond ~16cm patient scatter becomes dominant.
RELATIVE BIOLOGICAL EFFECTIVENESS (RBE)

What is the difference in biological effectiveness between particles and photons?

\[ RBE = \frac{D_y}{D_{ion}} |_{Isoeffect} \]

Dose [Gy]

Surviving Fraction

\[ RBE = \frac{D_x}{D_p} \]

X-rays

Particles
RELATIVE BIOLOGICAL EFFECTIVENESS (RBE)

RBE = 1.1 for protons (general consensus)

RBE for heavier particles (C12) can be as high as 3.5

$1.07 \pm 0.12$
RELATIVE BIOLOGICAL EFFECTIVENESS (RBE)

RBE increases with depth because linear energy transfer (LET) increases with depth.

For protons we assume 1.1 flat for the entire SOBP.

Biological effective range increases by 1-2mm.

Carbon 12
LINEAR ENERGY TRANSFER (LET)

LET of charged particle in a medium is the ratio of $dE/dl$, where $dE$ is the average energy locally imparted to the medium by a charged particle in traversing a distance of $dl$.

- LET $< 10 \text{ keV/}\mu\text{m}$ Low LET
- LET $> 10 \text{ keV/}\mu\text{m}$ High LET

- 260 kVp X-Rays: 2 keV/μm
- 3 MeV X-Rays: 0.3 keV/μm
- 14 MeV neutrons: 12 keV/μm
- heavy charged particles: 100-200 keV/μm
- 10 keV electrons: 2.3 keV/μm
Pencil beam formalism

Dose from a single beam at a point \((x',y',z')\) relative to the source position of the pencil beam
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Dose from a single beam at a point \((x', y', z')\) relative to the source position of the pencil beam

\[ d_p(x', y', z') = C(z') \cdot O(x', y', z') \]

Central Axis term

\[ C(z') = DD(d_{eff}) \left(\frac{ssd_0 + d_{eff}}{z'}\right)^2 \]

Broad beam depth dose distribution. Measured in the water phantom and modified by an inverse square law

Off-Axis term

\[ O(x', y', z') = \frac{1}{2\pi[\sigma_{tot}(z')]^2} \exp\left(\frac{x'^2 + y'^2}{2[\sigma_{tot}(z')]^2}\right) \]

Is the lateral flux distribution from the radial emittance suffered by protons directed along the axis of the pencil beam
Pencil beam formalism for broad beam - sum of multiple pencil beams
DOSE CALCULATION

Pencil beam formalism for broad beam - sum of multiple pencil beams
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Pencil beam formalism for broad beam - sum of multiple pencil beams

Dose at a point in a beam is a integral of over all pencil beams:

\[
D_p(x,y,z) = \int \int dx' dy' \frac{C(x',y',z)}{2\pi[\sigma_{tot}(x',y',z)]^2} \exp\left(-\frac{(x'-x)^2 + (y'-y)^2}{2[\sigma_{tot}(x',y',z)]^2}\right)
\]
FIELD DOSE SHAPING
FIELD DOSE SHAPING
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High-Density Structure

Body Surface

Beam

Target Volume

Critical Structure

water equivalent thickness sets the range for treatment
FIELD DOSE SHAPING

water equivalent thickness sets the range for treatment
FIELD DOSE SHAPING

- Aperture
- High-Density Structure
- Body Surface
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FIELD DOSE SHAPING

High-Density Structure

Beam

Aperture

Body Surface

Target Volume

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SOBP Fit

Mod 44.0B
N 9

Depth / mm
DOSE PLANNING

Typically 120 keV

CT-scan in Hounsfield units

It measures linear attenuation

\[ HU = \frac{\mu_X - \mu_{H_2O}}{\mu_{H_2O} - \mu_{air}} \cdot 1000 \]

<table>
<thead>
<tr>
<th>Substance</th>
<th>HU</th>
</tr>
</thead>
<tbody>
<tr>
<td>Air</td>
<td>-1000</td>
</tr>
<tr>
<td>Fat</td>
<td>-120</td>
</tr>
<tr>
<td>Water</td>
<td>0</td>
</tr>
<tr>
<td>Muscle</td>
<td>+40</td>
</tr>
<tr>
<td>Bone</td>
<td>+400 or more</td>
</tr>
</tbody>
</table>
DOSE PLANNING

CT vs relative electron density for photons

CT vs relative stopping power for protons
DOSE PLANNING

CT vs relative electron density for photons

CT vs relative stopping power for protons

CT vs relative electron density for photons

CT vs relative stopping power for protons

Any error in CT will result in uncertainty in proton range calculations
%5 error in CT calibration can have couple of % error in photon depth dose. Tumor is still covered
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5% error in CT can change the proton range.
- miss part of tumor
- overshoot tumor into critical structure like cord, brainstem
- RBE is also large at the end.

Unrealistic 5% error in CT conversion
SUMMARY

• Physics: Energy loss, scattering, nuclear interactions lead to Bragg peak shaped dose distribution.
• Pencil beam is converted to a broad beam by lateral and longitudinal spreading.
• Range straggling modifies the beam at distal end along the direction of beam ~1% of the Range.
• Lateral penumbra modifies the beam in a transverse direction to the beam ~2% of the Range.
• RBE modifies the does depths and increases range by ~2mm.
• Dose calculation based on pencil beam algorithm.
• Sculpting raw proton beam into clinical deliverable beam.
THANK YOU