Protons: Clinical Physics Implementation

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Protons stop.
Dark Blue: 45 Gy
Light Blue: 10 Gy

A proton beam and an electron beam with the same 90% distal dose

WHY PROTONS? It is a positive experience.

Protons have a limited range, which should limit toxicity

3 fields, Lateral and 2 Posterior obliques

Patient with T2, N0, MX COPD
87.5 CGE
Limited dose to the non-involved lung

Standard fractionation

Note: Penetration through lung
Charged Particles Interaction in Matter - Attix Chapter 8

- A charged particle, being surrounded by its Coulomb electric force field, interacts with one or more electrons or with the nucleus of practically every atom it passes.
- Continuous slowing down approximation (CSDA) – most charged particle interactions individually transfer only minute fractions of the incident particle’s kinetic energy.
- A 1 MeV charged particle would typically undergo approximately $10^5$ interactions before losing all of its kinetic energy.
- Range is the expectation value of path length, namely the mean value for a very large population of identical particles.

![Diagram of Charged Particle Interaction](image)

**A** – classic atomic radius
**b** – classic impact parameter

**Figure 8.1:** Important parameters in charged-particle collisions. (a) is the classical atomic radius; (b) is the classical impact parameter.
Types of Charged Particles Coulomb-Force Field Interactions

A. Soft Collisions (b>>a)
   Atom as a whole moves to a higher energy state
   very small energy transfer (a few eV)

Roughly half the energy transferred to the absorbing medium,
as large values of b are clearly more probable than are near hits on
individual atoms.

The finite range of protons is due to their almost continuous loss of energy as
they traverse matter. This allows the computation of the continuous slowing-
down approximation range of a proton of given energy by the integration of the
reciprocal of the stopping power along its entire path.

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Types of Charged Particles Coulomb-Force Field Interactions

A. Soft Collisions (b<<a)
   Protons also experience numerous Coulomb interactions with
   the charged nuclei of the atoms. Each of these interactions results
   in a usually very small deflection of the projectile proton. These
   interactions result in the finite deflection of a proton from a
   straight path.

A near monoenergetic proton beam traversing a thickness of material small
relative to its range will be scattered with an approximately Gaussian distribution
of angles for which sigma (standard deviation) is termed the characteristic
scattering angle, $\delta_0$.

Penumbra for deep tumors cannot be ignored.

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Nuclear Interactions by Heavy Charged Particles

A heavy charged particle having sufficiently high
kinetic energy (100 MeV) and an impact parameter
less than the nuclear radius may interact inelastically
with the nucleus.

When one or more individual nucleons are struck, they
may be driven out of the nucleus in an intra-nuclear
cascade process, collimated strongly in the forward
direction.

In solid organic materials for protons > 500 MeV, this
process dominates the energy loss.
Proton Interactions

- For protons with energies between 0.01 MeV and 250 MeV, interactions with electrons are dominant.
- For tissue equivalent material, the probability that protons will undergo a nuclear interaction while traversing a path length of 1 g cm\(^{-2}\) is on the order of 1%.
- At a depth of 20 cm, approximately 1 in 4 protons will have undergone a nuclear interaction. This will contribute a background of nuclear interaction products.

The interactions of a 200 MeV proton in water are only:

1. Electromagnetic
2. Electromagnetic and inelastic scattering
3. Electromagnetic, inelastic scattering and Rutherford scattering
4. Electromagnetic, inelastic scattering, Rutherford scattering, and nuclear scattering
5. Electromagnetic, inelastic scattering, Rutherford scattering, nuclear, and fusion

Mass Electronic Stopping Power, \(S/\rho\)

\[ S/\rho = 1/\rho \left(\frac{dE}{dx}\right) \text{ MeV M}^2/\text{kg} \]

\(S/\rho\) depends on the composition of the material and on the nature and energy of the charged particle.

Gottschalk: The Fundamental Equation

\[ D = \Phi \frac{S}{\rho} \]

Dose equals fluence times mass stopping power
### Proton Mass Electronic Stopping Power (MeV cm$^{-2}$ g$^{-1}$) ICRU 59

<table>
<thead>
<tr>
<th>E(MeV)</th>
<th>Water</th>
<th>Air</th>
<th>Bone</th>
<th>Polystyrene</th>
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<tr>
<td>250</td>
<td>3.911</td>
<td>3.462</td>
<td>3.646</td>
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<td>20</td>
<td>26.02</td>
<td>22.94</td>
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<tr>
<td>10</td>
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<td>222.9</td>
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<tr>
<td>0.1</td>
<td>916.1</td>
<td>791.2</td>
<td>791.2</td>
<td>916.4</td>
</tr>
</tbody>
</table>

### Proton stopping power in water for energies between 0.1 and 250 MeV

1. Vary by a factor of 10 to 100 with the higher energy protons having the greater ratios
2. Vary by a factor of > 100 with the higher energy protons having the greater ratios
3. Vary by a factor of 10 to 100 with the higher energy protons having the lower ratios
4. Vary by a factor of > 100 with the higher energy protons having the lower ratios
5. Vary in a linear manner as energy decreases

### Accelerators

**Cyclotrons – CW Units**

- **IBA – Isochronous cyclotron with resistive magnet**, 220 tons, 70 to 230 MeV/u
- **Varian – Isochronous superconducting cyclotron**, 90 tons, 70-250 MeV/u

*Isochronous cyclotron* is a cyclotron that maintains a constant RF driving frequency, and compensates for the relativistic mass gain of the accelerated particles by alternating field gradient in space but constant in time.
Accelerators
Synchrotrons - Pulsed Units

- Optivus – LLUMC solution
- Hitachi – slow-cycle synchrotron, 70 to 250 MeV protons, scattered beam spills 0.5 sec with 1.5 sec between spills, scanned beam spills up to 4.1 sec with 2.1 sec between spills
- Mitsubishi – 70 to 250 MeV, 2 Gy/min

Hitachi synchrotron

Gantry Treatment Rooms

- The gantry rings are 5.5 meters in diameter, the rotating mass is 190 tons, and the gantry rotates 360 degrees (+180 degrees with 10 degrees over travel) around the patient.
- The maximum speed is 1 RPM. Emergency stop will occur within 4 degrees at maximum speed.
- The gantry mechanical isocenter is required to be contained within a sphere of < 1 mm diameter.
- A correction algorithm will correct for residual gantry errors at each gantry angle; this correction is made by repositioning the couch when a correction request is made on the treatment control pendant.
The Gantry
A Significant Example of Mass

Counter weight Gantry diameter: 5.5 m

Gantry: 190 tons – Isocenter is held in part by adjusting the couch as a function of gantry angle.

ICRU 78
Beam Parameters (3.4.2.2)

- Passively scattered beams
  - Depth of penetration or range
  - Distal-dose fall off 80 to 20% in g cm\(^{-2}\)
  - SOBP length
  - Lateral penumbra
  - Target or treatment width
  - Lateral flatness

Range

- Depth of penetration or range is defined as the depth (in g cm\(^{-2}\)) along the central axis in water to the distal 90 percent point of the maximum dose.
Ranges (cm) (d 90%)
Protons loose energy when scattered for large fields.

<table>
<thead>
<tr>
<th>Energy (MeV)</th>
<th>Small Snout 10 cm²</th>
<th>Medium Snout 18 cm²</th>
<th>Large Snout 25 cm²</th>
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<tbody>
<tr>
<td>250</td>
<td>32.4</td>
<td>28.5</td>
<td>25.0</td>
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<tr>
<td>225</td>
<td>26.9</td>
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<td>20.6</td>
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<tr>
<td>200</td>
<td>21.8</td>
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<td>16.5</td>
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<tr>
<td>180</td>
<td>16.9</td>
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<td>13.4</td>
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<td>6.3</td>
</tr>
<tr>
<td>100</td>
<td>4.9</td>
<td>4.3</td>
<td>4.3</td>
</tr>
</tbody>
</table>

Distal-dose fall off (DDF)

- The distal dose fall off is defined as the distance (in g cm⁻²) in which the dose, measured in water along the beam central axis, decreases from 80% to 20% of the maximum dose value.
- In the example shown, this distance is 0.6 cm.

SOBP Length

- SOBP length is defined as the distance in water between the distal and proximal 90% points of the maximum dose value.
- The ICRU definition may be hard to implement if the proximal portion of the curve displays a gradual increase.

MDACC Definition: 95% proximal to 90% distal.
**Lateral Penumbra (LP)**

- The lateral penumbra is defined at a given depth as the distance (in mm) in which the dose, measured along the line perpendicular to the beam axis, decreases from 80 to 20% of the maximum dose value at that depth.
- The aperture to patient distance changes as the snout is moved from isocenter to 45 cm.

**Profiles**

**Scattered Beam**

- Lateral profile at depth of 14.9 cm for small snout for beam with range of 16.9 cm (180 MeV)
  - 6.3 mm. (Left)
- Lateral profile at depth of 11.9 cm for small snout for beam with range of 16.9 cm (180 MeV)
  - 4.3 mm. (Right)

**Scanned Beam Terms**

- Range: 94 different energies: 4 to 30.6 cm
- Spot Spacing: Generally based upon highest energy
- Dose per Spot: Variable
Spot Scanning: Creating a 3D dose distribution by combining spot location, weight, and energies

Two spots separated by 1 cm and two spots separated by 2 cm.

Spot Scanning 20 cm Uniform Dose File

- Energies: 26 energies
- Spots: 7943 spots
- Spot Spacing: 8 mm
- Penumbra at 10 cm depth: 10 mm
- Time to deliver 2 Gy: 1+ minutes

IAEA TRS-398

- Absorbed Dose Determination in External Beam Radiotherapy: An International Code of Practice for Dosimetry based on Standards of Absorbed Dose to Water.
- Published by the IAEA on behalf of IAEA, WHO, PAHO, and ESTRO.
- Authors are mainly from Europe but also Japan, New Zealand, and the US
- This is the recommended protocol for proton beam calibration.
IAEA 398 Chapters

- 1. Introduction
- 2. Framework
- 3. $N_{D,w}$ Based Formalism
- 4. Implementation
- 5. Code of Practice for Cobalt-60
- 6. Code of Practice for High Energy Photon Beams
- 7. Code of Practice for High Energy Electron Beams
- 9. Code of Practice for Medium Energy Kilovoltage X-Ray Beams
- 10. Code of Practice for Proton Beams
- 11. Code of Practice for Heavy-Ion Beams

IAEA 398 Appendices

- Appendix A. Relation between $N_k$ and $N_{D,w}$ based upon codes of practice
- Appendix B. Calculation of $k_{Q,Q_0}$ and its uncertainty
- Appendix C. Photon Beam Quality Specification
- Appendix D. Expression of Uncertainties

Recommended $w_p/W_Q$ Values in air from different protocols

<table>
<thead>
<tr>
<th>Protocol</th>
<th>Value</th>
<th>Date</th>
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<tr>
<td>AAPM</td>
<td>34.3 ± 4.0%</td>
<td>1986</td>
</tr>
<tr>
<td>ICRU 59</td>
<td>34.8 ± 2.0%</td>
<td>1998</td>
</tr>
<tr>
<td>IAEA 398</td>
<td>34.23 ± 0.4%</td>
<td>2000</td>
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</table>
IAEA 398: Absorbed dose to water at reference dept, $z_{\text{ref}}$

- The absorbed dose calibration of monitor at $z_{\text{ref}}$ is:

$$D_{w,Q}(z_{\text{ref}}) = M_Q N_{D,w} k_Q$$

$$M_Q = M_P k_{\text{TP}} k_{\text{elec}} k_{\text{pol}} k_{\text{recom}}$$

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**Percentage depth-dose distribution for a modulated proton beam.** Indicated on the figure are the reference depth $Z_{\text{ref}}$ (middle of the SOBP), the residual range at $Z_{\text{ref}}$ used to specify the quality of the beam, $R_{\text{res}}$, and the practical range $R_{\text{p}}$.

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Calculated values of $k_Q$ for various cylindrical and plan-parallel ionization chambers commonly used for reference dosimetry, as a function of proton beam quality $Q (R_{\text{res}})$. 

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IAEA 398 10.3.1

Beam Quality Index

- $R_{res}$ is chosen as the beam quality index.
- The residual range $R_{res}$ (in g cm$^{-2}$) at a measurement depth $z$ is defined as
  \[ R_{res} = R_p - z \]
  
  Where $z$ is the depth of measurement.

For protons, the quality $Q$ is not unique for a particular beam, but is also determined by the reference depth $z_{ref}$ chosen for measurement.

Proton Statement of Calibration at PTC H for Scattered Beams

- For a proton beam with a range of 28.5 cm (250 MeV beam medium snout), for a 10 cm x 10 cm, at the center of a 10 cm SOBP (which will be at a depth of approximately 24 cm) at a TSD of 246 cm, 1 MU will equal 1 cGy (water).
- This will put the point of calibration at approximately 270 cm, the nominal isocenter distance.
- For scanned beams, MUs are essentially a method to count protons.

The recommended protocol for the calibration of proton beams is:

1. AAPM 21
2. AAPM 51
3. IAEA Report 398
4. ICRU Report 59
5. ICRU Report 78
The ICRU Report 78 recommended dosimetry system for the calibration of proton beams is

1. Ambient air-filled Bragg peak chamber
2. Ambient air-filled cylindrical ionization chamber
3. Nitrogen filled TE chamber
4. Faraday cup
5. Calorimeter

Dose and Dose Equivalent

- Oncologists and dosimetrists only speak in terms of dose equivalent. The treatment plan is viewed in terms of dose equivalent.
- Physicists convert to physical dose by dividing dose equivalent by 1.1.
- $D_{RBE} = 1.1 \times D$  ICRU 78 2.1
- $D$ represents the proton absorbed dose in Gy.
- $D_{RBE}$ (in Gy) is the RBE weighted proton absorbed dose.
- Recommended RBE value is 1.1.
The recommended proton radiation prescription is provided in terms of:

1. Dose (Gy)
2. Dose (CGE)
3. Dose (RBE)
4. Dose (LET)
5. Dose (DRA)

The Proton Treatment Process

Similar to photons but more sensitive

- The proton "calibrated" CT scanner to establish the HU conversion to Stopping Power.
- Fixed kVp
- Curve is a compromise between large (body) and small (head) results.

Information Flow for Proton Treatments

DICOM RT ION is an evolving standard
Image Guided RT
No reticule – No Light Field Set up

- There are 3 x-ray tubes and flat panel detectors. The systems in the nozzle and the cage are used routinely.
- It is challenging to confirm the alignment of the proton beam and the x-ray beam to within 1 mm.
- The alignment of the x-ray system and the lasers are confirmed daily, together with the communication between the Patient Positioning Image and Analysis System (PIAS) and Mosaiq.

IGRT Work Flow

- Eclipse/Varian
- PIAS/Hitachi – DRR & X-ray images Alignment
- Pre and post shift
- X-ray System – Hitachi
- X-ray images
- Couch shifts
- Plan & DRR
- Mosaiq/IMPAC
- Plan: MU, range, SOBP...
- X-ray System – Hitachi
- G2 PIAS Monitor – Physician Work Room
- Zenkei/Hitachi – Couch movement
- Couch shifts
- Imaging Room
- X-ray
- X-ray Controls
- PIAS
Passive Scattering A well established method

- The pristine Bragg Peak is spread out using a rotating (400 revolutions per minute) modulation wheel (RMW) to produce the Spread Out Bragg Peak.
- There are 3 peaks (6 modulating slopes) on the RMWs and SOBPs from 2 cm to 16 cm can be obtained.
- For high energy proton beams, the RMWs are made from Al, while a plastic is used for lower energy beams.

Beam as it enters the nozzle is a spot.
Passive Scattering
A well established method
• Patient specific field shapes are made from bronze.
• An acrylic compensator is used to account for the heterogeneity of the human body.
• There are 8 different energies (100, 120, 140, 160, 180, 200, 225, and 250 MeV.)
• The range of protons in water can be controlled to within 1 millimeter from 4 cm to 32 cm using range shifting plates. (Note to Physicists: Patients are not water tanks.)

For passive scattering the Pristine beam passes through various thicknesses of the RMW to create the Spread Out Bragg Peak (SOBP).
120 MeV, Medium snout
Range: 4.4 to 6.4 cm

Note:
Limited penetration of beam

16 month old
Retinoblastoma
45 CGE (40.9 Gy)

Cranial spinal patient supine

Approximately 25 new cranial spinal patients per year. Each new field requires new apertures. Spinal fields change each week.

Patient Specific QA

5 cm/10 cm water box
Which is designed to hold a Farmer type chamber
Solid water plates to obtain the desired depths.
Note brass apertures and no compensator

The Physics Miracle transforming treatment plans into treatment delivery parameters, including MUs. Generally physics spends 1 to 2 hours after planning is finished to review and prepare for treatment. 27 field cranial spinal patients may require 8 to 10 hours.
### SOBP features
- Measured ranges agree within 1 mm with Hitachi set range
- Measured SOBP widths (Distal 90% to proximal 95% distance) are within 5 mm of the Hitachi set width. Mostly within 2 mm, large deviation for large modulation widths – Gating Off Table adjustments
- Distal portion of the SOBP is insensitive to aperture size and snout position
- Surface dose can be close to 90% for large modulation
- Very small field sizes can lead to a greater inhomogeneity

### Profile features
- Flatness and symmetry are within 3% for all scans except at depths close to the distal edge of the SOBP-mostly due to set up uncertainties
- Penumbra width is independent of energy aperture size and SOBP width, depends on depth in patient and snout position
- Penumbra measurements: 3.5 mm at 6 cm depth to 12.5 mm at 28.4 cm depth

### ICRU 78 Chapter 5
**Geometric Terms, and Dose, and Dose-Volume Definitions**
- GTV – gross tumor volume
- CTV – Clinical target volume includes GTV and suspected sub-clinical extension of the tumor
- ITV – Internal target volume is the volume that includes the CTV plus an allowance for internal component of uncertainty.
- Planning Target Volume – a geometrical concept, introduced for treatment planning. It surrounds the CTV with additional margins to compensate for different types of variations and uncertainties of beams relative to the CTV.
ICRU 78 Chapter 5
Geometric Terms, and Dose, and Dose-Volume Definitions

• Proton-specific issues regarding the PTV
  – PTV is primarily used to determine the lateral margins for photon beams.
  – For charged particle beams, some margin in depth must be left to allow for range uncertainties.
  – "It is therefore proposed that, in proton therapy, the PTV be defined relative to the CTV on the basis of lateral uncertainties alone. An adjustment must then be made with the beam-design algorithm to take into account the differences, if any, between the margins needed to account for uncertainties along the beam direction (i.e. range uncertainties) and those included in the so-defined PTV (i.e. based on lateral uncertainties)."
  PTV remains a valuable concept in protons, according to the ICRU and others.

ICRU 78, Chapter 6
Treatment Planning

• The differences between proton beam planning and photon beam planning derive from the differences in the physics of protons and photons, namely
  – That protons have a finite and controllable penetration in depth
  – That the penetration of protons is strongly affected by the nature (e.g. density) of the tissues through which they pass, while photons are much less affected... Therefore, heterogeneities are much more important in proton-beam therapy than in photon-beam therapy
  – The apparatus for proton beam therapy is different and its details affect the dose distributions.
Pristine Bragg Peak TPS Input Data for Scanning Beam MC Calculated/Measured Dose in Gy/MU versus range

Note that the lower ranges have many more peaks than the higher ranges, as the peak width diminishes with lower energy.

IMPT
SFO vs. MFO

**SFO**
- “Open Field” for “simple” volume
- Uniform dose distribution (SFO and SIB)
- Less sensitive to uncertainties
- Should use SFO plan if MFO plan is not significantly better

**MFO**
- “Patch Field” for complex volume
- More versatile to get a good plan
- More sensitive to uncertainties
- Robustness of MFO is important
- MFO presents a true 3D dosimetry challenge.

Number of Beams
Fewer than with photons. High skin dose is a concern.

- 67 yr old male
- Squamous cell carcinoma
- Right base of tongue
- CTV66, CTV60 & CTV54
- 3 fields: G280°/C15°, G380°/C345° & G180°/C0°
IMPT H&N - Example
- Simultaneous spot optimization
- Optimized with constraints only
- Spot spacing = 1 cm
- Distal & prox. margins = 0 cm
- Lateral margin = 0.8 cm

DVH – H&N IMPT

IMPT MFO
Planning and Patient QA
- Histocytosis – 26 yo female
- Three Fields: 70 Gy in 33 Fxs
- Field Range(cm) SOBP(cm) Layers Spots MU
  - RAS 11.38 6.68 24 759 24.36
  - LAS 14.97 9.88 33 595 19.68
  - A Vertex 17.16 10.72 21 290 9.29
3 Fields MFO
70 Gy in 33 Fxs

Red: 7696 cGy, Green 7346 cGy, Orange 6996 cGy, Yellow 5700 cGy

3 Fields MFO
70 Gy in 33 Fxs

Orange 6996 cGy: Prescription Isodose line

Depth Dose Curves

Depth dose curves. Red diamonds are MatriXX in plastic water. Error bars correspond to 2% and 2 mm.
Anterior Vertex Field
Note: 2 different dose peaks

- Gamma analysis for field CAVPB (Gantry = 285°). Upper left pane: measured dose plane; lower left pane: calculated dose plane; upper right pane: isodose line-comparison; lower right pane: gamma index map, 99.7% passes for 2% and 2 mm criteria.

Motion Management
ICRU 78, Chapter 7
- Support and Immobilization ("... bulky immobilization devices can be problematic.")
- Localization (Skin marks, bony anatomy, relative to immobilization device, and identification of target-volume markers or tumor itself.)
- Verification (Radiography and PET)
- Organ Motion (4D CT, Respiration Gating, Tumor Tracking)
- Compensation for Patient and Organ Motion
  - This is an ongoing challenge in proton therapy.

Uncertainty in Dose Delivered
ICRU 78 Recommendations
- Those involved in designing radiation treatments should analyze the uncertainties, make an effort to minimize them to the extent practicable; ensure that a quality assurance program is in place to give assurance that the treatment can be given as prescribed; and document their assessment of the remaining uncertainties.
- For normal reporting purposes, in uncomplicated cases, the uncertainties in the full 3D dose distribution need not be presented, but those in summarizing quantities should be estimated, together with their corresponding confidence intervals. “Doses are judged to be accurate to X percent of the prescription dose, or to be within y mm of the true location (at the z percent CL).”
Uncertainty in Dose Delivered
ICRU 78 Recommendations

• For cases where unacceptably large uncertainties might exist, and for illustrative purposes in scientific reports: the uncertainties in the dose distribution(s), as well as those in summarizing quantities should be estimated and presented, together with a statement of corresponding confidence intervals.

• Actual Practice: Medical Director request to Clinical Physicists: Tell me when you are more uncertain than usual.

Summary of Typical Penetration Uncertainties

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<thead>
<tr>
<th>Parameter</th>
<th>Uncertainty</th>
</tr>
</thead>
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<tr>
<td>Standard energy (or range)</td>
<td>±0.6 mm</td>
</tr>
<tr>
<td>Energy (or range) reproducibility</td>
<td>±1.0 mm</td>
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<tr>
<td>Bolus WET</td>
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<tr>
<td>Alignment devices*</td>
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<td>CT# accuracy (after scaling)</td>
<td>±2.5%</td>
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<tr>
<td>RLSF of tissues and devices</td>
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<td>Energy dependence of RLSF</td>
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<td>CT# to RLSF (soft tissues only)</td>
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<td>Bolus position relative to patient</td>
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<tr>
<td>Heterogeneity straggling</td>
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Planning

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<tr>
<td>Planning</td>
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Moyers PTCOG 2008

Protons

Full Employment Act for Physicists

• Theoretical physicists – Many new calculation opportunities – finally a application for Monte Carlo
• Experimental physicists – A large number of measurements to make – 3D systems, feathered field edges, neutrons, etc.
• Discrete spot scanning: 94 energies, 360 gantry angles, an infinite number of different scanning patterns

"The principle difference between men and boys is the price of their toys."
It is difficult to imagine more satisfying toys than those offered by supporting proton therapy systems.
140 MeV Protons and 50 MeV Electrons (U of Michigan)

Protons: Flat peak, sharp drop off. Range controlled to within 1 mm in water. What clinical sites benefit from these characteristics?

Electron vs. Proton: 50 Gy