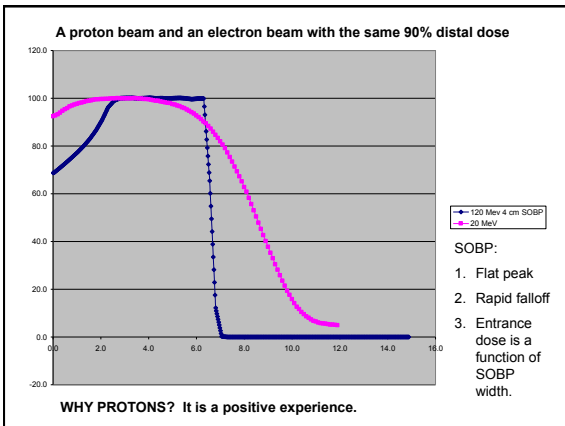


Protons: Clinical Physics Implementation

Michael T. Gillin, Ph.D.
 Professor, Deputy Chair,
 Chief of Clinical Services
 Department of Radiation Physics

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



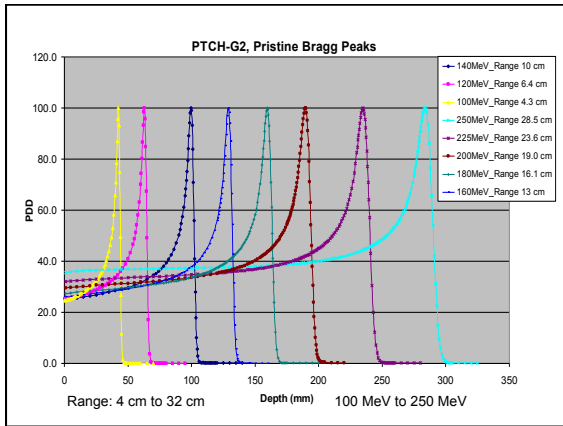
Protons have a limited range, which should limit toxicity

3 fields,
Lateral
and 2
Posterior
obliques

Standard fractionation

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

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.

A – classic atomic radius
b – classic impact parameter

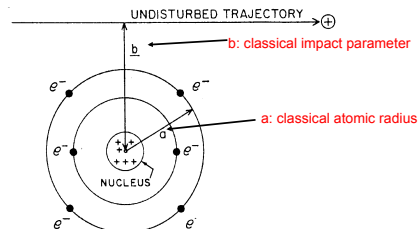


FIGURE 8.1. Important parameters in charged-particle collisions with atoms: a is the classical atomic radius; b is the classical impact parameter.

Types of Charged Particles Coulomb-Force Field Interactions

A. Soft Collisions ($b \gg a$)

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.

Types of Charged Particles Coulomb-Force Field Interactions

A. Soft Collisions ($b \ll a$)

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, δ_0 .

Penumbra for deep tumors cannot be ignored.

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.

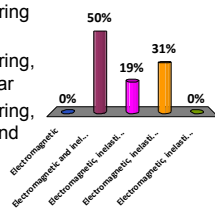
In solid organic materials for protons > 500 MeV, this
process dominates the energy loss.

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
5. Electromagnetic, inelastic scattering, Rutherford scattering, nuclear, and fusion



Mass Electronic Stopping Power, S/ρ

$$S/\rho = 1/\rho (dE/dx) \text{ MeV M}^2/\text{kg}$$

S/ρ depends on the composition of the material and on the nature and energy of the charged particle.

Gottschalk: **The Fundamental Equation**

$$D = \Phi S/\rho$$

Dose equals fluence times mass stopping power

Proton Mass Electronic Stopping Power (MeV cm⁻² g⁻¹) ICRU 59

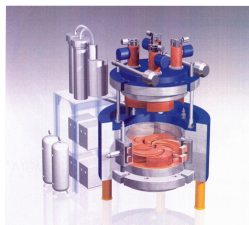
E(MeV)	Water	Air	Bone	Polystyrene
250	3.911	3.462	3.646	3.827
200	4.492	3.976	4.186	4.397
150	5.445	4.816	5.070	5.331
100	7.289	6.443	6.778	7.140
75	9.063	8.006	8.420	8.882
50	12.45	10.99	11.55	12.21
25	21.75	19.15	20.10	21.36
20	26.02	22.94	24.06	25.62
10	45.67	40.06	41.96	45.00
5	79.11	69.09	72.28	78.20
1	260.8	222.9	233.9	257.7
0.1	816.1	730.1	791.2	916.4

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

- 8% 1. Vary by a factor of 10 to 100 with the higher energy protons having the greater ratios
- 19% 2. Vary by a factor of > 100 with the higher energy protons having the greater ratios
- 19% 3. Vary by a factor of 10 to 100 with the higher energy protons having the lower ratios
- 38% 4. Vary by a factor of > 100 with the higher energy protons having the lower ratios
- 15% 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

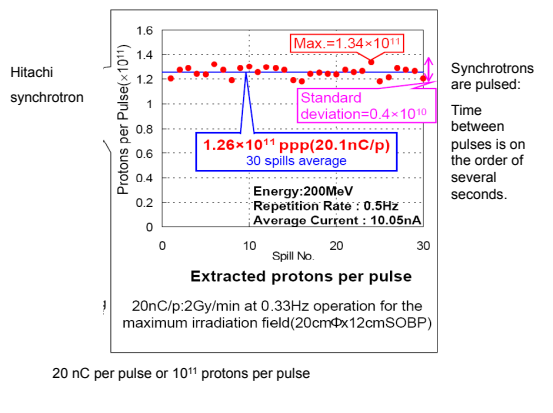


Isochronous cyclotron is a cyclotron that maintains a constant RF driving frequency, and compensates for the relativistic mass gain of the accelerated particles by alternating field gradient in space but constant in time.

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





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



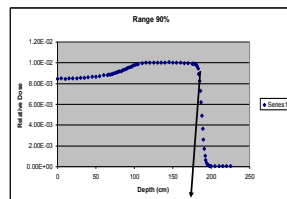
Gantry: 190 tons – Isocenter is held in part by adjusting the couch as a function of gantry angle.

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.



Range: 90%
distal depth.

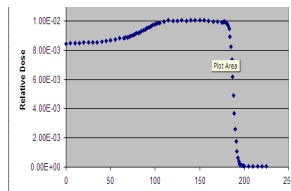
Ranges (cm) (d 90%)

Protons loose energy when scattered for large fields.

Energy (MeV)	Small Snout 10 cm ²	Medium Snout 18 cm ²	Large Snout 25 cm ²
250	32.4	28.5	25.0
225	26.9	23.6	20.6
200	21.8	19.0	16.5
180	16.9	16.1	13.7
160	13.4	13.0	11.0
140	10.2	10.0	8.4
120	6.9	6.4	6.3
100	4.9	4.3	4.3

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.



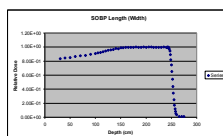
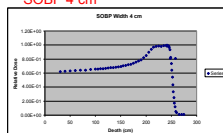
Distal-dose fall off will be smaller than lateral penumbra.

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.

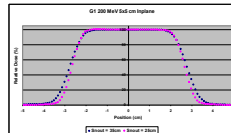
SOBP 4 cm



SOBP 14 cm

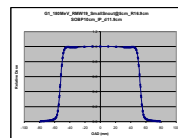
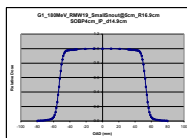
Lateral Penumbra (LP)

- 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.



Blue: Snout 35 cm Pink: Snout 25 cm

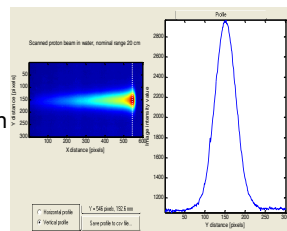
Profiles Scattered Beam



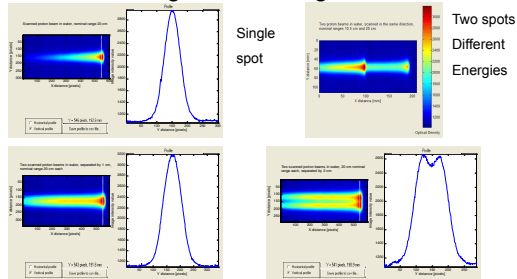
- Lateral profile at depth of **14.9 cm** for small snout for beam with range of 16.9 cm (180 MeV) 6.3 mm. (Left)
- Lateral profile at depth of **11.9 cm** for small snout for beam with range of 16.9 cm (180 MeV) 4.3 mm. (Right)

Scanned Beam Terms

- Range: 94 different energies: 4 to 30.6 cm
- Spot Spacing:
Generally based upon highest energy
- Dose per Spot:
Variable



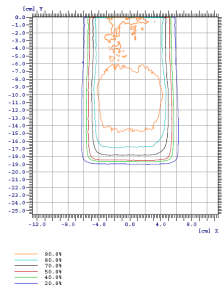
Spot Scanning: Creating a 3D dose distribution by combining spot location, weight, and energies



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
- 8. Code of Practice for Low Energy Kilovoltage X-Ray 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

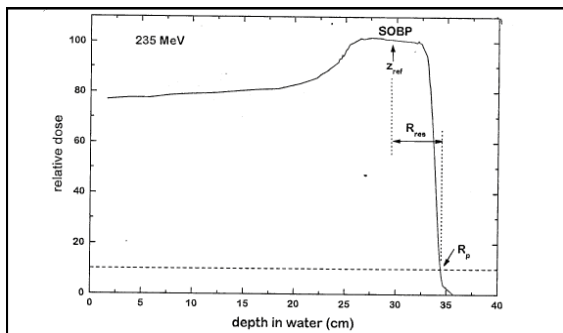
Protocol	Value	Date
• AAPM	$34.3 \pm 4.0\%$	1986
• ICRU 59	$34.8 \pm 2.0\%$	1998
• IAEA 398	$34.23 \pm 0.4\%$	2000

IAEA 398: Absorbed dose to water at reference dept, z_{ref}

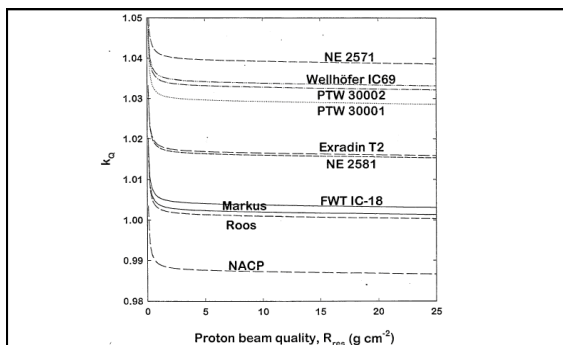
- The absorbed dose calibration of monitor at z_{ref} is:

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

$$M_Q = M_1 k_{TP} k_{elec} k_{pol} k_{recom}$$



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



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_{res}).

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

$$R_{\text{res}} = R_p - z$$

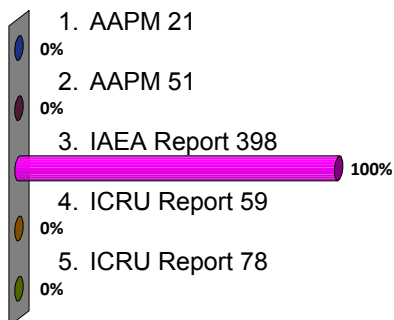
Where z is the depth of measurement.

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

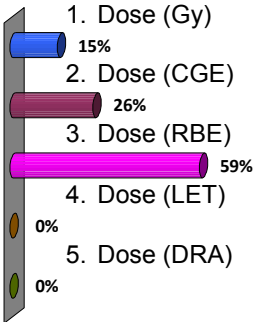
Proton Statement of Calibration at PTC H for Scattered Beams

- 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:



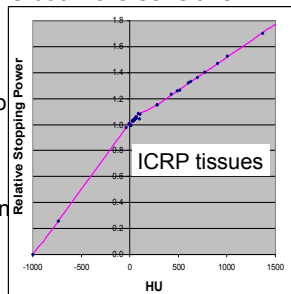
The recommended proton radiation prescription is provided in terms of:



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

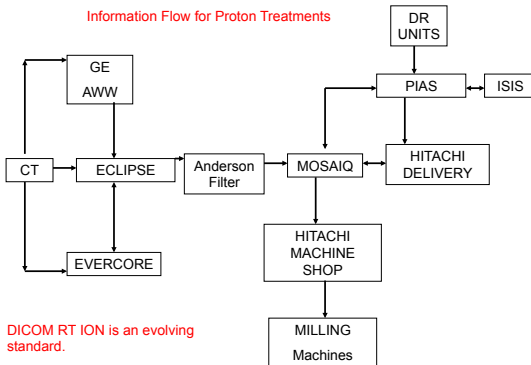
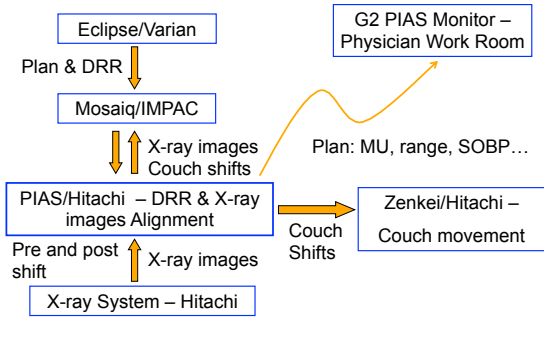


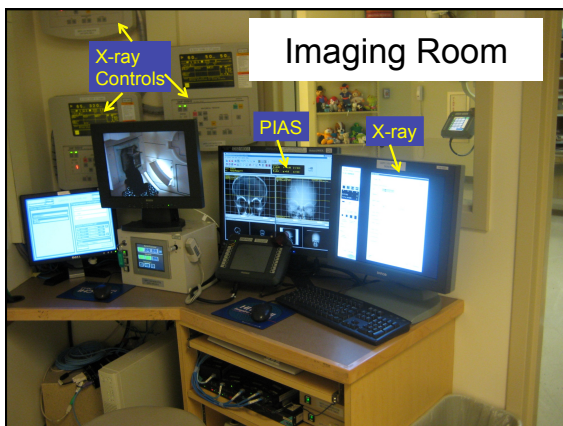
Image Guided RT No reticule – No Light Field Set up

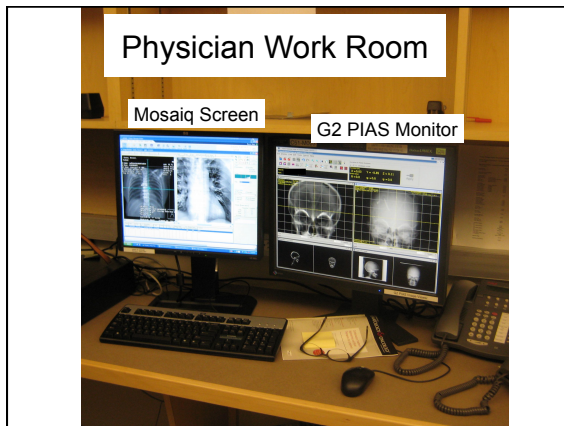
- There are 3 x-ray tubes and flat panel detectors. The systems in the nozzle and the cage are used routinely.
- It is challenging to confirm the alignment of the proton beam and the x-ray beam to within 1 mm.
- The alignment of the x-ray system and the lasers are confirmed daily, together with the communication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

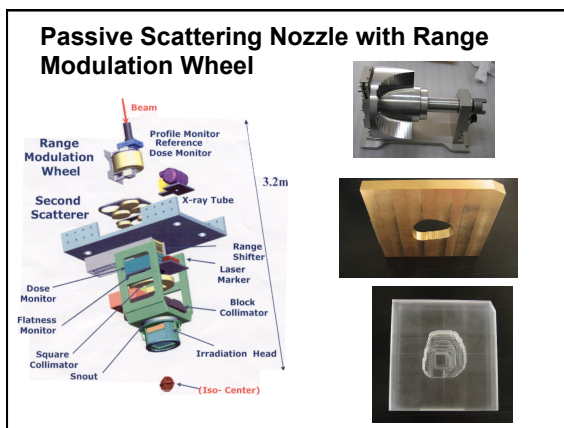


IGRT Work Flow









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.

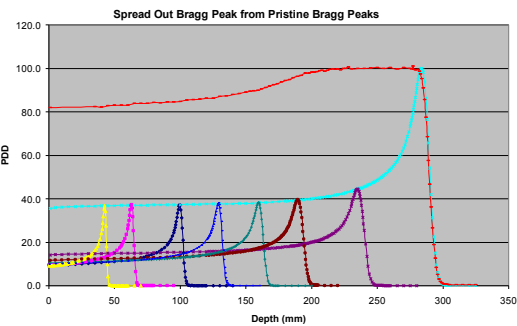
Scanned proton beam in air at exit beam line, E = 221.8 MeV

Beam as it enters the nozzle is a spot.

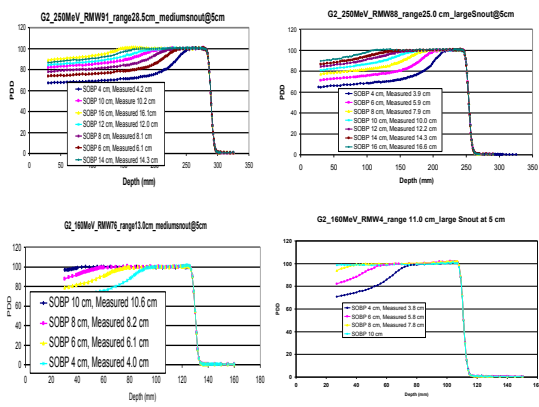
Passive Scattering

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.)

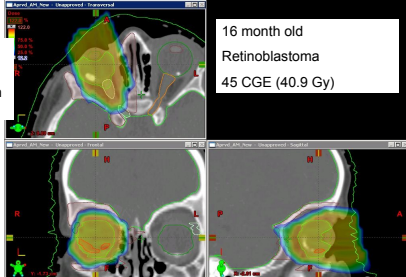


For passive scattering the Pristine beam passes through various thicknesses of the RMW to create the Spread Out Bragg Peak (SOBP).

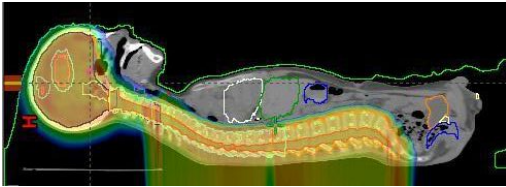


120 MeV, Medium snout
Range: 4.4 to 6.4 cm

Note:
Limited
Penetration
of beam



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).”

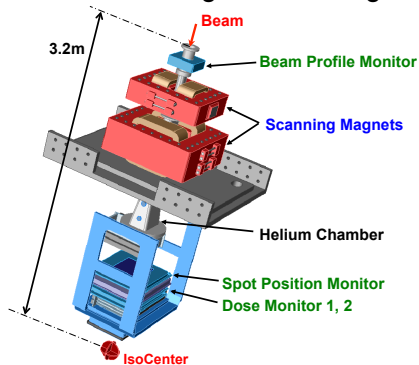
PTV remains a valuable concept in protons, according to the ICRU and others.

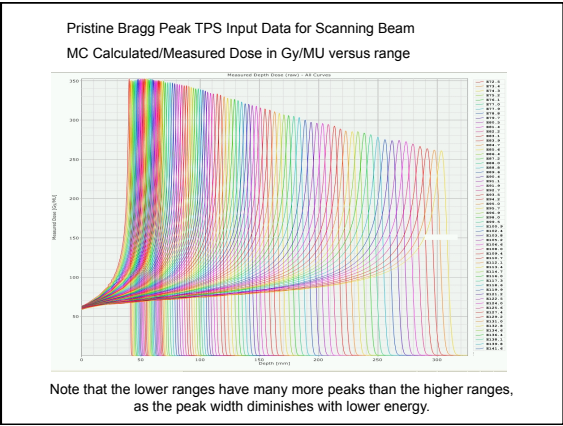
ICRU 78, Chapter 6

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.

Schematic Drawing of Scanning Nozzle





IMPT

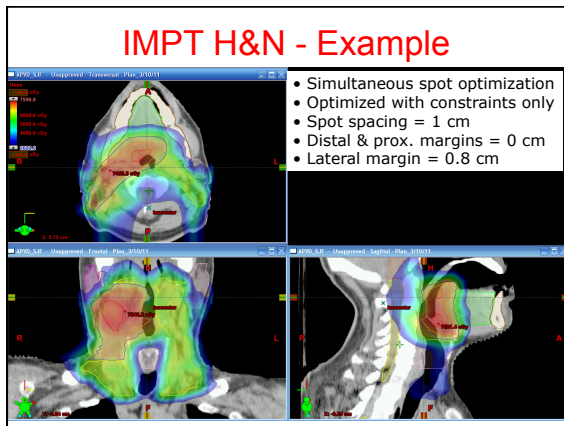
SFO vs. MFO

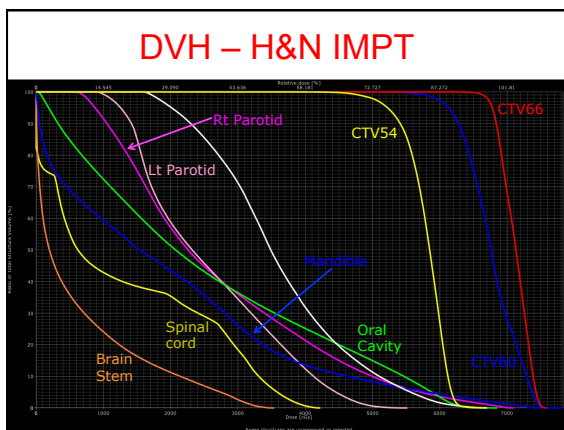
SFO	MFO
• “Open Field” for “simple” volume • Uniform dose distribution (SFO and SIB) • Less sensitive to uncertainties • Should use SFO plan if MFO plan is not significantly better	• “Patch Field” for complex volume • More versatile to get a good plan • More sensitive to uncertainties • Robustness of 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°, G80°/C345° & G180°/C0°



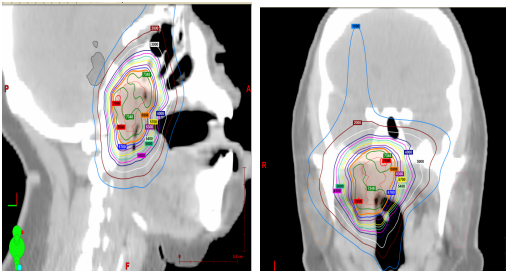


IMPT MFO Planning and Patient QA

- Histocytosis – 26 yo female
- Three Fields: 70 Gy in 33 Fxs

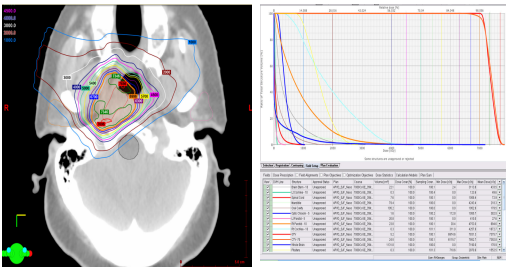
	Field	Range(cm)	SOBP(cm)	Layers	Spots	MU
• RAS	11.38	6.68	24	759	24.36	
• LAS	14.97	9.88	33	595	19.68	
• A Vertex	17.16	10.72	21	290	9.29	

3 Fields MFO 70 Gy in 33 Fxs



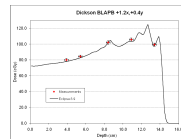
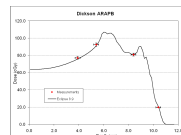
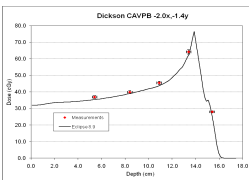
Red: 7696 cGy, Green 7346 cGy, Orange 6996 cGy, Yellow 5700 cGy

3 Fields MFO 70 Gy in 33 Fxs



Orange 6996 cGy: Prescription Isodose line

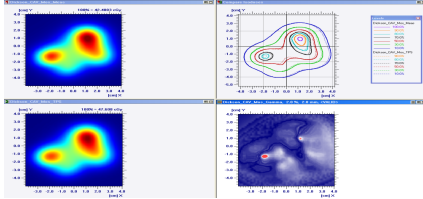
Depth Dose Curves



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

standard energy (or range) ± 0.6 mm
energy (or range) reproducibility ± 1.0 mm
bolus WET ± 0.9 mm
alignment devices* ± 1.0 mm

CT# accuracy (after scaling) $\pm 2.5\%$
RLSP of tissues and devices $\pm 1.6\%$
energy dependence of RLSP $\pm 1.0\%$
CT# to RLSP (soft tissues only) $\pm 1.5\%$

bolus position relative to patient variable
heterogeneity straggling variable
patient motion variable

Range Uncert.
2 mm

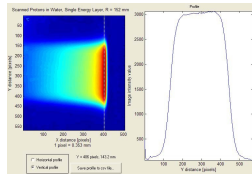
CT Uncert.
3.5%

Planning
bolus expansion
multiple angles

Moyers PTCOG 2008

Protons Full Employment Act for Physicists

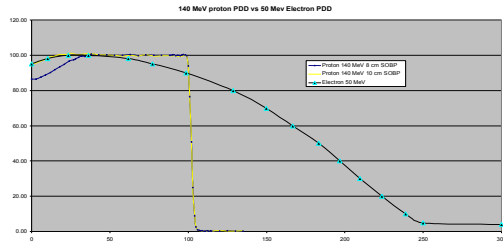
- Theoretical physicists – Many new calculation opportunities – finally a application for Monte Carlo
- Experimental physicists – A large number of measurements to make – 3D systems, feathered field edges, neutrons, etc.
- Discrete spot scanning: 94 energies, 360 gantry angles, an infinite number of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

