PROTON THERAPY

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Topics Covered

• History of Proton Therapy
• Worldwide Facilities
• Rationale for Proton Therapy
• Physics of Proton Beams
• Treatment Delivery Techniques
• Proton Treatment Technology
• Clinical Commissioning
• Treatment Planning
History and Current Status of Proton Therapy
Abbreviated History of Protons

- 1919: Rutherford proposed existence of protons
- 1930: E. O. Lawrence built first cyclotron
- 1946: Robert Wilson proposed proton therapy
- 1955: Tobias et al treated patients at LBL
- 1961: Kjellberg et al treated patients at HCL
- 1972: MGH received first NCI grant for proton studies at HCL
- 1991: First hospital-based proton facility at LLUMC
- 2006: 28 facilities worldwide treating patients; over 55,000 patients treated with protons.
25 facilities worldwide are treating patients.

- 6 in Japan (4 hospital-based)
  - Chiba, NCC East-Kashiwa, HIBMC-Hyogo, PMRC-Tsukuba, WERC-Wakasa, Shizuoka Cancer Center
- 6 in the United States (4 hospital-based)
  - LLUMC, MGH, MDACC, Univ. of Florida, Univ. of Indiana, UC Davis
- 9 in Europe/Russia
- 4 Additional facilities (UK, China, Korea, South Africa)
- 15 additional institutions worldwide are either building a new facility or are seriously planning to have a particle therapy facility.
Particle Therapy Facilities Worldwide

Treating: Protons 25, Carbon ions 3

In operation  In preparation  Considering

Courtesy of Takashi Ogino, MD, PhD, NCC Kashiwa, Japan
Rationale for Proton Therapy
### Need for Improved Local Control in Cancer Treatment (selected sites)
(all numbers are estimates)

<table>
<thead>
<tr>
<th>Tumor Site</th>
<th>Deaths/ year</th>
<th>Deaths due to Local Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head/Neck</td>
<td>22,000</td>
<td>13,200 (60%)</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>135,000</td>
<td>54,000 (40%)</td>
</tr>
<tr>
<td>Gynecologic</td>
<td>28,000</td>
<td>14,000 (50%)</td>
</tr>
<tr>
<td>Genitourinary</td>
<td>55,000</td>
<td>27,500 (50%)</td>
</tr>
<tr>
<td>Lung</td>
<td>160,000</td>
<td>40,000 (25%)</td>
</tr>
<tr>
<td>Breast</td>
<td>41,000</td>
<td>4,920 (12%)</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>20,000</td>
<td>2,400 (12%)</td>
</tr>
<tr>
<td>Skin, Bone, Soft Tissue</td>
<td>15,000</td>
<td>5,000 (33%)</td>
</tr>
<tr>
<td>Brain</td>
<td>12,000</td>
<td>10,800 (90%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>488,000</strong></td>
<td><strong>171,820 (35%)</strong></td>
</tr>
</tbody>
</table>

Over 1,350,000 new cancer patients per year in the US
Fundamental Things to Remember about Protons

- Protons Stop!
- Photons don’t stop.
- Proton dose at depth (target) is greater than dose at surface.
- Photon dose at depth (target) is less than dose at $d_{max}$.
Rhabdomyosarcoma of Paranasal Sinus (7 y old boy)

- 6 MV Photons (3 field)
- 160 MeV Protons (2 field)
- Photon IMXT (9 field)
- Proton IMRT (9 field)
Proton Physics

- The physics of proton beams
- Passive scattering systems
- Pencil beam scanning systems
Electromagnetic energy loss of protons

Mass Electronic Stopping Power is the mean energy lost by protons in electronic collisions in traversing the distance $dx$ in a material of density $\rho$.

$$\frac{S}{\rho} = \frac{1}{\rho} [\frac{dE}{dx}] \propto \frac{1}{v^2}$$

Where $v =$ proton velocity
Normalized (at peak) Bragg Curves for Various Proton Incident Energies

Range Straggling will cause the Bragg peak to widen with depth of penetration

Normalized (at entrance) Bragg Curves for Various Proton Incident Energies
Dose depositions in water from 160 MeV protons. Beam slit delimiters with width $W$ cm. Uniform particle distributions.

Loss of in-scattering (charged particle equilibrium) results in deterioration of Bragg peak and non uniformity of SOBP.

George Ciangaru

Narayan Sahoo
Multiple Coulomb Scattering

- Protons are deflected frequently in the electric field of the nuclei
- Beam broadening can be approximated by a Gaussian distribution

**Lateral dose fall-off: Protons vs. Photons**

\[
\text{80/20 Penumbra Comparison}
\]

- Protons
- 15 MV Photons

\[\approx 17 \text{ cm}\]
Nuclear interactions of protons

- A certain fraction of protons undergo nuclear interactions, mainly on $^{16}\text{O}$
- Nuclear interactions lead to secondary particles and thus to local and non-local dose deposition (neutrons!)
- In passive scattering systems neutrons are produced in the first and second scatterers, modulation wheel, aperture, range compensator in addition to those produced in the patient.
Effect on the lateral dose distribution

Pedroni et al. PMB, 50, 541-561, 2005

Depth in Water [cm]

Relative Dose [%]

230 MeV protons

Total Absorbed Dose

'Primary' Dose

'Secondary' Dose

Depth in Water [cm]
Physics of the Passive Scattering Mode of Proton Beam Delivery

Passive Scattering Nozzle with Range Modulation Wheel
How a Spread Out Bragg Peak (SOBP) is formed.

- Modulation wheel rotates in the beam.
- Pull-back (energy shift) determined by height of step.
- Weight determined by width of step.
- Multiple SOBPs can be obtained by gating beam.
Deficiencies of Proton Passive Scattering Techniques

- Uniform SOBP - excess normal tissue dose.
- Requires custom aperture and compensator
- Inefficient - high proton loss produces activation and neutron production.

The Pencil Beam Scanning Mode of Proton Beam Delivery

ACTIVE SCANNING

Dynamic changes of the proton energy

Dynamically varying sweeping magnets (in and out of plane)

No compensator, and generally no collimator needed

Evolution of the lateral beam profile

No wasted protons
Pencil Beam Scanning Nozzle

Performance

Range \(4 \text{ – } 36 \text{ g/cm}^2\)

Adjustability \(0.1 \text{ g/cm}^2\)

Max. field size \(30 \times 30 \text{ cm}\)

Beam size in air \(6 \text{ – } 10 \text{mm }\sigma\)

SAD \(> 2.5 \text{ m}\)

Dose compliance \(+/- 3\% \text{ (2 }\sigma)\)

Irradiation time \(< 2 \text{ min to deliver }2 \text{ Gy to }1 \text{ liter}\)
Proton Accelerators
Isocentric Gantries
Typical Facility
Typical Accelerators used in proton therapy facilities

Hitachi 250 MeV synchrotron ring
7 MeV Linac injector

IBA 230 MeV Cyclotron

ACCEL Superconducting Cyclotron

250 MeV
Proton and Carbon Ion Gantries

M. D. Anderson Gantry
Hitachi
190 tons

NPTC GANTRY
120 tons

Siemens
Heidelberg
600 tons
Proton Therapy Center - Houston

PTC-H
3 Rotating Gantries
1 Fixed Port
1 Eye Port
1 Experimental Port

Pencil Beam Scanning Port
Passive Scattering Port
Accelerator System (slow cycle synchrotron)
Experimental Port
Large Fixed Port
Eye Port
Clinical Commissioning

- Tests for system functionality and safety
- Treatment Planning System commissioning
  - Collection of data for input to planning system
  - Validation of planning system output
- Beam calibration
  - Calibration of transmission ionization chambers
  - Measurement of dependence of dose on range modulation, field size, etc.
- Patient treatment and machine QA
PTCOG 46 Educational Workshop

Pristine Bragg Peaks

**160 MeV**

- **PTCH-G2, Pristine Bragg Peaks**
- **G2_250MeV_RMW88_range25.0 cm_largeSnout@5cm**

**120 MeV**

- **160 MeV**
  - PDD
  - SOBP 10 cm: Measured 10.6 cm
  - SOBP 8 cm: Measured 8.2 cm
  - SOBP 6 cm: Measured 6.1 cm
  - SOBP 4 cm: Measured 4.0 cm

**250 MeV**

- **G2_250MeV_RMW88_range25.0 cm_largeSnout@5cm**
- **SOBP 4 cm, Measured 3.9 cm**
- **SOBP 6 cm, Measured 5.9 cm**
- **SOBP 8 cm, Measured 7.9 cm**
- **SOBP 10 cm, Measured 10.0 cm**
- **SOBP 12 cm, Measured 12.2 cm**
- **SOBP 14 cm, Measured 14.3 cm**
- **SOBP 16 cm, Measured 16.6 cm**

**Depth in Water [mmH2O]**

**Pristine Bragg Peaks**

**250 MeV**

- **SOBP 8 cm, Measured 2.9 cm T0522L+M+P**
- **SOBP 10 cm, Measured 3.8 cm T0521R**
- **SOBP 12 cm, Measured 4.0 cm T0521T**
- **SOBP 14 cm, Measured 1.9 cm T0521U**

**Depth in Water [mmH2O]**
The CT scanner used to acquire treatment planning images should be calibrated.

**Relative Stopping Power & Calibration Curve**

**Comparison of measurements with treatment planning calculations**

250 MeV, depth = 23.3 cm, Cross Plane Scan

**Comparison of Measurements and Treatment Planning Calculations**

Bone-Water Interface Profile, 250 MeV, Depth = 17.9 cm

**Bone-Water Interface Profiles**

250 MeV, Range 28.5 cm, SOBP Width 16 cm

**ICRP tissues**

The CT scanner used to acquire treatment planning images should be calibrated.
Prostate Patient Treatment Plan

Measurements in water phantom using EBT film, patient aperture, and range compensator

QA of Prostate Treatment using patient treatment parameters/appliances and EBT film in water phantom.

Treatment plan on CT anatomy converted to dose distribution in water phantom.

Patient Treatment QA – Measurements compared with treatment planning calculations converted to water phantom.

Data measured in water phantom using Pin-Point ion chamber. Treatment aperture and range compensator were both inserted.
Treatment Planning

- Acquisition of imaging data (CT, MRI)
- Conversion of CT values into stopping power (not electron density)
- Delineation of regions of interest
- Selection of proton beam directions
- Optimization of the plan
Treatment Planning

• Passive scattered proton beams
• Scanned Proton Beams
• Intensity modulated proton beams
• Comparative Treatment Plans
Dose shaping: Range compensator

Double scattering system

Beam

Aperture

High-Density Structure

Target Volume

Critical Structure

Body Surface

© Hanne Kooy, MGH
SOBP Modulation

© Hanne Kooy, MGH
Aperture and Range Compensator

To be ‘designed’ by the planning system!

© Hanne Kooy, MGH
Compensator smearing to account for uncertainties

© Hanne Kooy, MGH
Dosimetry and QA for SOBP proton fields

Beam range: 17.19 cm
Modulation width: 6.78 cm

Beam range: 13.47 cm
Modulation width: 8.65 cm

Beam range: 12.0 cm
Modulation width: 4.0 cm
Field dependent (!) absolute dosimetry

Volume for absolute dosimetry

\[ \text{Output} - \text{Factor} \approx \frac{D_{\text{cal}}}{i_c} \left[ \frac{cGy}{MU} \right] \]
EXAMPLE 1: Para-spinal case using 3 fields
EXAMPLE 2: Para-spinal case using 6 fields (involves metal CT artifacts)
Field Patching

- Abutting the distal dose edge of one field to the dose boundary of other field(s).
- Useful if target is close to critical structures
- Not necessarily homogeneous dose to the target for each beam (IM!)
- Range an penumbra uncertainties need to be considered

"THROUGH" Field A followed by "PATCH" field B, followed by "PATCH" field C

Match at 50% isodose, lateral + distal, levels
EXAMPLE 3: Nasopharynx case using 14 fields (plus additional photon fields to the lower neck)
• GTV 76 Gy
  – CTV1 60-66 Gy
  – CTV2 60 Gy
• Nodes 54 Gy
Treating moving targets with protons
Effect of respiration on dose

Range fluctuations due to respiration in the lung

© Shinishiro Mori, MGH
Effect of respiration on dose

Range Fluctuation on Cardiac MRI

© Shinishiro Mori, MGH
Burr Proton Therapy Center (2001-)

Patient Population

- Brain 32%
- Spine 23%
- Prostate 12%
- Skull Base 12%
- Head & Neck 7%
- Trunk/Extremity Sarcomas 6%
- Gastrointestinal 6%
- Lung 1%

In general, 1-3 fields / day

© Thomas DeLaney, MGH
Treatment Planning

- Passive scattered proton beams
- Scanned Proton Beams
- Intensity modulated proton beams
- Comparative Treatment Plans
Typical Spot Beam in Water

Depth Dose

Beam Profile

© G. Ciangaru, MDACC
Beam Scanning

No compensator, no aperture, no scattering system required
A major problem with spot scanning: The target can move!

Remedies:

• Rescanning
• Beam Gating
• Real time tumor tracking with markers

© Alfred Smith, MDACC
1. Evenly spaced/weighted spots to achieve uniform field
2. 1mm spot error due to delivery error or patient motion.
3. Optimum spacing/weighting to achieve sharper penumbra
Dosimetry and QA of pencil beams

- Energy/Range
  - large number of energies required.
  - energy spacing must provide dose uniformity over all depths
- Spot size and shape
  - spot size/shape dependence on energy
  - spot orientation as a function of gantry angle
- Spot position accuracy
- Validation of treatment planning calculations
- Validation of treatment delivery
- Measurements require methods for rapid collection large amounts of data
- Real-time beam information
Orthogonal IC array measurements performed at different water depths using a computer controlled water column and compared with calculations.

'Beam's-eye-view' of dose in water

U axis profile

T axis profile

© Eros Pedroni, PSI
Scintillating Plate, Mirror and CCD Camera used for pencil beam scanning QA.

MD Anderson Cancer Center

Scintillating screen viewed with a CCD through a 45° mirror – ideal for non homogeneous dose distributions

Measurement vs. Calculation

WER 6.65 CM
W= 6.65 cm

WER 7.82 CM
W= 7.82 cm

© Eros Pedroni, PSI, Switzerland

© Martin Bues, MDACC
Treatment Planning

- Passive scattered proton beams
- Scanned Proton Beams
- Intensity modulated proton beams
- Comparative Treatment Plans
IMPT Treatment Planning

- Bragg peaks of pencil beams are distributed throughout the planning volume
- Pencil beam weights are optimized for several beam directions simultaneously (inverse planning)
IMPT Delivery

Spot scanning at PSI (Switzerland)
IMPT Delivery

- Built-in magnets for IMPT
- Two (red) “dipole” magnets to deflect the beam in X and Y respectively
- Two (yellow) “quadrupole” magnets to focus the beam in X and Y respectively

© Hanne Kooy, MGH
IMPT in clinical practice

+ great flexibility and variability
+ no need for apertures/compensators
+ easy delivery of large fields
+ beamlet optimization routines

- requires very high degree of precision
Treatment Planning

- Passive scattered proton beams
- Scanned Proton Beams
- Intensity modulated proton beams
- Comparative Treatment Plans
Example
(IM protons vs. IM photons)
Example
(protons vs. IM photons)

Nasopharynx
(case shown earlier)
A Composite plan
(14 proton fields, 4 photon fields)

- **proton fields**
  - CTV to 59.4 GyE (33 x 1.8 Gy)
  - GTV to 70.2 GyE (+ 6 x 1.8 Gy)

- **Photon fields**
  - lower neck, nodes to 60 Gy
B IMXT plan
(7 coplanar photon beams)
C IMPT plan
(4 coplanar photon beams)
DVH for target structures

Comparable target coverage

© Alex Trofimov, MGH
• Critical normal structures (always outlined):
  – brain stem, spinal cord, optic structures
  – parotid glands, cochlea

• ‘Extra’ structures were outlined on 3 data sets
  – esophagus, base of tongue, larynx
  – minor salivary, sublingual and submand. glands
  – mastication and suprahyoid muscles
DVH for some critical structures

© Alex Trofimov, MGH
DVH for some critical structures

© Alex Trofimov, MGH
Example
(standard protons vs. photons)

Medulloblastoma
Medulloblastoma

- Irradiation of the whole cranium and spinal axis
  - Low Risk – 23.4 CGE
  - High Risk – 36.0 CGE
  - Spine
    - Include Vertebral Body
  - Cranium
    - Constrain Auditory System < 40 CGE
    - Pituitary / Hypothalamus ~ 45 CGE
- Posterior Cranial Fossa Boost
  - Total 54 CGE
Example
(protons vs. IM photons)

Prostate
Prostate carcinoma:
(GTV + 5mm) to 79.2 Gy
(CTV + 5mm) to 50.4 Gy
Summary

• Proton planning offers more options in terms of beam directions and field shaping than photon planning
• For specific sites IMRT and protons can be comparable in terms of dose conformality
• Protons are able to reduce the dose to most critical structures compared to photons
• Proton therapy is able to reduce the integral dose compared to photons by up to a factor of 3
• IMPT is the method of choice
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