Proton Treatment Planning:

*From Physics to Clinical Reality*

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Proton Treatment Planning

OUTLINE

• Proton beam delivery techniques

• Treatment Planning Commissioning

• Differences between photons an protons treatment planning

• Managing uncertainties in proton therapy.
Principles of Proton Therapy

ICRU 78
Principles of Proton Therapy
ICRU 78
Principles of Proton Therapy

- Ranges of 4 - 38 cm (70-250 MeV) are required to irradiate all possible target volumes in adult patient
Delivery Methods

- Accelerated protons are near monoenergetic and form a beam of small lateral dimension and angular divergence.

- There are two approaches to form a desired dose distribution:
  
a. Passive Scattering and modulation (referring to the method of spreading the beam laterally and with method of spreading the beam in depth)
Delivery Methods

b. Dynamic Scanning of a pencil beam laterally and in depth involves scanning of a PB both laterally and in depth (by changing its energy) => in a near arbitrary dose distribution laterally and dose sharpening in depth (Pedroni et al.)
- lateral distribution determined by the lateral positions and weights of each pencil beam of a chosen energy
- distribution in depth is determined by weighting the pencil beam at each position within the field.

Note: Beam Scanning is the only practical technique which enables IMPT to be performed.
Proton Treatment Planning
Beam Parameters/ TX length/width

(Gall et al. 1993)
Proton Treatment Planning Commissioning

- The machine specific data are acquired, imported, modeled and validated in the TPS by the Physicist.

- The commissioning plan of the TPS is develop by the Physicist based on the clinical requirements.
Proton Treatment Planning Commissioning

• The number of measurements performed for passive scattering commissioning is higher than the PBS due to the number of options and suboptions available.
• The options are given by the combination of a range modulator and second scatter used in a given span/energy.
• The suboption is a subspan of the option using its own beam current modulation.
Proton Treatment Planning Commissioning

• Most commercial TPSs are based on a Pencil Beam Algorithm.
• The data to be acquired for passive scattering are:
  - Pristine peak, PDD/SOBP
  - Open field profiles => Virtual SAD
  - Fluence Along Beam Axis => Effective SAD
  - Half Beam Profiles=> Effective source Size
Proton Treatment Planning Commissioning

- Dose calculation has to be validated against measurements:
  - In water phantom
  - Inhomogeneities
  - Oblique beams
  - Different geometries
  - Etc..
Proton Treatment Planning Commissioning

• Figures for: sigma, PDD and measured vs calculated lateral profiles, compensator test
• Is any golden beam data available for DS?
• Golden Beam Data
• PBS Data Measurements requirement reduced to the measurement of energy spread and initial phase space as a function of energy.
Proton Treatment Planning Beam Parameters

- Protons have a sharp lateral beam penumbra which decreases with increasing beam energy and, hence, depth of penetration.
- Proton beam penumbra is widest in the Bragg peak region where the proton energy is least.
- Penumbra is narrower for proton than photon beam for penetrations up to 17-18 cm
Planning of Proton Therapy

• Illustration of the volume and margins relating to the definition of the target volume per ICRU 62:
Planning of Proton Therapy

- Volumes and margins related to the OARs:
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Proton –specific issues related to the PTV

• For photon beam the PTV is primarily used to delineate the lateral margin
• For protons in addition to lateral margins a margin in depth has to be left to allow for uncertainties in the knowledge where the distal 90% IDL would fall
• Proton Beam Energy should be selected in a way that the CTV is within the irradiated volume taking into account both motion and range uncertainties
• Since the lateral and the margins in depth solve different problems each beam orientation would need a different PTV
• Alternatively the beam parameters are determined based on the CTV adding the lateral and range margins to the TPS alg.
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• In practice the beam parameters are determined based on the CTV adding the lateral and range margins to the TPS alg for each beam.
• For Scatter beam treatments, the lateral margins would be designed into the aperture in the BEV and depth n the compensator
• For scanned Beams and IMPT these margins would influence which pencil beam would be used and each one’s depth of penetration
• It is “required” that the dose distribution within the PTV is recorded and reported, therefore a PTV relative to CTV based on lateral uncertainties alone is proposed by ICRU 78
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• Individual proton beams can be shaped three dimensionally to the target:
  a. Perpendicular to the beam axis- aperture
  b. Along the beam axis- range and SOBP

**Beam specific PTV margins MUST be related to the range uncertainties!**

Lateral margins are set to ensure that the prescribed dose from each proton beam encompasses the CTV and take in account IM, SM and penumbra margins.

\[ \text{IM+SM} = 5 \text{ mm} \]
\[ \text{Penumbra (90%-50%)} = 9-12 \text{ mm} \]
\[ \text{Lateral margin} = 14-17 \text{ mm} \]
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- **Beam specific PTV margins** are related to the range uncertainties

Distal and proximal margins are set from CTV:

- \[ DM = (0.035 \times CTV_{distal}) + 3 \text{ mm} \]
- \[ PM = (0.035 \times CTV_{proximal}) + 3 \text{ mm} \]

3.5% uncertainty in the CT# and their conversion to relative proton linear stopping power
3 mm added to correct for range uncertainty due to compensator manufacturing, etc.

*Moyers et al. 2001*
Uncertainties in Proton Therapy

Why are uncertainties dangerous in PT vs. XT?

• Protons STOP
• Protons scatter differently (charged particle)
• Their assessment is not trivial

What are the consequences?

• Affect optimality of treatments due to restriction on beam directions, uncertain delivery of the prescribed dose...etc..
Uncertainties in Proton Therapy

Sources of uncertainties:

• Patient related: Setup, movements, organ motion, body contour, target definition, etc...

• Physics related: CT number conversion, dose calculation, etc...

• Machine related: Device tolerances, beam energy, delivery method, etc...

• Biology related: Relative biological effectiveness (RBE), etc.
Uncertainties in Proton Therapy

“If something goes wrong in the planning process it starts usually at the CT Simulator ...”

Physics Issues:

• CT Calibration Curve:
  - Proton interaction ≠ Photon interaction
  - Multisegmental curves are in use
  - No unique SP values for soft tissue HU range
  - Tissue substitutes ≠ real tissues
  - Statistical and systematic variations in CT numbers
  - Image reconstruction artifacts (High Z materials)
Uncertainties in Proton Therapy CT
Calibration Curve Stoichiometric Method

Schneider U. et al. PMB, 47, 487

Step 1: Parameterization of H
Choose tissue substitutes
Obtain best-fitting parameters A, B, C

\[ H = N_{rel} \{ A (ZPE)^{3.6} + B (Z_{coh})^{1.9} + C \} \]

Step 2: Define Calibration Curve
select different standard tissues with known composition (e.g., ICRP)
calculate H using parametric equation for each tissue calculate SP using Bethe Bloch equation fit linear segments through data points

Uncertainties in Proton Therapy CT Calibration Curve Stoichiometric Method - ICRU 78
Uncertainties in Proton Therapy

CT Calibration Curve Stoichiometric Method

Is the 3.5% CT# correction for proton range uncertainty conservative? Experimental evaluation of the relationship between the CT# and proton stopping power ratio was done at PSI using a stoichiometric method (Schaffner et al 1998, PMB)

Conclusion: There is a 1.1 % uncertainty in soft tissue and 1.8% in bone.

Reality...A decade later it is still NOT the current clinical practice!
3.5% standard...Further investigations needed.
Uncertainties in Proton Therapy

CT numbers

• For Siemens CT only in RM mode a 180 degree rotation is performed => CT # generated for the other 180 degrees inaccurate.
  Correction: Create a correspondence curve

• HUs vary within 3% as function of localization (Schneider 1996, PMB 41)

• HU for homogeneous materials vary between 1% to 2%
  (Schneider 1996, PMB 41)

• CBCT data can NOT be used for plan calculations
Uncertainties in Proton Therapy CT

High Z artifacts

• Artifacts due to high Z materials (metal clips, fiducials, Calypso beacons, prosthesis, dental fillings, etc.) are common in RT.
Uncertainties in Proton Therapy CT

High Z artifacts

- Siemens CT technology provides different phenomenological approaches for suppression of metal artifacts. For example:

  a. Imaged base beam hardening corrections (corrected attenuation data by means of Fourier transformations)

  b. Iterative correction of corrupt data (projected data through metal replaced by modified values)

  c. Streak balancing (identify radial streaks and subtracts them)
Uncertainties in Proton Therapy CT

High Z artifacts

Note: Image quality improvement for diagnostic purpose do not account for HU corrections at an accuracy level required for calculations in RT
Proton Treatment Planning: Inhomogeneities

- The effect of tissue inhomogeneity is greater for protons then for photons (Goitein et al., Med. Phys. 5)

- Failure to allow for a higher density along the proton path may result in a near zero dose in a distal segment of the target due to the reduced range of the protons.

- Penumbra is minimally affected for the materials limited to the human body, but it changes significantly for other material as it is caused by multiple scattering.

- Conversely neglecting to account for an air cavity upstream of the target => in high dose deposited in distal normal structures.

ICRU 78
Correction through SMEARING

Compensator design based on radiological path — Urie et al., PMB 1984

Setup and motion corrected through smearing of the compensator based on:

\[ ((\text{Internal margin} + \text{Setup Margin})^2 + [0.03 \times (\text{distal CTV depth} + \text{bolus thickness})]^2)^{0.5} \]

Corrects for Motion

Corrects for proton scattering

Moyers, et. al, IJROBP 49, 2001
Uncertainties in Proton Therapy Motion and Setup uncertainties

- What happens if the beam is nearly tangential to the target?

Per ICRU 78
Uncertainties in Proton Therapy
Motion and Setup uncertainties

What do we know so far?

- Smearing improves dose distribution but increase the irradiated volume
- Smearing degrades the distal end => increased range uncertainty
- Smearing may increase dose heterogeneity

- Tangential beams to the surface may alter dose distribution an MUST be controlled carefully
- It is desirable to avoid directions that bring the beam in line with large/variable heterogeneities or complex structure regions
- Beams should not point towards critical structures
- Imaging must be used for guidance
Planning of Proton Therapy
Patched Fields

- Patched = Feathering ≠ Smearing
- Targets wrapping around critical structures
- Spare OARS
- Each beam treats a part of the target
- NO perfect match possible
- Hot & Cold regions possible
- Must know lateral and distal penumbra
- Clinical judgment required

Planning of Proton Therapy
Patched Fields

• Patched beams should be selected:
  a. with short path lengths
  b. min. range uncertainties
  c. QAed

BEST: Avoid them!
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• This effect can be easily achieved using PBS, however the less sharper penumbra may be disadvantageous.

• The interplay effect (fig)
• The interplay effect for moving targets can be overcome though
• Repainting

• Fig.
Planning of Proton Therapy
Dose calculation

Dose calculation algorithms comparison:

Ray-tracing
Pencil beam
Monte Carlo

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RBE Uncertainties

• Clinical RBE: 1 Gy proton dose ≡ 1.1 Gy Cobalt γ dose (RBE = 1.1 in the middle of SOBP)

• RBE weighted dose concept introduced by ICRU 73

• RBE vs. depth (LET) is not constant

• RBE also depends on
  – dose
  – biological system (cell type)
  – clinical endpoint (early response, late effect)
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RBE Uncertainties

• Single RBE value of 1.1 may not be sufficient

• Biologically effective dose vs. physical dose

• Effect of proton nuclear interactions on RBE

• Energy deposition at the nanometer level - clustering of DNA damage
Proton Treatment Planning: From Physics to Reality

SUMMARY

• TPS commissioning process has to be developed based on the technology to be used and clinical applications.

• Setting up a realistic commissioning plan is important

• Uncertainties have a significant impact on dose distributions actually delivered and may affect outcome

• It is KEY to educate ourselves about the impact of uncertainties and how we account for them in the planning process for different delivery technologies.

• PBS may be easier to commission and plan, however it is most difficult to mange uncertainties related to the actual treatment.

• There many differences among photons and protons, however there are many similarities.