Treatment Planning and Protons

Radhe Mohan, PhD
To Save Time, Let’s Just Assume I Know Everything
The more you learn, the more you realize how little you know ...

Attributed to by Plato
Outline

- Characteristics of protons
- Dose calculations
- Uncertainties
- Passively scattered protons strategies
- Scanning beam and IMPT strategies
- Limitation of the concept of PTV
- Plan robustness
- Some clinical results
- Proton therapy research at MDACC
Characteristics of Protons

- Pristine Bragg peak due to a pencil beam of protons in homogeneous phantom

- Loose energy continuously

- Deposit less energy per unit pathlength in plateau and more near the end of the range

- Have a finite range – they stop
To Make Protons Useful for Radiotherapy

... Thin pencil beams must be spread laterally and longitudinally
The Passive Scattering Mode of Proton Beam Delivery
Dose Calculations for Passively Scattered Proton Therapy

- SOBP is decomposed into pencils and layers of energy
- Integral of each pencil across a plane for each energy is its depth dose
- Lateral dose distribution approximated by multiple Gaussians to account for MCS, nuclear interactions, etc.
- Ray tracing used to approximately account for inhomogeneities
- Empirical corrections and fitting of parameters leads to acceptable accuracy in most situations
Uncertainties in Proton Therapy

- Inter-and intra-fractional variations
- Dosimetric: CT numbers, high-Z artifacts, conversion to stopping powers, dose computation approximations
- Assumption of Radiobiological Effectiveness (RBE) to be 1.1
- ...
Proton Therapy of Moving Lung Tumors

Solution: Respiratory gating and breath-hold

Treatment plan based on single free-breathing CT image (perceived dose distribution)

The same treatment plan calculated on 10 phases of the 4D CT image
Inter-Fractional Variations

Original Plan

After Two weeks of Radiotherapy

IMRT: 7 beams plan

Proton: 3 beams plan

Solution: Repeat Imaging and Adaptive Replanning
Vulnerability of Protons to Uncertainties

- Protons more sensitive to uncertainties than photons
- Importance recognized early (in the 1980s)
  - Limited by tools by today’s standard (repeat CTs, 4D CT) to obtain quantitative information about the consequences and find solutions
- Rudimentary early solutions were developed
Accounting for Uncertainties

Margins, Apertures and Compensators
Beam-Specific Margins for Uncertainties -

Proximal Margin

Protons

CTV

Lateral Margin = PTV Margin

Distal Margin
Compensator “Smearing” to Account for Lateral Position Changes in Inhomogeneities

Scanning Beams and Intensity Modulated Proton Therapy
Scanning Beams and IMPT

3.2m Beam

Beam Profile Monitor

Scanning Magnets

Helium Chamber

Spot Position Monitor
Dose Monitor 1, 2

Isocenter

174 MeV Beamlet

σ = 0.8 cm

20 cm
Scanning Beams and IMPT

- Range of energies (72 – 221 MeV for Hitachi)
- Spots positioned by magnetic steering
- Discrete spot scanning or raster scanning
- Spots from placed in layers in the target for each of multiple fields
- Spot intensities determined using optimization techniques
Layer-by-Layer Scanning of Proton Beamlets for IMPT
Dose Calculations for Intensity Modulated Proton Therapy

- Beamlets are assumed to be Gaussian
- Approximations related to
  - Scattering from beam line components
  - Nuclear interactions
- Contributions from thousands of “spots” of specified energies and intensities constituting the scanned beam are summed
- Minor inaccuracies can add up to significant discrepancies
Intensity Modulated Proton Therapy

Three possible IMPT optimization strategies

- Single field uniform dose (SFUD)
  - Robustness similar to PSPT
- 3D IMPT
  - In-between robustness
- Distal edge tracking
  - Most vulnerable to uncertainties

- No need for compensator
- Normally, no aperture
Accounting for Uncertainties in IMPT

- No such thing as smearing - consequences of lateral variations in inhomogeneities ignored
- For SFUD, distal and proximal margins = those for PSPT
- For 3D IMPT and DET, no current solution
- Future solution - Robust optimization
Evaluation of Proton Plans
The PTV Concept is Not Valid for Protons

- Main reason: Planning margins to CTV are different in different directions and for different beams
- Then how do we
  - Evaluate plans using DVHs
  - Compare proton plans with photon plans
  - Add proton dose distributions to photon dose distributions
PTV Concept is Not Adequate Even for Photons

DVH for PTV represents the “worst” case scenario
DVH for CTV represents the “best” case scenario

Levegrun et al, IJROPB 2000: No prostate dose response
One Solution

“Uncertainty” (or “Worst Case”) Analysis
Parallel Opposed Prostate – Transverse Prescription (75.6 CGE) Isodose Range ±3.5% Nominal 5 mm Ant. 5 mm Post.
Some Clinical Results
Planning Study (23 patients) to Design Randomized PSPT vs. IMRT NSCLC Trial

Dose-volume indices are averaged over 23 patients

- PTV95%V
- PTV2cc
- LungVat 5Gy
- LungVat 20Gy
- MLD
- CordDose 1%/y
- EsoD1/3Gy
- Heart D1/3
D-V Indices of the First 5 Patients Enrolled on Randomized PSPT vs. IMRT NSCLC Trial

Dose-volume indices are averaged over 5 patient
Proton Therapy vs. 3D CRT & IMRT of Locally Advanced NSCLC

- Median Total Dose
  - 3D CRT & IMRT: 63 Gy
  - Proton therapy: 74 CGE

<table>
<thead>
<tr>
<th></th>
<th>3D CRT</th>
<th>IMRT</th>
<th>Protons</th>
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<tbody>
<tr>
<td>Esophagitis Gr ≥ 3</td>
<td>40.00%</td>
<td>35.00%</td>
<td>31.00%</td>
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<tr>
<td>Tx Related Pneumonitis Gr ≥ 3</td>
<td>35.00%</td>
<td>30.00%</td>
<td>25.00%</td>
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Reduction of Bone Marrow Toxicity in Patients with LA NSCLC treated with Concurrent ChT/ PBT compared to IMRT

Ritsuko Komaki, M.D
## Tumor Volume and BM toxicity

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<thead>
<tr>
<th>GTV (cc)</th>
<th>N</th>
<th>% of ≥2 Grade Hemoglobin Events (%)</th>
<th>P value</th>
<th>% of ≥2 Grade Platelets Events (%)</th>
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<td>≥100</td>
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<td>&lt;0.001</td>
<td>1 (5%)</td>
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<td>IMRT = 64</td>
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<td>2 (8%)</td>
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<td>1 (5%)</td>
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<tr>
<td>GTV (cc)</td>
<td>N</td>
<td>% of ≥2 Grade Neutrophil Events (%)</td>
<td>P value</td>
<td>% of ≥2 Grade WBC Events (%)</td>
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<td>0.813</td>
<td>50, 44</td>
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Current Research at MDACC
(In Collaboration with MGH)

- Reduction in uncertainties and accounting of residual uncertainties
  - Stopping powers improvement
  - Gating and breath-hold
  - Adaptive replanning
  - Dose calculation accuracy
- IMPT development
- Robust optimization
- Evaluation of robustness of treatment plans
- Dose accumulation
- Trials and studies
Summary

- Abundant room for improvement of efficiency, cost-effectiveness, accuracy and quality of treatments
- A boon and a bain for physicists
- Even in the current state of the art PT has the potential to be significantly superior for certain sites
  - Lung
  - Pediatrics
  - ...
- Future potential is great
However, Be Mindful of Irrational Exuberance Lest ...
Parachute use to prevent death and major trauma related to gravitational challenge: systematic review of randomised controlled trials – Smith et al, BMJ 2003;327:1459-1461

- **Conclusion:**
  - As with many interventions intended to prevent ill health, the effectiveness of parachutes has not been subjected to rigorous evaluation by using randomised controlled trials.
  - Advocates of evidence based medicine have criticised the adoption of interventions evaluated by using only observational data.
  - We think that everyone might benefit if the most radical protagonists of evidence based medicine organised and participated in a double blind, randomised, placebo controlled, crossover trial of the parachute.
Thank You