Proton Stereotactic Radiotherapy: Clinical Overview

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Acknowledgements

- Radiation Oncologists and Physicists at various institutions (MGH, MDACC, PSI, Clatterbridge, many more)
SRS History

- Gamma Knife original photon treatment (1950’s)
- Ten years later (1960’s): proton radiosurgery
- Linac based begun in 1980’s and Cyberknife later
- Thousands of patients treated with Photon SRS—clinically proven technique
Stereotactic Proton Therapy

- Limited fractions (1-5)
- Higher doses/fraction
- Often smaller treatment volumes and smaller field sizes
- Magnified effects of random uncertainties
Why Proton SRT?

- Generally with respect to photon SRT
  - Distal Edge
  - Conformal for concave/complex geometries
  - Penumbra**
  - Integral Dose
- Higher TCP/Lower NTCP
Dose Comparisons

- 18 MeV Electrons
- 10 MV Photons
- SOBP Protons
- Single Bragg Peak
Complex Geometries
Penumbra

- Proton Penumbra can be sharper than photons but...
  - Air Gap
  - Range Compensator
  - Apertures
  - Spot Size
  - Beam Optics
Integral Dose
Integral Dose

- The V40% for protons is smaller than photons
- Due to the incorporation of uncertainties in planning, the conformality is tighter with photons for most SRT targets
- Abnormally shaped targets or targets close to an OAR can have tighter conformality
- Clinical Significance?
# Proton SRT for Benign Cases: Secondary Cancer Risks

<table>
<thead>
<tr>
<th>Risk of 2nd cancer</th>
<th>SRT</th>
<th>2-field photon</th>
<th>3-field photon</th>
<th>IMRT</th>
<th>2-field proton</th>
<th>3-field proton</th>
<th>4-field proton</th>
<th>5-field proton</th>
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</thead>
<tbody>
<tr>
<td>EUD (Gy)</td>
<td>32.1</td>
<td>5.7</td>
<td>11.2</td>
<td>26.8</td>
<td>1.5</td>
<td>4.3</td>
<td>6.1</td>
<td>6.8</td>
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<tr>
<td>NTCP (%)</td>
<td>23</td>
<td>48</td>
<td>38</td>
<td>34</td>
<td>30</td>
<td>29</td>
<td>27</td>
<td>26</td>
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<td>Right temporal lobe</td>
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<td>NTCP (%)</td>
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<tr>
<td>Left temporal lobe</td>
<td>28</td>
<td>48</td>
<td>40</td>
<td>37</td>
<td>35</td>
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<td>EUD (Gy)</td>
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<td>NTCP (%)</td>
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<td>Clinical symptoms</td>
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</tbody>
</table>

**Acoustic** → **Sarcomatous Hanabusa, 2001**

**Acoustic** → **Glioblastoma Shamisa, 2001**

**AVM** → **Glioblastoma Kaido, 2001**

**Acoustic** → **Meningiosarcoma Thomsen, 2000**

**NF2** → **Malignant schwannoma Baser, 2000**

**NF2** → **Malignant meningioma Baser, 2000**

**Mening** → **Glioblastoma Yu, 2000**

**Acoustic** → **Malign Schwannoma Shih, 2000**

**Cav hem** → **Glioblastoma Salvati, 2003**

**Acromeg** → **Meningioma Loeffler, 2003**

**Acromeg** → **Vestibular Schwannoma Loeffler, 2003**

**AVM** → **Meningioma Sheehan 2006**

Many more studies...

**Winkfield, et al, 2011**
Integral Dose and Risks: Mets

- Liver and lung toxicity
- Mediastinum
- Stomach and intestinal tract
- Spinal Cord
- Optics
- Brain dose and cognitive health
What is *not* a benefit of protons versus photon SRT?

<table>
<thead>
<tr>
<th>Percentage</th>
<th>Benefit</th>
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<tbody>
<tr>
<td>20%</td>
<td>1. Distal dose reduction</td>
</tr>
<tr>
<td>20%</td>
<td>2. Lower NTCP</td>
</tr>
<tr>
<td>20%</td>
<td>3. Conformal for Complex Geometries</td>
</tr>
<tr>
<td>20%</td>
<td>4. Less uncertainty in the dose delivery</td>
</tr>
<tr>
<td>20%</td>
<td>5. Lower integral dose.</td>
</tr>
</tbody>
</table>
Uncertainties?

- Range uncertainties (CT, SPR, Motion, Setup, Geometric Patient Daily Variations)
- Motion-Miss Targets
- Field Size Effects
- Penumbra
- Online Imaging Limited
- ∴ Affect the conformality (Rx dose)
Proton range changes: Cranial SRT

- Fluids in sinuses
- Scattering from heterogeneities
- Setup Uncertainties
- Air gap
- Onyx for AVM
  - Artifacts
  - WET
Intrafractional Motion

Cranial Intrafractional Motion

Impact on MFO Planning
Less impact on Passive Scattered

Lei Dong, Ph.D.
1.5 mm setup error
Perils Due to MCS

- Multiple Coulomb Scattering (MCS)
- Range Uncertainties, especially along a heterogeneous boundary
- Motion Uncertainties in Heterogeneous Materials
- Differences in Output, PDD, and Penumbra compared to Photons
Liver Motion

H-M Lu, Ph.D
LET/RBE

- Danger of the distal edge

Bednarz, et al 2013

RBE for a single fraction??
Uncertainty Mitigation

- What do we do with all of this information:
  - Margins: Distal/Proximal
  - Beam angle selection
  - Smearing
  - Feathering
  - Gating
  - OARs
Beam Angle Selection

1. Avoid beam entrance angles along and through heterogeneous boundaries
2. Avoid distal edge sparing.
3. Use multiple beams to reduce uncertainty of a single beam!
OARs

- AVOID distal edge sparing!
- If unavoidable, use multiple fields to spread the risk and reduce the dose to the OAR if there is an error.
Gating

- Gating can greatly reduce the range uncertainties of targets close to the diaphragm where motion is typically the greatest.
Large Margins:
Range, Motion, Smearing
What is the best method to minimize the effects of dose delivery uncertainties in proton SRT?

<table>
<thead>
<tr>
<th>Percentage</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>20%</td>
<td>1. Increased image guidance</td>
</tr>
<tr>
<td>20%</td>
<td>2. Use multiple beams</td>
</tr>
<tr>
<td>20%</td>
<td>3. Use a single beam</td>
</tr>
<tr>
<td>20%</td>
<td>4. Increase the margins</td>
</tr>
<tr>
<td>20%</td>
<td>5. If it moves, don’t treat it.</td>
</tr>
</tbody>
</table>
Using Multiple Beams

- Spreads uncertainty due to range, patient setup, LET, and patient motion
- Difference in lateral and distal uncertainties
- Increases conformality for both scanned and scattered delivery
- Increased Robustness
Patient Setup

- Immobilizations similar to photons
  - Vac Lock bags
  - Masks and Frames
- **Need to be aware of proton WET**
- Image guidance:
  - Most 2D currently available
  - CT and CBCT coming soon
  - Patient motion, target motion, gantry wobble, Apertures, etc.
Routine QA

- Some QA common to Photons:
  - Output, flatness, symmetry, mechanical, isocentricity, etc.

- Differences:
  - Energy/Range dependent variables and device sensitivities
  - Machine specific factors (timing, feedback, scattering devices, etc)
  - Scanning versus Scattering
Treatment Sites

- Cranial and ocular targets are the most documented and historically most common
- Spines treated later (attached to rigid body surrogate)
- Recently: Body sites of lung, liver and pancreas
Cranial Patients Treated

- Benign Neoplasms:
  - Acoustic Neuromas
  - Meningiomas
  - Pituitary Adenomas
- Arteriovenous Malformations
- Metastatic Lesions
  - Multiple Lesions
  - Close proximity to surface or critical structures (optics, brainstem)

Eyes: very high LC
Extra-cranial Patients Treated

- Spine
  - Mets
  - Small primary lesions

- Lung
  - Multiple trials
  - Reduced V5 and V20
  - Reduces dose to contralateral lung

- Liver: Reduced liver toxicity
- Pancreas: Reduced digestive tract dose
Which Proton SRT site is the most technically challenging?

<table>
<thead>
<tr>
<th>Rank</th>
<th>Site</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Eyes</td>
<td>20%</td>
</tr>
<tr>
<td>2</td>
<td>AVM</td>
<td>20%</td>
</tr>
<tr>
<td>3</td>
<td>Spine</td>
<td>20%</td>
</tr>
<tr>
<td>4</td>
<td>Lung</td>
<td>20%</td>
</tr>
<tr>
<td>5</td>
<td>Pituitary</td>
<td>20%</td>
</tr>
</tbody>
</table>
Lung Challenges

- Motion
- Density variations
- Range uncertainties
- Treatment planning
- Image Guidance
- OARs
Lung Challenges

- Motion
- Density variations
- Range uncertainties
- Treatment planning
- Image Guidance
- OARs
- Robustness
- Interplay

Grassberger, et. al.
Robustness

- Include probability estimates in the treatment planning optimization
- Reduce high gradients in close proximity to OARs
- Include Range Uncertainties, Setup Uncertainties, and Motion
Summary

- Proton SRT is a viable option for SRT.
- Benign cases probably have the most benefits with protons → Integral Dose, late effects.
- Malignant:
  - Close proximity to OARs/Quality of life or necrosis concerns.
  - Multiple brain metastases: is quality of life affected?
  - Volume toxicities in the body.
- Currently, less conformal due to uncertainties:
  - Online range verification.
  - Robust planning.
  - Patient Imaging.
Thank You!

http://gray.mgh.harvard.edu