Pencil Beam Proton Therapy for Head and Neck Cancer: Lessons Learned, Current Applications, Future Directions

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PTCOG 2014
June 10, 2014
Treatment of Major Salivary Gland Cancers/Unilateral Neck with non-PBS PT

DVH Comparison Proton (□) vs. Rapid Arc (△)
Outline

- Background/Introduction
- Patient selection
- Simulation
- Treatment Planning
- Treatment Delivery/Quality Assurance
- Future Directions
- Conclusions
Outline

- **Background/Introduction**
  - Rationale for PBS proton therapy for locally advanced HNC (requiring bilateral neck RT)

- Patient selection

- Simulation

- Treatment Planning

- Treatment Delivery/Quality Assurance

- Future Directions

- Conclusions
Why consider proton therapy for the head and neck cancer?

- **Treatment is morbid**

- **Side effects**
  - Acute
    - Mucositis
    - Dysgeusia
    - Dysphagia
    - Odynophagia (requiring opioids and/or supplemental nutrition)
    - Xerostomia
    - Weight loss, dehydration, malnutrition
  - Chronic
    - Dysgeusia
    - Xerostomia
    - Dysphagia (risk of feeding tube dependence)
    - Fibrosis
    - Lymphedema
    - Dental caries and Osteoradionecrosis
    - RT-induced malignancy
    - Cerebrovascular accident
Why consider proton therapy for the head and neck cancer?

- Treatment is morbid
- Increasing incidence
Why consider proton therapy for the head and neck cancer?

- Treatment is morbid
- Increasing incidence

**Improving disease outcomes**
- Many people cured, living longer after treatment
- Late toxicities are important
A  Overall Survival According to Tumor HPV Status

Overall Survival (%)  

0 25 50 75 100

No. at Risk

<table>
<thead>
<tr>
<th>HPV-positive</th>
<th>205</th>
<th>193</th>
<th>179</th>
<th>165</th>
<th>151</th>
<th>73</th>
</tr>
</thead>
<tbody>
<tr>
<td>HPV-negative</td>
<td>117</td>
<td>89</td>
<td>76</td>
<td>65</td>
<td>51</td>
<td>22</td>
</tr>
</tbody>
</table>

Hazard ratio for death, 0.38 (0.26–0.55); P<0.001

B  Overall Survival According to Risk Group

Overall Survival (%)  

No. at Risk

<table>
<thead>
<tr>
<th>Low risk</th>
<th>114</th>
<th>111</th>
<th>106</th>
<th>102</th>
<th>95</th>
<th>46</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intermediate risk</td>
<td>79</td>
<td>70</td>
<td>64</td>
<td>54</td>
<td>44</td>
<td>24</td>
</tr>
<tr>
<td>High risk</td>
<td>73</td>
<td>52</td>
<td>43</td>
<td>33</td>
<td>28</td>
<td>8</td>
</tr>
</tbody>
</table>

Ang et al., NEJM 2010
Outline

- Background/Introduction

- **Patient selection**
  - Definitive vs Postop: implications on quality assurance, need for adaptive replanning, etc.

- Simulation

- Treatment Planning

- Treatment Delivery/Quality Assurance

- Future Directions

- Conclusions
Impact of anatomic changes during proton therapy?

Baseline

12 weeks post-CRT
Selecting Patients for HN Proton RT

❖ Definitive CRT?
  • Concerns:
    – Anatomic changes due to disease response
      ○ Inability to image soft tissue (no CBCT)
      ○ Resources required (contouring, replanning)

❖ Postoperative, HPV+, oropharynx cancer
  • Advantages:
    – Excellent disease outcomes, long-term f/u
    – Anatomy favorable for proton therapy
    – Anatomic changes during treatment limited to weight loss
Outline

- Background/Introduction
- Patient selection
- Simulation
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- Future Directions
- Conclusions
Simulation

- Supine, head extended
- Thermoplastic mask (3-pt)
- Shoulders immobilization with rope pulls
  - Reinforced with a U-bolus
- Non-contrast scan
Outline

- Background/Introduction
- Patient selection
- Simulation
- Treatment Planning
- Treatment Delivery/Quality Assurance
- Current trials/Future Directions
- Conclusions
Obtaining optimal spot size

- Need high level of conformity
  - Small spots

- Shallow targets in PBS require a range shifter

Conclusion: try to shift range close to the patient

Plot courtesy of L. Lin, UPenn
Universal Bolus
Universal Bolus vs Range Shifter

- Clinically, is it worth the effort to shift the range close to the patient?

- More conformal and homogeneous target dose

- Better normal sparing of normal tissues
Choosing Beam Arrangement

- Need a reproducible beam path which minimizes uncertainties

- Anterior beam should be avoided
  - Uncertainty caused by dental artifacts and implants
  - Goal of decreasing dose to oral cavity (mucositis, additional sparing of taste buds, minor salivary glands)
Choosing Beam Arrangement

- **Best option:**
  - High density table used as a range shifter
  - Two posterior oblique beams

U-shaped bolus for possibility of lateral fields when target volumes do not extend inferiorly beyond the shoulders
Planning: Benefits and Limitations

**Benefits:**
- Oral Cavity (~20 Gy mean reduction)
- Submandibular Glands (contralateral)
- Parotid glands (contralateral)

**Limitations**
- Central structures (when targets approach or cross midline)
- Limited angles
- Inability to use anterior beam
- Uncertainty (robustness)
  - Worse with IMPT
Planning: Benefits, Limitations, Uncertainty

- Goal is to use single field optimization (SFUD) whenever possible

- If target crosses midline, cord is proximal to the target making it difficult to reduce dose

- Use some portion of IMPT treatment to reduce cord dose
Cord constraints can be met on most cases with <20% of the fractions using IMPT.

Doing a shift study to assess uncertainties, determined 20% IMPT resulted in clinically acceptable uncertainty in target dose and low uncertainty in critical OAR doses.

Clinically, we often combine SFUD+ IMPT for cord constraints and to improve proton conformality in certain OARs (larynx, for example).
Contralateral Submandibular Gland

Stage 4a, T1N2b, HPV+, R tonsil SCCA

PBS: 80% SFUD, 20% IMPT
Rapid Arc IMRT: Backup plan
Mean Doses: IMRT (39 Gy), PBS (32 Gy)
Contralateral parotid
Mean Doses: IMRT (18 Gy), PBS (9 Gy)
Oral Cavity
Mean Doses: IMRT (19 Gy), PBS (3 Gy)
Outline

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Imaging/Setup Verification

- **Daily Imaging**
  - Medcom
    - Orthogonal kv-kv

- **Weekly imaging**
  - Verification CT scan
    - Plan overlay on CT to assess effect of anatomic changes
  - Performed weekly on first 10 pts
  - Now limited to pts with weight loss approaching 5%
Daily imaging: Medcom

- Limitations: Limited to bony anatomy. Inadequate evaluation of soft tissue.
CT verification

- Through verification CT scans we find the most uncertainty in the lower neck:
  - Loose skin
  - Shoulder positioning
  - Inability to see neck skin position with kV-kV setup
Outline

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Anterior Bolus

- Use a smeared match to combine an anterior field for treatment of low neck nodes

- Requires range shifter or anterior bolus device

- More robust treatment path, less subject to setup uncertainty. Improvements sparing of central structures.
CBCT Image Guidance for Proton Therapy

- All the advantages of CBCT in photon therapy:
  - Visualization of soft tissue, tumor size, or location
  - 3D anatomic matching

- AND
  (1) Assessment of dose delivery deviations due to anatomical change/setup error
  (2) Dose calculation using CBCT
  (3) Dose guided adaptive proton therapy

Challenges:
  (1) CBCT HU variation: patient size, scatter, beam hardening
      --> Large uncertainty in proton stopping power and thus calculated range

Solution: Use deformable image registration tools to map HU of Planning CT to CBCT
CBCT Image Intensity Correction

*Linac CBCT is used in this study. Proton CBCT under development.

Original CBCT

Planning CT

Advanced Normalization Tools

Image Difference (corrected)

Intensity Corrected CBCT = Deformed planning CT

Image Difference (uncorrected)
Good Agreement of WETs in regions with minimum physiological changes: Mean WET difference $=1.26$ mm (Corrected) vs $3.38$ mm
Detecting Proton Range Differences

- Identified range discrepancy highlighted by red circle
Patient-reported toxicity/QOL

1. Have you experienced a change in taste? Check all of the following statements that apply to you now:
   - [ ] Normal
   - [ ] Diminished
   - [ ] Absent
   - [ ] Distorted
   - [ ] Heightened

   My sense of taste is: [ ]

2. I sometimes experience a taste when nothing is there (phantom taste): [ ] YES  [ ] NO

3. For each of the following taste qualities, indicate with a check whether your perception of it is currently normal, diminished, absent, distorted, heightened, or present when nothing is there (phantom taste):

<table>
<thead>
<tr>
<th>Taste</th>
<th>Normal</th>
<th>Diminished</th>
<th>Absent</th>
<th>Distorted</th>
<th>Heightened</th>
<th>Phantom Taste</th>
</tr>
</thead>
<tbody>
<tr>
<td>SWEET</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>SALTY</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>SOUR (e.g., lemon, vinegar)</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
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<td>[ ]</td>
</tr>
<tr>
<td>BITTER (e.g., tonic water, medicine)</td>
<td>[ ]</td>
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<td>[ ]</td>
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<tr>
<td>ROTTEN</td>
<td>[ ]</td>
<td>[ ]</td>
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<tr>
<td>BURNING</td>
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<tr>
<td>TINGLING</td>
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<td>[ ]</td>
</tr>
<tr>
<td>OTHER (if other, specify)</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
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<td>[ ]</td>
</tr>
</tbody>
</table>

4. If you have phantom taste (taste when nothing is there), indicate with a check where your perception of it is (check all that apply):
   - [ ] FRONT OF TONGUE
   - [ ] BACK OF TONGUE
   - [ ] ROOF OF MOUTH
   - [ ] SALIVA
   - [ ] THROAT
   - [ ] WHOLE MOUTH
   - [ ] GUMS
   - [ ] DENTURES OR CAPS
   - [ ] OTHER (specify) [ ]

   My sense of smell is: [ ]

   If phantom smell (smell when nothing is there), please describe [ ]

5. My changes in taste or smell have resulted in my eating (check all that apply):
   - [ ] The same amount of food
   - [ ] Less
   - [ ] More
   - [ ] Different types of food (specify the change) [ ]

Collected at baseline, 3, 6, 12, and 24 mos
Conclusions

- **Proton therapy**: promising tool to improve the therapeutic ratio for our pts.

- **Head and neck**: ideal disease site for proton therapy, often in a multimodal setting

- **Need for comparative evidence generation**
  - Collaborative efforts

- **Technical advances required for future improvements**
  - Treatment of difficult sites (sinonasal), bulky, intact disease
    - CBCT
    - Adaptive RT
Acknowledgements

♦ Clinical
  • Steve Hahn
  • Zelig Tochner
  • Peter Ahn

♦ Physics
  • Tim Solberg
  • Jim McDonough
  • Maura Kirk
  • Kevin Teo
  • Richard Maughan
  • Stefan Both