Proton Therapy for Head and Neck Cancer: Current Status

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Basics of Proton Therapy

A little bit of physics (yuck!) and biology (yum!)

Why Protons are Superior to Photons

Protons are **clinically superior** to X-rays:

X – Rays do not stop

- Excess radiation to healthy tissue results in costly side effects and secondary tumors
**Protons Stop, Unlike Photons**

Maximize Tumor Dose and **Spare Healthy Tissue**

![Protons Stop, Unlike Photons Diagram]

**How Protons are Produced**

- Hydrogen atoms are separated into electrons and protons.

- Proton beams stay in the vacuum tube as a **cyclotron**, where acceleration occurs and increases proton energy.

- After leaving the cyclotron, the protons move through a beam-transport system comprised of a series of bending magnets that shape, focus and direct the proton beam to the appropriate treatment room.
From the Cyclotron to the Patient

- In the cyclotron, the acceleration increases proton energy to a total of 70 to 250 million electron volts.

- At maximum energy, a proton beam travels 125,000 miles per second, which is equivalent to two-thirds the speed of light.

- From the hydrogen canister to the patient, a proton typically travels 313,000 miles.

Facility Layout
Proton Therapy Status Report

• Interest started taking off in the 1990s
• Currently, **18 operational facilities in the US**, and >40 additional ones in ~15 other countries
• Countries with (or in construction/planning) USA, Canada, UK, France, Norway, Sweden, Denmark, Germany, Switzerland, Italy, Russia, Poland, Czech Republic, Slovak Republic, Austria, Japan, China, S Korea, Taiwan, India, Saudi Arabia, S Africa
Head and Neck Applications of Proton Therapy

Ocular Melanoma Phase III

- I 125 Plaque vs Helium (2 protons) phase III (Char, et al, Ophthalmology, 1993) trial
  - Equivalent survival
  - Equivalent visual preservation
    - Proportion of eyes >20/40 = 21 vs 23%
  - Fewer recurrences with He (0 vs 13.3%)
  - Fewer enucleations with He (9.3 vs 17.3%)
Chordoma: Skull Base

- Rare tumors
- Difficult to achieve gross total oncologic resections
- RT doses are limited by critical surrounding brain, brainstem, cranial nerves, and cord
- Low to modest doses of RT rarely produce durable and sustained local control

Chordoma: Results

- Mayo (Krishnan, Neurosurg, 2005): **32% 5Y LC** with surgery + 3D CRT + GK SRS (n = 25); 10% symptomatic temporal lobe injury
- PSI, Switzerland (Ares, IJROBP, 2009): **81% 5Y LC** with surgery + scanning PBT (n = 42); 6% symptomatic temporal lobe injury
- MGH (Munzenrider, Strahlenther Onkol, 1999): **73% 5 Y LC with surgery + PBT**; 8% symptomatic temporal lobe injury
- **With such large differences for a tumor that kills, would you want to be randomized?**
**OPC: Gastrostomy Tubes ↓ by >50%**

- Case-control study, matched on based on unilateral vs bilateral therapy, tonsil vs BOT primary, T-category, N-category, concurrent chemo, induction chemo, smoking status, sex and age.

- 26 IMPT cases precisely matched to 26 IMRT.
- Gastrostomy tubes needed in 5 (19%) IMPT vs. 12 (46%) IMRT cases (P < 0.039).
- IMPT = less G3 dysphagia vs. IMRT.
- Phase 3 randomized trial is ongoing.


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**Proton Therapy for OPC: 50% reduction in feeding tubes**

Frank SJ et al. JROBP 2014
How many extra intra-oral x-ray equivalents is IMRT over IMPT?

How many intra-oral x-rays is 25 Gy?

1. 5
2. 50
3. 500
4. 5000
5. 5,000,000
Eligibility
1) Stage III-IV oropharyngeal cancer
2) Squamous cell carcinoma
3) ECOG≤2
4) Target volume delineation

Treatment 33 days
Recovery 10 wks
PROs

IMPT (70 Gy(RBE))
Chemotherapy (locally advanced disease)

IMRT (70 Gy)
Chemotherapy (locally advanced disease)

Frank – PI
Trial Activated – Sept 2013
Belmont Principle: Maleficence/Informed Consent

*25 Gy (25 Sv) of Unnecessary Radiation =

12,500 H&N CTs (2 mSv)
5,000,000 Intraoral X-Rays (0.002 mSv)
25,000x General Public Annual Limit (1.0 mSv)

+83% Additional Cancer Risk*
(12,500 CTs, 65 yo)

Equipoise: The Parachute Story

Hazardous Journeys

• Hazardous Journeys: Parachute use to prevent death and major trauma related to gravitational challenge: systematic review of randomised controlled trials: BMJ 2003;327:1459

• 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.

Dosimetric Conformality is Not a Trial Question but Intuitively Hippocratic
## Conclusions

- Radiotherapy using photons provides excellent outcomes for many patients
- Advances in proton technology will allow for treatment of more complex tumors/treatment sites
- Clinical trials are ongoing to better define which patients benefit most from protons and will be offered to all patients at the MPTC
- Partnering with regional providers and making proton therapy easily accessible for their patients is a priority of the MCI