Proton Therapy: Science Fiction or Science Fact

John Han-Chih Chang, MD
Director of Clinical Research
CDH Proton Center

Primary Investigator - Radiation Therapy Oncology Group
Primary Investigator - Children's Oncology Group
Lurie Children's Hospital
Vice Chair of the Midwest Children's Brain Tumor Clinic
Cancer Treatment
High End Image Guided
“Glorified Tanning Booths”
Modality and Delivery Must Work Together

Radiation Modality
- 3D CRT
- IMRT
- Stereotactic RT/RS
- Brachytherapy
- Particle Therapy

Techniques to Improve Radiation Delivery
- IGRT
- Gating
- Adaptive RT

OPTIMAL RADIATION THERAPY
The goal of radiation oncology for the past century has been to get:
- More radiation in the tumor
- Less radiation in the healthy tissue surrounding the tumor

Protons are the next evolutionary step in improving this ratio

Diagram:
- Therapeutic ratio
  - Dose to tumor
  - Dose to healthy tissue
The Next Step of Radiation Darwinism

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Protons through the Ages
Scientists have been perfecting proton therapy as a treatment for cancer for over 60+ years.

- Robert R. Wilson, PhD (1914-2000)
  - "Radiological Use of Fast Protons" (Radiology 1946:47:487-91)
  - A group leader of the Manhattan Project
  - Berkeley and Harvard
  - Architect for Fermilab
Protons: “Modern” History 101

- Loma Linda Univ Medical Center – Loma Linda, CA  1990
- HCL closes ⇔ NPTC opens  2001
- MPRI (Now the IUHPTC) – Bloomington, Indiana  2004
- MDAH – Houston, Texas  2006
- FPTI – Jacksonville, Florida  2006
- PPC – Oklahoma City, Oklahoma  2009
- RPTC – Philadelphia, Pennsylvania 2010
- HUPTI – Hampton, VA  2010
- CDH – Chicago, IL  2010
- Princeton – Somerset, NJ  2012
Mechanism of Action
The Value of Protons

- Protons have a physically *superior* dose distribution vs X-rays
- Protons behave differently than x-rays:
  - Protons
  - X-Rays do not!
- Protons improve the “therapeutic ratio”
  - maximizing tumor control *while minimizing side effects*
- At a given radiation dose to a tumor protons deliver, on average, less than half the radiation dose to normal tissues than do x-rays

(1) Jay Loeffler, Massachusetts General Hospital, “Proton Therapy 2009”
Protons have Fewer Side Effects than Photons

There is no reason to irradiate healthy tissue

- Photons deposit only 20% of their energy in the tumor

- Protons deposit more than 80% of their energy in the tumor

In order for photons to reach a prescribed dose at the tumor depth, healthy tissue gets four times the radiation as the tumor

Protons put 80% of their energy into the tumor and only 20% into healthy tissue
The Physics of Protons

Depth Dose Curves for Different Treatment Types

- High Energy X-Rays
- Spread Out Bragg Peak (SOBP)
- 200 MeV Protons
- Healthy Tissue
- Tumor

Depth in Tissue (cm)

Relative Dose
How a Cyclotron Works

1. Protons (ionized hydrogen) are injected at low energy.

2. Voltage alternates to give the protons a “kick” every time they cross the gap.

3. Magnetic field keeps protons bound in a circular orbit.

4. As the proton’s energy increases, its orbital radius increases.

High energy protons are kicked out.
Proton Therapy

Inclined Beam Room

Gantry Room
Treatment Delivery
Why would we chose Protons?
Clinical Indications

◆ Current
  • Pediatrics
    ❖ Ewing’s Sarcoma
    ❖ Ocular/Optic neoplasms
    ❖ Sellar/Suprasellar neoplasms
    ❖ Rhabdomyosarcoma
    ❖ Base of Skull Tumors
    ❖ Low Grade Gliomas
    ❖ Craniospinal Irradiation
    ❖ Germ Cell Tumors
  • Prostate
  • Head and Neck/Base of Skull
  • Intracranial
    ❖ Meningioma
    ❖ Benign and Malignant
  • Paraspinal/Sacrum
    ❖ Chordoma/Chondrosarcoma

◆ New/Future Indications
  • Lung
    ❖ Stage III/Locally Advanced
    ❖ Localized
  • Lymphoma
    ❖ Mediastinal
  • GI
    ❖ Esophageal
    ❖ Pancreas
    ❖ Hepatobiliary
  • Ocular
    ❖ Melanoma
  • Breast
    ❖ Left sided Chest Wall Radiation
    ❖ Accelerated Partial Breast Irradiation
Protons Are More Precise and Spare Healthy Tissue

6 Field IMRT PLAN

Exit dose unnecessarily radiates healthy tissues that may cause harmful side effects or secondary malignancies

3 Field Proton PLAN

Zero exit dose and high degree of conformity eliminates excess radiation
Craniospinal Irradiation (CSI) for Medulloblastoma, etc…
CLINICAL INVESTIGATION

TREATMENT PLANNING WITH PROTONS FOR PEDIATRIC RETINOBLASTOMA, MEDULLOBLASTOMA, AND PELVIC SARCOMA: HOW DO PROTONS COMPARE WITH OTHER CONFORMAL TECHNIQUES?

Catherine T. Lee, M.D.,* Stephen D. Bilton, C.M.D.,† Robin M. Famiglietti, C.M.D.,† Beverly A. Riley, C.M.D.,† Anita Mahajan, M.D.,* Eric L. Chang, M.D.,* Moshe H. Maor, M.D.,* Shiao Y. Woo, M.D.,* James D. Cox, M.D.,* and Alfred R. Smith, Ph.D.†

Departments of *Radiation Oncology and †Radiation Physics, The University of Texas M. D. Anderson Cancer Center, Houston, TX
Medulloblastoma, composite of craniospinal plus posterior fossa: Dose–volume histogram comparisons across treatment modalities. (Lee CT et al)

CSI – 23.4 Gy – 13 fractions
Boost – 30.6 Gy – 17 fractions
Total – 54 Gy – 30 fractions
Medulloblastoma, posterior fossa irradiation alone: Dose–volume histogram comparisons across treatment modalities. (Lee CT et al, IJROBP 2005)
Cranial-spinal Treatment
Protons v. Photons
Evidence of Distal Range Stopping

Before treatment

Treatment plan

After treatment

Stephanie C. Krejcarek, B.Sc., 1 P. Ellen Grant, M.D., 2 John W. Henson, M.D., 2, 3 Nancy J. Tarbell, M.D., 1 and Torunn I. Yock, M.D., M.C.H. 1
Pediatric Brain

Protons

IMRT

IMRT-Protons: showing extra dose for IMRT

50% more than protons
Base of Skull Chordoma
Base of Skull Clival Chordoma

Protons  IMRT  IMRT-Protons: showing extra dose for IMRT
Orbital Rhabdomyosarcoma and Retinoblastoma
PROTON RADIOThERAPY FOR ORBITAL RHABDOMYOSARCOMA: CLINICAL OUTCOME AND A DOSIMETRIC COMPARISON WITH PHOTONS

Torunn Yock, M.D., M.C.H., Robert Schneider, C.M.D., Alison Friedmann, M.D., Judith Adams, C.M.D., Barbara Fullerton, Ph.D., and Nancy Tarbell, M.D.

Department of Radiation Oncology, Massachusetts General Hospital, Harvard Medical School, Boston, MA

Torunn Yock et al
International Journal of Radiation Oncology*Biology*Physics
Volume 63, Issue 4, 15 November 2005, Pages 1161-1168
(a) Coronal and axial photon plan (left). (b) Coronal and axial proton plan (right). The tumor is outlined in red, and the high-dose regions have a red colorwash that fades to lower-dose regions depicted in blue. The colorwash dose legend is given in the middle of the picture.
Dose wash comparison. The areas in red, yellow, green, and aqua depict where the dose to tissues is saved by using a proton technique, whereas the bright blue areas show very little difference in dose between the two plans (i.e., in the tumor itself). The red areas show where using the proton technique saves the greatest dose to normal tissue. The navy blue shows the area treated by protons but not by photons.
Retinoblastoma

Concerns Regard Treatment Induced Secondary Malignancies
SMN in Retinoblastoma Patients

Graph showing cumulative incidence over time after retinoblastoma diagnosis. The graph compares patients who received radiotherapy and those who did not. The graph indicates that 26.5% ± 10.7% of patients who received radiotherapy experienced a certain event within 50 years after diagnosis, compared to a lower percentage for those who did not receive radiotherapy.
Bilateral Retinoblastoma Treatments

Protons - single fields

%  
10  
30  
50  
90  
100  
105  

Photons - multiple arcs
Spinal/Paraspinal/Axial Skeletal Tumors
Spine

Protons

IMRT

IMRT-Protons: showing extra dose for IMRT

20% more than protons

40% more than protons
Sacral Chordoma
Axial Skeletal Lesions

- DeLaney et al. IJROBP 2009
- MGH phase II data with axial skeleton soft tissue tumors
  - Mainly Chordomas & Chondrosarcomas
    - Tx’d with Proton beam alone
    - 6% sacral neuropathy
    - 5 year data with 48 mos median F/U:
      - LC 78%
      - PFS 63%
      - OS 87%
What does this ALL mean?!

- Do numbers and charts result in patient outcome improvement?
- “Direct Radiation Complications Never Occur In Unirradiated Tissues”
Drawing Parallels

- Surgery: a tool where you would NOT damage any of tissues as you approach your intended area of resection.
  - Robotic assisted surgery

- Chemotherapy: an agent concentrated at the cancer and the not the rest of the body
  - Targeted therapy
  - Chemoembolization
## Pediatric Malignancies

### Complications Associated with Pediatric Radiation Treatment

<table>
<thead>
<tr>
<th>Complication</th>
<th>Protons</th>
<th>Photons</th>
</tr>
</thead>
<tbody>
<tr>
<td>Restrictive Lung Disease</td>
<td>0%</td>
<td>60%</td>
</tr>
<tr>
<td>Reduced Exercise Capacity</td>
<td>0%</td>
<td>75%</td>
</tr>
<tr>
<td>Abnormal EKGs</td>
<td>0%</td>
<td>31%</td>
</tr>
<tr>
<td>Growth Abnormality</td>
<td>20%</td>
<td>100%</td>
</tr>
<tr>
<td>IQ drop of 10 points at 6 yrs</td>
<td>1.6%</td>
<td>28.5%</td>
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Source: James Metz, MD, Abramson Cancer Center of the University of Pennsylvania
Savings of 23,200 Euro per year in long-term survivors
Dose Volume Modeling

- Whole Brain (IQ)
- Hypothalamus (Endocrine function)
- Temporal Lobe (IQ)
- Cochlea (hearing)

- IQ was modeled taking into account dose (mean and total) to whole brain and temporal lobe along with age and time interval
Dose Volume Modeling

- Whole Brain (IQ)
- Hypothalamus (Endocrine function)
- Temporal Lobe (IQ)
- Cochlea (hearing)

- Benefit seen in all patients across all parameters.
Parting Shots

◆ Take home points:
  • All cancers should be approached in a multi-specialty or multi-disciplinary fashion (drawing parallels)
  • Patient care should be performed in team approach:
    ◆ Concierge, Nurses, Therapists, Physics/Dosimetrists, Physicians
  • State of the Art Radiation Therapy @ CDH/Procure
    ◆ FULL Spectrum of Radiation Treatment options
      ◇ HDR Brachytherapy
      ◇ SBRT/SRS
      ◇ IMRT/3D CRT//IGRT
      ◇ Proton Beam Therapy
Parting Shots

❖ Research

❖ Proton Collaborative Group (PCG)
  ❖ Procure Proton Centers
  ❖ University of Pennsylvania
  ❖ Indiana University Health Proton Therapy Center
  ❖ McLaren Health Care – Flint, MI
  ❖ Washington University
  ❖ Walter Reed Army Medical Center

❖ International Sites
  ◇ Paul Scherrer Institute – Switzerland
  ◇ University Medical Center Groningen – The Netherlands
Parting Shots

❖ Research

❖ MGH Program Project Grant (NCI)
  ❖ In collaboration with MDACC
  ❖ Pediatric Registry Study
  ❖ Prostate Cancer
  ❖ Lung Cancer
  ❖ GI Cancers
  ❖ CNS Malignancies
  ❖ Head and Neck Cancers
Parting Shots

- Research
  - Children’s Memorial Hospital – Ann and Robert H. Lurie Children’s Hospital of Chicago
    - Children’s Oncology Group Trials
    - Pediatric Brain Tumor Consortium Trials
Parting Shots

- Photons/Electrons will still be needed.
- Brachytherapy will still be utilized.
- Image guidance will remain critical for all modalities of radiation therapy.
- Proton beam therapy can improve the side effects profile in many of the disease we currently treat with photon radiation.
- Research will validate this as another treatment option in our armament in our fight against cancer.