Where are all the Proton Centers?

David Raubach
AAMD 2017
Nashville, TN
An Okie in the Smokeys
It Costs More, but Is It Worth More?
By EZEKIEL J. EMANUEL and STEVEN D. PEARSON

If you want to know what is wrong with American health care today, exhibit A might be the two new proton beam treatment facilities the Mayo Clinic has begun building, one in Minnesota, the other in Arizona, at a cost of more than $180 million dollars each. They are part of a medical arms race for proton beam machines, which could cost up to a billion dollars for treatment that probably costs much less.

Publix, Florida Blue sued over denial for cancer treatment at Mayo Clinic

Mayo's proton beam therapy adds to debate over high-tech costs

Proton beam therapy zaps cancer but draws criticism for making care more costly.

By Dan Browning Star Tribune | MARCH 19, 2014 — 5:21AM
“Proton therapy can deliver its destructive energy to the targeted tumor while largely sparing the healthy tissue surrounding it....You also have to consider the costs to society of dealing with patients who have complications from conventional radiation therapy. **That alone makes any extra costs worthwhile.**”

- **Dr. Herman Suit** *(father of the MGH proton program)*

“To be fair to Herman [Suit], when he first came and talked about this, **he said there’s not a photon plan that he could not improve upon with protons and he was absolutely right.** So I have become convinced and am now at least as strong an advocate in support of his viewpoint as anybody. And then I realized, well, gosh, I mean, protons are a natural evolution of that progress going from 2-D to 3-D to IMRT and beyond, the natural progression of that I think is proton therapy and now IMPT.”

- **Dr. James Cox** *(father of the MD Anderson proton program; editor-in-chief of the Red Journal)*
The more you know about the past, the better prepared you are for the future

- *Theodore Roosevelt*
• Discovered the Proton
• Charged Particles will have a definitive range in a medium
• Bragg Peak
• First Cyclotron 1931
“Dr Livingston has asked me to advise you that he has obtained 1,100,000 volt protons. He also suggested that I add ‘Whoopee’!"

—Telegram to Ernest Lawrence, 3 August 1931

- The first cyclotron (January 1931)
  - Diameter – 4.5 inches
  - Energy - 80,000 Electron Volts (.08 MeV)

Ernest O. Lawrence – The First Cyclotron
“In the Radiation Laboratory we count it a privilege to do everything we can to assist our medical colleagues in the application of these new tools to the problems of human suffering.”

- Ernest Lawrence
“An American Genius”

Ernest Lawrence – inventor of the cyclotron and Nobel Prize winner, standing next to a 27” cyclotron at the Berkeley Laboratory (1932)
“I have read with much interest the newspaper accounts of your recent discovery....It would seem to me that with sodium chloride radioactive, it could be injected ...around a tumor and thus perhaps attack cancer where it is generalized.... Let me know what you think about this. I certainly think it might possibly be worth trying on an advanced case of malignant disease, and I would like to try it.”

-Dr. John Lawrence, 1934, in a letter to his brother Ernest Lawrence
“[Robert] taught us to build an accelerator to be modified with the ongoing developments of science, always looking ahead.”

-Physicist Timothy Toohig, U.S. Department of Energy

Wilson joined Berkeley Lab in 1936
German troops march through occupied Warsaw, Poland, after invading on Sept 1, 1939 and igniting WWII
Pearl Harbor

December 7th, 1941
"V.B.

OK – returned – I think you had best keep this in your own safe.

FDR"

- President Roosevelt responding to a proposal from Vannevar Bush, head of the U.S. Office of Scientific Research and Development, to begin production of an atomic bomb (Jan 19th, 1942)
“He hesitated only a moment. ‘If you tell me this is my job, I’ll do it.’”

- Arthur Compton on Lawrence’s commitment to a bomb project

“If ever the forces of darkness could be said to be lined up against the forces of light, it was at that time.”

- Robert Wilson, a pacifist, on his decision to join the war effort
“I learned of British measurements that indicated that a nuclear bomb could actually be built if a small quantity of U-235 could be separated from the more prevalent U-238. To my astonishment and horror, I invented a method of doing just that.”

- Robert R Wilson

Ernest Lawrence designed Alpha 1 racetrack utilizing cyclotrons to enrich uranium
“I determined at that moment that having played even a small role in bringing it about, I would go all out in helping to make it a positive factor for humanity.”

- Robert R. Wilson
“It will be easy to produce well collimated narrow beams of fast protons and since the range of the beam is easily controllable, **precision exposure of well defined small volumes within the body will soon be feasible.**”

**Radiological Use of Fast Protons**

ROBERT R. WILSON  
Research Laboratory of Physics, Harvard University  
Cambridge, Massachusetts
The First Proton Treatment

(above) E.O. Lawrence in front of a 60” cyclotron;
(right) Dr. John Lawrence using the 60” cyclotron to treat a patient
Proton Therapy Early History

• 1954 – First proton treatment at Berkeley Laboratory

• 1957 – First proton treatments in Europe at Uppsala in Sweden

• 1958 – First neurological treatments

• 1961 – Harvard treats first patient at the Harvard Cyclotron Laboratory (HCL)

• 1967 – First large field proton treatments in Sweden

• 1974 – First large field fractionated treatments - HCL
First proton treatments

What Wilson Proposed

First Treatments

- Lack of density information
- Treatment planning challenges
- Easy setup + verification

Portal X-Ray
The first scanner was installed in Atkinson Morley Hospital in Wimbledon, England, and the first patient brain-scan was done in October 1971. It was publicly announced in 1972.
Axial CT of the brain circa 1975

Axial CT of the brain modern day
Michael Goitein, while at MGH, develops:

1) 3D Treatment Planning
2) DVH’s
3) DRR’s
CT Scanning + Computerized 3D treatment Planning became available at MGH/ HCL

Figure 1-4 Patient treated at HCL over time indicating the growth and popularity of for patient treatments. Data adapted from reference [15].
Dr. James Slater with help from Dr. Robert Wilson develops the first hospital based proton center which opens in 1990
Illustration of US / DS

- Patient Contour
- Compensator
- Target Area
- Inhomogeneity (Air Pocket)
- SOBP extent
- Aperture

Diagram showing the components and areas related to US/DS technology.
Illustration of PBS

- Target Area
- Patient Contour
- Inhomogeneity (Air Pocket)
- Scanning Magnet
- Individually controlled pencil beams scanned across the target
- No high dose spots outside of Target Area
Advantage of Pencil Beam scanning

- PBS offers Proximal and distal beam shaping
- Dose outside the target (integral dose) is reduced significantly
- Reduction of integral dose even more significant for large targets

Dose Difference DS/US – PBS dose
Another Technology Jump → Robust Optimization
the “certainty” of proton dose delivery

• Evaluate the uncertainties in the dose delivered by a single spot +
• Give higher weights to those spots with less uncertainty
• Instead of setting margins – specify uncertainties – no need for a PTV
• Robust optimization is also referred to as “Inverse planning of Margins”
"Direct Radiation Complications Never Occur In Unirradiated Tissues"

“There is no advantage whatsoever to irradiating uninvolved healthy tissue”

Proton Therapy Reduces Esophagitis in Lung Cancer

MD Anderson Cancer Center Study

Proton Therapy vs. 3D CRT & IMRT of Locally Advanced NSCLC

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

Esophagitis Gr ≥ 3

- 3D: 15.0%
- IMRT: 35.0%
- Protons: 5.0%

Tx Related Pneumonitis Gr ≥ 3

- 3D: 35.0%
- IMRT: 20.0%
- Protons: 5.0%

Proton data from Chang, et al, ASTRO 2009 Abstract
Head and Neck – Reduction in Side Effects

Gastrostomy Tubes Decrease by Over 50% With Intensity Modulated Proton Therapy (IMPT) During the Treatment of Oropharyngeal Cancer Patients: A Case-Control Study


Purpose/Objective(s): A potential advantage of intensity modulated proton therapy (IMPT) over photon therapy (IMRT) in the treatment of oropharyngeal carcinoma (OPC) is a decrease in toxicity. The purpose of this study was to quantify the incidence of gastrostomy tube use in our OPC patients treated with IMPT and compare this to gastrostomy use in patients treated with IMRT.

Materials/Methods: The study design was case-control. Twenty-six patients newly diagnosed with OPC were treated with IMPT between 2011 and 2012. IMRT-treated controls were extracted from our database of patients with OPC treated between 2000 and 2009. Cases were matched based on the following criteria, in order: Unilateral vs bilateral therapy, tonsil vs base of tongue primary, T-category, N-category, concurrent chemotherapy, induction chemotherapy, smoking status, sex and age. Comparisons of categorical variables were done with the chi-square test, and the t-test was used for comparison of means.

Results: Twenty-six cases treated with IMPT were matched to 26 controls treated with IMRT. There were no differences between the groups on matching per laterality of therapy (21 bilateral; 5 unilateral), primary site (18 tonsil; 8 base of tongue), stage, chemotherapy [induction (IMPT-65%; IMRT-58%), concurrent (IMPT-50%; IMRT-58%)], smoking and sex, with exact matches on the first 3 variables. The IMPT

Proton Therapy for Oropharyngeal Tumors

• **58% REDUCTION** in feeding tubes when compared to IMRT

1Frank, SJ et al, MD Anderson, IJORBP 2014

Proton Therapy for Nasopharyngeal Tumors

• **60% REDUCTION** in feeding tubes when compared to IMRT

2Holliday, EM & Frank, SJ ASTRO 2014
Correlation between Heart Dose and Coronary Artery Disease

“Significantly higher rate of fatal and non-fatal diagnosis of coronary artery disease seen in left-sided patients compared with right-sided XRT”

Fig 2. Freedom from coronary artery disease. A significantly higher rate of fatal and nonfatal diagnoses of coronary artery disease was seen in left-sided patients compared with right-sided patients using Kaplan-Meier analysis.

Late Cardiac Mortality and Morbidity in Early-Stage Breast Cancer Patients After Breast-Conservation Treatment

Eleanor E.R. Harris, Candace Correa, Wei-Ting Hwang, Jessica Liao, Harold I. Litt, Victor A. Ferrari, and Lawrence J. Solin
Large Intact Breast with DIBH

- Protons
- Protons minus V-MAT 6 MV Photons
- V-MAT 6 MV Photons
- Protons minus V-MAT 6 MV Photons
Second Malignancy

Clinical Investigation: Late Effect

Incidence of Second Malignancies Among Patients Treated With Proton Versus Photon Radiation

Christine S. Chung, MD, MPH,* Torunn I. Yock, MD, MCh,† Kerrie Nelson, PhD,‡ Yang Xu, MS,§ Nancy L. Keating, MD, MPH,¶ and Nancy J. Tarbell, MD†,¶

558 proton pts treated from MGH (1973 to 2001) compared with 558 matched photon pts (SEER)

558 proton pts treated from MGH (1973 to 2001) compared with 558 matched photon pts (SEER)

Hazard ratio

=0.52

(CI 0.32-0.85, p=0.009)
7 of 10 Top Cancer Centers provide or are developing Proton Therapy

<table>
<thead>
<tr>
<th>Rank</th>
<th>Center</th>
<th>Proton Therapy</th>
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<tbody>
<tr>
<td>1.</td>
<td>MD Anderson Cancer Center</td>
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<tr>
<td>2.</td>
<td>Memorial Sloan Kettering Cancer Center</td>
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<tr>
<td>3.</td>
<td>Mayo Clinic MN &amp; AZ (2 Proton Centers)</td>
<td>✔️</td>
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<tr>
<td>4.</td>
<td>Dana-Farber Cancer Center</td>
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<td>5.</td>
<td>UCLA Cancer Center</td>
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<td>6.</td>
<td>Moffitt Cancer Center &amp; Research Institute</td>
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<td>7.</td>
<td>University of Washington Cancer Center</td>
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<td>8.</td>
<td>Cleveland Clinic Cancer Center</td>
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<td>9.</td>
<td>Johns Hopkins Cancer Center</td>
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<tr>
<td>10.</td>
<td>Univ. of CA – San Francisco Cancer Center</td>
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Rankings from U.S. News and World Report
2016 Top Cancer Hospitals
Proton Therapy Today

- Long Track Record of Safety
- Clear Clinical Benefit
- 100,000+ patients treated
- Refinement of treatment techniques
- Historical Precedent of adoption of new radiation technology based on DVH
Proton Therapy Industry Growth

Proton and Photon Rooms in the U.S.

~5,000 LINACs in the U.S.
"Well, I've got good gnus and I've got bad gnus."
Cost of Computing – A Decreasing Cost Curve

*Graph showing the decreasing cost of hard drives per gigabyte over time, with a steep decline from the 1980s to the 2010s.*

*Source: mkomo.com*
Proton Gantry and Cyclotron
The Solution

• Willingness of vendors to push down the cost curve

• Economies of Scale in Production

• Paradigm shift in treatment philosophy
Economies of Scale – The Model T
Proton Vendors

**EQUIPMENT**

- Varian Medical Systems
- Hitachi
- Pronova
- IBA
- Mevion Medical Systems

**DEVELOPMENT**

- Provision Solutions
- Proton International
- Proton Partners International
- Providence Proton
Seated Treatment Reduce Tumor Motion in Lung Cancer Patients

Figure 2: The amplitude of motion in the superior-inferior (S-I) direction for landmark points was plotted as a function of normalized distance to the diaphragm at end-exhalation for 20 volunteers. The vertical distance between the apex of the supine lung and the diaphragm was set to 1. A linear regression to these data indicates a reduction of tumor motion by 4.0 mm when the participant was in the supine position.

“Practically every one of our patients is saying ‘wow, it’s so much easier’”
Of 104 PBS treatments, all but 1 could be reproduced with FIXED geometry.
The Revolution over the next few years

From Harald paganetti
Conclusion

• Proton Therapy has been in continuous use since 1954
  • Well over 100,000 patients have been treated worldwide

• Proton Therapy has proven clinical benefit

• Proton technology continues to evolve
  • RBE Painting
  • In–vivo verification
  • Real time Adaptive planning

• Proton Therapy is still expensive

• Increased utilization, vendors pushing the cost curve, and a paradigm shift in treatment philosophy will bring down the price

• Proton therapy WILL eventually be the standard of care for most radiation therapy patients
“If I gave the people what they asked for it would have been faster horses.”
-Henry Ford