THE CUTTING EDGE: KILLING CANCER WITH PROTONS

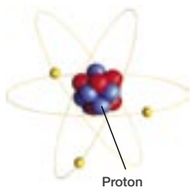
Proton therapy is one of the most intriguing developments in cancer treatment, offering new hope to patients around the globe.

by Patrick Perry

Like most patients when first diagnosed, Phil Thompson was in shock.

"It was such a dark, negative kind of day," Phil recalls. "Just the C–word is frightening to anyone."

Diagnosed with prostate cancer in 2004, Phil was presented with a variety of cancer treatment options—prostatectomy, seed implants, and a combination of seed implants and standard radiation. However, in an unusual twist of fate, Phil already knew his treatment of choice. It was called proton radiation beam therapy, a pinpoint-accurate form of radiation that delivers the exact dose of radiation needed to treat a tumor. Protons are subatomic particles that are accelerated by a device called a cyclotron to specific speeds in beams that penetrate the body. As positively charged protons enter the body, they slow down and interact with negatively charged electrons, releasing energy (also known as radiation).



Swords into plowshares: doctors are using the atomic energy of protons to treat disease.

Phil was very familiar with the cyclotron. He helped build it during his 30-year career. Today, the Indiana University Cyclotron Facility (IUCF) is home to the Midwest Proton Radiotherapy Institute (MPRI), one of only five such centers in the entire country.

After speaking with MPRI's medical director and his physician, Phil opted for proton therapy and began a six–week course of 44 treatments. Three years later, Phil remains cancer–free and an outspoken advocate for proton therapy.

Proton therapy is a pinpoint-precise form of treatment that radiates the tumor site, leaving surrounding healthy tissue and organs intact, unlike conventional x-ray radiation that often affects healthy tissue in its path.

First used to treat cancer patients half a century ago, research into proton therapy, coupled with significant technological advances, has made the science more focused—like proton therapy itself. The results are impressive. For example, use of proton therapy has turned a 90 percent fatality rate for patients with certain forms of brain tumors into an 80 percent survival rate. Today, researchers are discovering more and more applications for the lifesaving treatment.

To learn more about the promise of proton therapy, the *Post* spoke with Dr. Allan Thornton, medical director of MPRI and a nationally recognized radiation oncology expert.

Allan Thornton, M.D.
Medical Director of MPRI

***Post:* What are the unique attributes of proton therapy in terms of precision, side effects, and impact on surrounding tissue?**

Dr. Thornton: It is a fundamentally different and, we believe, better form of therapy for delivering radiation that reduces the side effects through the sparing of normal tissue. It is also a wonderful application of technology from the nuclear weaponry age brought down to the humanitarian level of peacetime applications.

At Harvard, we have used proton therapy for about 50 years. It is a very well-established therapy with greater precision in terms of delivery, resulting from the basic physics of the beam. We can aim it more accurately and, most important, we can stop or control the beam, which is important because we want to avoid treating normal tissue as much as possible.

***Post:* Does it differ dramatically from traditional x-ray radiation therapy?**

Dr. Thornton: It does—and from all other forms of irradiation used today, whether they be gamma knife, cyber knife or any of the other conventional x-ray-based radiations.

***Post:* For what forms of cancer is the therapy used?**

Dr. Thornton: Historically we treat tumors of the spinal cord or, more applicably, tumors of tissue around the spinal cord. These are tumors of the bone up and down the skeleton—the vertebrae. We treat tumors of the eye, base of the brain, under the skull, around the optic system, and tumors of the paranasal sinuses, in particular. We also treat a variety of pediatric tumors employing the unique characteristics of protons. Finally, we offer therapy for prostate tumors and rectal cancers, particularly ones that are considered unresectable, or difficult to treat, with traditional methodologies and surgery.

***Post:* Is the therapy curative? What are the cure rates among the different forms of cancer?**

Dr. Thornton: Absolutely it is curative. Most of our patients are curable, and we generally do not treat palliative patients. The cure rates at the Harvard Cyclotron Laboratory, when analyzed over a 35-year period, were 73 percent for the entire patient population over that length of time.

***Post:* Because it is used for both benign and malignant disease, could proton therapy work in cases like Mrs. Elizabeth Edwards?**

Dr. Thornton: If I understood the news reports correctly, Mrs. Edwards has metastatic breast cancer—I believe in the bone. Proton therapy certainly could be useful. In fact, I just saw a patient in whom the tumor eroded into the vertebrae and grew into the spinal canal right next to the spinal cord. We can give twice the dose you can maximally give with conventional therapy. Many patients have previously been treated with conventional therapy, and the tumors came back. They have no options at this point, but we may be able to re-radiate those patients with proton therapy.

In 2007, the Midwest Proton Radiotherapy Institute (MPRI) treated the first patient in the world using an industrial robotic patient-positioning system with a rotating gantry, so protons aimed at the tumor can enter the patient's body from multiple directions. Since 1954, when proton therapy was first introduced for human treatment, about 55,000 patients have been treated in the U.S. and around the world.

***Post:* Are physicians and clinicians simply not aware of this therapy, or is it that there are so few centers doing it?**

Dr. Thornton: Both statements are true. We are the third proton therapy center in the country; we started up in February 2004. We have been very quiet for the last three years because we have been treating under what we call a Food and Drug Administration IDE, so we have not been allowed to advertise.

But in general, patients and physicians in the Midwest are not aware of it because there was no proton therapy center here until 2004. Many physicians in New England know about the treatment because it has been present since 1961 in Boston. However, despite the relative nascency of Midwest Proton to the heartland, I have been very impressed with the appropriateness of the referrals that physicians in the Midwest are giving. They are right on target.

***Post:* What about colon, pancreatic, liver and brain cancers?**

Dr. Thornton: There are actually 130 different forms of brain cancer, each quite unique in its requirements. The bulk of these brain tumors are gliomas, tumors of the brain itself. Those have been frustrating to radiation oncologists and oncologists in general. We completed a trial at Massachusetts General in the 1990s during which we treated brain cancer patients to twice the amount of radiation ever delivered with conventional therapy, and we had very good results. The patients lived almost 2½ times as long as the longest trial to date—simply because we could administer a higher dose of radiation and confine it to the tumor with greater accuracy due to the physics of the beam. I intend to reincarnate that trial in the near future here at IU for patients in the Midwest.

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We have treated a patient with very early pancreatic cancer. Pancreas tumors are very frustrating and difficult because the pancreas is right next to the duodenum—the bowel—and that limits the dose of conventional therapy. But we have a technique using proton therapy that we believe can help patients with pancreatic tumors.

With regard to liver cancer, proton therapy is used much more in Europe and the Far East than in the United States. In Japan, they have seven proton facilities and are building six more. They have a high rate of primary liver cancer—tumors starting in the liver, not spread to the liver from the colon, as is generally the case in the United States. They use proton therapy for a large segment of that patient population with curative results, using very, very high doses of radiation. They are essentially doing radiosurgery with their proton beam. We have treated two patients like this here. We are also treating selected patients with metastatic disease from the bowel to the liver.

***Post:* Is proton therapy proving useful in treating macular degeneration?**

Dr. Thornton: Adult macular degeneration comes in two varieties: the dry and the wet (exudative) form. Proton therapy is used for only the exudative form. There was a completed trial at Loma Linda University, as well as at Harvard. In Indiana, we also treated 42 patients in the late 1990s. The trial was a positive trial, showing that it was effective for exudative AMD. The trial is complete, and they are analyzing the results. Ophthalmologists are looking at the data very critically before they weigh in positively, but

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it does appear it is able to stop the exudation of the degeneration. It may be something we offer, but we are not ready as yet to treat routinely.

Post: **What are the general eligibility criteria for proton therapy?**

Dr. Thornton: You need to have a localized tumor. It needs to be generally in one spot, so we can address and cure the tumor by treating that location. There are exceptions. We do treat metastatic disease, but for the most part, we try to limit ourselves to curative patients who have a good quality of life because they need to come daily for the treatments over potentially a long period. Some patients require as many as 45 treatments; some as few as four or five. Generally, it is a four- to eight-week course of treatment.

The patient needs to be somewhat flexible to get onto the table and work with us, because we use a tremendous amount of exactitude and verification in our process. We use an industrial robot to move our patients around the beam. We are the only place in the world that has an industrial robot coupled with a gantry—a large device that rotates the beam around the patient.

Frankly, I also spend a great deal of time with my patients, because I want them to understand what we are doing and to truly understand their disease. We want a truly well-informed patient. Those are the main criteria. There is no age restriction. Twenty percent of our patients right now are children. Our patient population ranges from babies to very spry 95-year-olds.

Post: **Is planning the treatment time consuming?**

Dr. Thornton: What I do is computer-aided design of people—CAD. It is similar to building a car part or an engineered part in industry. Basically, I do the same technology employing the human skeleton and anatomy. Protons are even more challenging in that my physicists have to generate a true three-dimensional perception of where the tumor is located and calculate how that proton is going to scatter in all three dimensions. Many of the tumors I treat are literally adjacent to critical structures, so they have to verify and prove that they have a good model to explain that scattering. That process may take up to a month in challenging cases.

Post: **Why is this therapy so beneficial to the pediatric population?**

Dr. Thornton: First, we do not like treating children with radiation. If we have to, we want to do it in the kindest, gentlest way that treats the absolute least of normal tissue as possible. That is important for a couple of reasons. First, we are realizing the potential for radiation to cause tumors later in life, as with chemotherapy. Fifteen years ago, we thought the risk was small, but now we're realizing that the risk may be as much as three percent over 20 to 40 years after treatment. Many children will go on to live normal lives and potentially realize that risk. With that understanding, proton therapy treats, on average, one fifth the normal tissue that even the most elegant of standard therapy treats. My common sense tells me that significant savings of normal tissue will translate into a significant savings of second tumors over the lives of these children.

Secondly, children obviously have not grown. For example, one of the side effects of treating young patients with eye tumors is that their cheekbones do not grow afterwards. When they become adults, they have sunken faces, misshapen foreheads, and eye sockets as a result. We have a better way of treating the tumor with radiation. We treat them in a way that avoids the cheekbone. It spares that bone so that it develops proportional growth.

Post: **How many centers are in the United States, and how many are planning to build facilities like yours in the near future?**

Dr. Thornton: Now there are five centers in the United States. We are the third; the fourth was M.D. Anderson Cancer Center in Houston, and the fifth facility was built at the University of Florida, in Jacksonville, Florida.

Interestingly, the first cyclotron was built at Harvard University in 1937, and it was decommissioned and moved to Los Alamos, where it made the plutonium for the first three atom bombs in 1939 through 1945. Its replacement was built in 1946, and I used that machine to treat my patients in the 1990s at Harvard.

In 1975, the Indiana University cyclotron was built to take over from the Harvard cyclotron for high-energy physics research in the United States. It has provided many years of successful physics investigations, and now has been modified to treat patients.

Post: **How many people is your facility capable of treating in the course of a day, and how many are on a waiting list?**

Dr. Thornton: Until just recently, we have been limited by the fact that there has only been one physician, and we have been treating in only one room. Right now, we are treating 15 patients a day. Realistically, when we are fully built out in two to three years, we will be capable of treating 75 patients a day. As far as a waiting list, it has varied anywhere from one month to six months or longer, depending on our throughput. We are averaging a month or two, which is pretty standard across the industry.

Post: **The therapy sounds so promising. Why aren't more facilities popping up?**

Dr. Thornton: It is a reflection of our medical economics system as much as anything else. Our country is not set up to distribute and share medical resources on a regional basis. Every hospital tries to do everything. These are very expensive facilities that each country in Europe or Japan has, and shares. The Midwest Proton Radiotherapy Institute is intended to be a regional resource, a shared resource by a number of university and pediatric hospitals in the country. The short answer to your question is, it is a high-cost capital investment and, up to this point, has been a little too large for hospitals to afford. But that is changing. It is a reflection of changes in the economics of the healthcare system, and the lowering of technology costs.

Post: **If people would like to learn more, how would they get in touch with the facility?**

Dr. Thornton: Our telephone number is (812) 349-5074. Or they can go to the website at www.mpri.org.