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CONTENTS

Deadly Accuracy

BY KATY HUMAN

Proton beam therapy kills cancer cells without the collateral damage of traditional radiation.

Skin burns. Second cancers. Sterility.

The possible side effects of conventional radiation therapy are frightening. It's a potent weapon against cancer, physicians say, especially with today's technical advances, and it's less damaging to healthy tissues than it was 10 years ago.

But an accumulating pile of studies are drawing attention to an older radiation treatment that pounds cancer with far more energy at the tumor's exact location than conventional radiation and saves normal tissues from extensive injury. It's called proton beam therapy, and medical experts call it the next generation of radiation therapy.

Despite its modern precision, proton beam therapy has actually been around since the 1950s, when physicists began to understand the compelling differences between proton beams and intense X-ray beams, called photons, used in conventional therapy. Those differences let doctors control the depth of proton beams more precisely and deliver more cancer-killing radiation to tumors—a particularly appealing effect for discrete tumors of the eye and for treating children, who are most vulnerable to the damaging side effects of radiation. Proton beam therapy is also used to treat some prostate, brain, lung, esophageal and head and neck cancers, among others.

"I don't love military analogies, but it really is like having a smart bomb. You can avoid collateral damage," says James Cox, MD, head of the radiation oncology division at M.D. Anderson Cancer Center in Houston and medical director of its new Proton Therapy Center.

Physics and Cancer

Protons are minute particles with a positive charge, accelerated to great speed by

equipment once familiar only to research physicists. Because protons have mass, they work on impact with the tumor and don't travel all the way through the body.

Conventional X-rays are a form of electromagnetic radiation with short wavelengths. Without charge or mass, X-rays irradiate cells continually as they pass through the body, delivering injury both at the surface of the body where they enter, and in tissues behind the cancer.

"Protons are different. Their dose is deposited with a burst of energy where you want it—in the tumor," Dr. Cox says. "The location is determined by the energy of the proton beam."

Doctors can determine exactly where they want to deliver the bulk of the cancer-busting power of protons. By accelerating protons to different speeds, they can target a tumor just under the surface of the skin, or one deep inside a body cavity. Some call this the "depth charge effect," because it's akin to dropping a bomb into the water, and determining the precise depth at which it detonates.

Although side effects are still possible, they are considerably less intense than with conventional radiation and are far less likely to be long-term. More common symptoms include skin irritation and hair loss in the direct path of radiation, and fatigue if a large area is treated. Loss of appetite, diarrhea and headache occur more rarely. Proton beam therapy is also used in combination with other cancer treatments that carry their own side effects.

Last summer, M.D. Anderson opened its $125 million proton beam therapy facility following three years of construction and testing, and Dr. Cox says the patients are flowing in. Officials calculate the center can accommodate 3,500 cancer patients a year.

Today, cancer patients with the "right" kind of tumor can receive proton beam therapy in six centers in the United States: M.D. Anderson in Houston; Loma Linda University Medical Center in California; the Midwest Proton Radiotherapy Institute in Bloomington, Indiana; Massachusetts General Hospital in Boston; the University of Florida Proton Therapy Institute in Jacksonville; and the University of California Davis Cancer Center in Sacramento (offered only for patients with ocular melanoma). There are more than 20 proton beam therapy facilities elsewhere around the world, and at least six other medical centers have plans to open the expensive facilities in Philadelphia, West Chicago, St. Louis, Seattle, Oklahoma City and Hampton, Virginia.

Popularity Boost

The Food and Drug Administration approved proton beam therapy as a cancer treatment in 1988, and most medical insurers cover proton beam treatment for specific cancers. So why all the fuss now?

Jerry Slater, MD, chair of the radiation department at Loma Linda, which has been treating cancer with proton beams since 1990, says the current excitement is a byproduct of better imaging techniques that are finally accurate enough to let

physicians take advantage of the precision of proton beam therapy.

“You could have done proton therapy in the ’50s if you had PET (positron emission tomography) and MRI (magnetic resonance imaging),” Dr. Slater says, referring to two key imaging methods. Those images let doctors understand the three-dimensional structure of a tumor, which is necessary for guiding proton beams to exactly the right place. “It’s also just such a high-tech thing. There was a perception you couldn’t do something this complicated in a hospital. We believed it could be done, and showed it.”

Long-term clinical studies are finally being published that demonstrate the effectiveness of proton beam therapy. Studies have shown doctors can use proton beams to control ocular melanomas while letting many patients retain vision; to control acoustic neuromas while avoiding nerve injury; and improve survival rates from chordomas and chondrosarcomas of the skull base, among many other results.

For the more common cancers, such as prostate cancer, studies indicate proton beam therapy offers about the same tumor control as X-ray radiation. Dr. Slater expects studies will soon demonstrate improved survival. “Start with a better treatment and you’ll get better outcomes,” he says. “There’s going to be a lot more [data]. We’re still in our infancy.”

Six years ago, when Bob Marckini’s doctor called to tell him he had prostate cancer, Loma Linda was the only medical center in the United States offering proton beam therapy.

Marckini, 57, had just watched his brother go through surgery for prostate cancer. “I was scared to death,” Marckini says of seeing his brother in the recovery room after surgery. “He was the patriarch of our family. Strong, healthy and athletic. I watched him go through his slow recovery.”

Bob Marckini chose proton beam therapy to treat his prostate cancer because of its lower risk of side effects. Photo by Andy Gallagher

With his own prostate cancer diagnosis, Marckini dug into medical literature and sought advice from doctors and prostate cancer patients who had undergone a variety of radiation therapies, including conventional X-ray therapy, intensity-modulated radiation therapy and brachytherapy. Although each therapy

seemed to have an equal chance of getting rid of the cancer, proton beam therapy was non-invasive and by far promised the fewest side effects. For instance, more than 60 percent of prostate cancer patients suffer impotence after conventional radiation compared with 30 percent after proton beam therapy.

After 10 weeks of research, Marckini traveled from his home in Massachusetts to California for proton beam treatment. He's now cancer-free and has created an online support community for prostate cancer patients at www.protonbob.com. The only side effect he experienced was temporary rectal bleeding after radiologists irradiated the healthy cells in a thin margin around his prostate to catch stray cancer cells. Since this area of the body houses organs close together, some radiation can reach the inside rectal wall.

Proton beam therapy is not appropriate for all cancer patients. In a series of papers published in *Acta Oncologica*, Swedish doctors estimated proton beam therapy would benefit "one in seven patients for whom radiation therapy is indicated."

Its power lies in its precision, so proton beam therapy typically can't help patients whose cancers have metastasized, or those with diffuse tumors. But for isolated tumors, studies have shown proton beam therapy is at least as powerful as its conventional radiation counterpart without damage to sensitive structures near a tumor. And because side effects often limit the ability to deliver strong radiation doses by X-ray, proton beam therapy often means more powerful doses can be delivered at one time, which may mean fewer treatments.

Pediatric patients' developmental stage makes them particularly vulnerable to the side effects of radiation, so researchers are excited about the possibilities of proton beam therapy in children.

Dr. Cox says proton beam therapy is especially promising for children. Pediatric patients' developmental stage makes them particularly vulnerable to the side effects of radiation, including later cancers induced by treatment, so researchers are excited about the possibilities of proton beam therapy in children. The technique has shown tremendous success in pediatric head and neck cancers, in particular, increasing tumor control and survival.

Over the past decade, key improvements to conventional X-ray therapy, specifically three-dimensional conformal X-rays and intensity-modulated radiation therapy, have increased dose delivery to tumors and lessened side effects. "The same things are going to happen with protons," Dr. Slater says. "Everybody's goal is 100 percent of dose delivery to the tumor, zero elsewhere."