FEATURE STORY

A Direct Hit

BY MELISSA KNOPPER

Technology propels radiation therapy to a new status: targeted therapy.

Five years ago, Alvaro Martinez, MD, a radiation oncologist at Beaumont Hospitals in Royal Oak, Michigan, was attending a medical conference in Dearborn when he happened to wander into the wrong conference room. There, he found a group of Ford Motor Company engineers talking about how to check for defects in engine blocks with CT (computed tomography) scans.

Martinez, who had been looking for a way to improve radiation therapy, had a brainstorm. Today, Beaumont cancer patients are benefiting from that idea: The $3.3 million Omnibeam is helping doctors treat hard-to-reach tumors deep inside the body. The machine combines a powerful CT scan with robotic technology that automatically adjusts for movement—the way a patient's chest rises and falls while breathing, for example.

Beaumont radiologists like Frank Vicini, MD, treat a tumor with much more confidence than they have in the past. "The Omnibeam's robotic couch moves the patient in unison with the beam," Vicini says. "So it really affords you tremendous precision."

In the past, radiation oncologists radiated a broad volume of tissue—both healthy and cancerous—to make sure they didn't miss any stray cancer cells, explains Robert Kuske, MD, a Scottsdale, Arizona, radiation oncologist. In the process, healthy tissues were at risk for side effects or complications just because they were in the way of the radiation beam. Treating cancer in the pancreas, for example, could cause bowel problems.

Researchers knew they needed to innovate—to hit their targets more precisely and avoid excess damage. Doing so would cut down on side effects for the patient and allow dose escalation to prevent recurrence.

Now, cancer patients are seeing the benefits of cutting-edge (although costly) radiation technology. Instead of relying solely on external treatments that send radiation into the body from an outside source, radiation oncologists now have newer techniques that target cancer cells from inside the body. Plus, new imaging techniques and devices, as well as various forms of energy, are allowing physicians to deliver radiation in a more precise way that is making life better for patients.

“[These innovations] bring a decrease in side effects, an increase in quality of life. And it’s more user-friendly for the patients,” Kuske says. “It is indeed a very exciting time.”

High-Tech Machines

Research has pointed to the great need for new and better technology. One study of 803 patients with cancer of the prostate, head and neck, or brain showed patients given external beam radiation therapy routinely received the wrong dose. Results showed 46 percent of the patients were given 10 percent more radiation than physicians had intended, while 63 percent received 10 percent less than the prescribed dose.

Plus, the long-term side effects of external beam’s broad coverage approach can be serious, especially for patients with cancer in the left breast. “In the past, the radiation beam penetrated the anterior surface of the heart in order to cover the entire left breast,” Kuske explains. “It exposed a coronary artery to full doses of radiation, increasing the risk of fatal heart attacks 10 to 15 years later.”

These challenges led to a new way of thinking about radiation treatment, starting with three-dimensional conformal radiation therapy (3-D CRT), the first innovation to address the need for a more precise dose. Using digital imaging—typically with computerized tomography (CT)—the treatment team creates a three-dimensional image of a tumor inside the patient’s body. A virtual computer model lets technicians try out different angles and different doses to make sure they will be able to hit the target without damaging healthy tissue. Finally, they aim several powerful beams of radiation at the tumor. By attacking it from different angles, they decrease the chance the cancer will return.

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Intensity-modulated radiation therapy (IMRT) takes 3-D CRT a step further. With IMRT, physicians can choose a different number of beams and set them at different angles, but they can also adjust the intensity of the dose. When treating prostate cancer with IMRT, for example, radiation oncologists use as many as 36 beams (compared with four using traditional techniques) to match the shape of the prostate and miss the bladder, avoiding future problems with incontinence. One example of IMRT is TomoTherapy, a CT-like machine with a radiation source that moves around the patient in a circle as it hits the tumor with thousands of tiny beams, or beamlets.

James Cox, MD, head of the radiation oncology division at M.D. Anderson Cancer Center in Houston, has already seen positive results from this new 3-D technology, especially in lung cancer. Cox says the facility's three-year survival rate for non-small cell lung cancer has approximately doubled since 3-D CRT and IMRT became available. Three-dimensional radiation therapy is also particularly suited to prostate cancer and certain brain tumors.

Many of the nation's largest cancer centers are investing millions of dollars in similar machines, such as CyberKnife and Gamma Knife. With this technology, known as stereotactic radiosurgery, surgeons use high-dose X-ray beams or laser beams to treat tumors without making an actual incision. The beams are guided by digital imaging. These techniques are also used for patients who need surgery in areas such as the brain and spine.

Harnessing Energy Sources

The exciting thing about all of these new delivery methods, says Cox, is they can be used with different types of energy sources. For example, external beam radiation therapy uses both X-rays and electrons. But now, more facilities, such as M.D. Anderson, are experimenting with proton beams as well.

The benefits of proton beams have been clear for many years now, Cox says, but it hasn't been possible to transfer the technology from physics research facilities to hospitals and cancer centers until recently. M.D. Anderson invested $125 million to build its proton therapy center, which opened in 2006, and Cox feels it was well worth it.

"What we're seeing with these advances and new technologies is we can give higher doses and get better tumor control with less side effects," he says. "We wanted to chart a course for the future, not wait for the future to catch up with us."

With traditional external beam radiation, X-ray beams hit the target but then pass all the way through the body, leaving a trail of damage behind them, Cox explains. Protons, by contrast, hit the tumor and stop, making proton beam therapy much safer for pediatric cancer patients and for patients with brain, prostate, or lung cancer. Pediatric patients, for example, have less risk of secondary cancers, infertility, and bone deformity later in life. Avoiding normal tissue is important in children, Cox says, because growing structures, like bone and soft tissue, are very susceptible to radiation damage.

A typical complication of external beam radiation for lung cancer is pneumonitis (inflammation of lung tissue), a potentially life-threatening problem. By using IMRT, M.D. Anderson physicians cut the rate of pneumonitis to 9 percent. Now, with proton therapy, Cox has seen no cases of pneumonitis so far. "It's hitting the target and avoiding normal lungs better," he says.

View Illustration: Radiation Manipulation

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Besides M.D. Anderson, at least five other hospital-based facilities in the United States offer proton therapy, and nearly a dozen new centers are in the works. Beaumont Hospitals just received state approval to build one on its Royal Oak campus.

Heat and light are other energy sources being explored as treatment. Protons and electrons are examples of ionizing radiation, while heat and photodynamic therapy are non-ionizing, meaning they cannot disrupt chemical bonds and cause DNA mutations.

Through various studies, researchers have shown the therapeutic use of heat, or hyperthermia, has an additive effect in radiation. Health care providers increase the body temperature by using energy sources such as microwaves, ultrasound, or radiofrequency energy. While studies are not conclusive on the benefits of hyperthermia, some believe it can alter the proteins in cancer cells and make them more susceptible to traditional radiation therapy.

Photodynamic, or light, therapy often uses lasers, fiber optics, and light-sensitive drugs, to treat a variety of cancers, including skin, brain, and gynecologic. Photofrin (porfimer), a drug used in photodynamic therapy, is absorbed by cancer cells and becomes briefly activated when exposed to light. The cancer cells are killed, and damage to normal cells is minimized. Light sensitivity can be a side effect of Photofrin, so patients are usually advised to avoid sunlight until the drug is out of the body.

Looking Inside

While external approaches began to take shape, physicians also started to look for internal solutions. Intraoperative radiation therapy is a newer type of internal radiation that helps patients who have a tumor that cannot be completely removed because of its location in the body (near the heart, optic nerve, or brain). During surgery to remove the tumor, radiologists aim an electron beam at the remainder of the tumor.

Physicians can also place radioactive material directly inside the body that emits a type of radiation that only travels a few millimeters, a technique called brachytherapy. Arizona’s Kuske and Beaumont’s Vicini were among those who experimented with placing tiny pellets of radiation, or “radioactive seeds,” directly into the surgical cavity after tumor removal.

Brachytherapy has led to advances in prostate cancer, such as TheraSeed, and multicatheter interstitial brachytherapy for breast cancer. More modern breast cancer techniques include MammoSite (see illustration), Contura balloon catheters, and expandable, single-entry strut catheter devices.

View Illustration: The MammoSite Method

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Another form of brachytherapy called radioembolization uses tiny glass spheres smaller than a human hair that are filled with radioactive compounds. The tiny bubbles can move into the circulatory system and shut down the blood supply to a tumor deep inside the liver.

Brachytherapy, however, is not a new science, Kuske points out. The British surgeon Sir Geoffrey Keynes (younger brother of economist John Maynard Keynes) offered patients brachytherapy for several years in the 1920s when the only delivery choice was radium seeds or needles, Kuske says.

Keynes' work with this new technique halted during World War II, when fears that his lab would be bombed caused him to bury all of his radioactive -materials in the English countryside.

Since then, Kuske, Vicini, and others have turned to brachytherapy, which they consider the ultimate precision conformal radiation delivery method, in their search for a potentially better way to treat breast cancer. Kuske realized physicians were already using an abbreviated form of brachytherapy by giving patients a "boost" with radioactive needles to intensify external beam radiation treatment at the lumpectomy site.

"In 1991, we got the idea to do the whole thing with brachytherapy for select breast cancers," says Kuske, who was working in New Orleans at the time. "With the help of two prominent biologists, we figured out the dose, and the rest is history."

Kuske estimates half of his early-stage breast cancer patients opt for lumpectomy and partial breast irradiation, a five-day alternative to conventional six-week external beam whole breast irradiation. In partial breast irradiation, physicians typically use brachytherapy as the method for delivering radiation.

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Partial breast irradiation, however, remains open to debate as researchers and physicians anticipate definitive data from several phase III clinical trials now under way. Current data suggest the technique is as effective as standard external beam whole breast radiation, but the small number of patients followed for limited lengths of time hinders a definitive conclusion.

Another new trend in breast cancer is hypofractionated radiation, which gives patients the option of taking a stronger dose of radiation in about half the time as the standard treatment schedule. Most physicians use external beam radiation for this type of treatment.

Hypofractionated radiation has been popular in the United Kingdom and Europe for years, but is just now catching on in the United States. A study presented at last year's San Antonio Breast Cancer Symposium revealed 12-year data that showed the recurrence rate for early-stage breast cancer patients was about the same with hypofractionated radiation (6.7 percent) compared with the standard schedule (6.2 percent). Despite the appeal of more convenient treatment, American physicians are still concerned about the cardiac risks of irradiating the left breast with strong doses.

They borrowed ideas from the auto industry and revived an old technique from the past, and now, radiation oncologists must continue to find new energy sources and better ways to deliver radiation therapy. The buzzword for the future is synergy—combining radiation with other treatment methods and other specialties to shut down cancer growth from different angles.

"Across the spectrum of many types of cancer, we're now going to more targeted therapy," Kuske says. "We're targeting the dose just to the tissues at risk. In other words, we're getting better at avoiding collateral damage."