

Doctors try heat treatment for tumors

Ultrasound and electrical heating seem to help some cases, in conjunction with other therapies

By Peter Bates
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In Cambridge, a woman's neck tumor has been markedly reduced, allowing her to swallow on her own for the first time in years.

In St. Louis, a man's recurrent larynx tumor was treated externally and disappeared — perhaps for good.

And in Boston, two lung cancer patients have lived three years longer than doctors expected because of a new "whole body" treatment along with conventional radiation.

These apparent successes all resulted from hyperthermia — the selective heating of parts of the body using ultrasound or electromagnetic devices. But it's still too early to tell whether the process has actually cured these patients. And the possibility of toxic side effects has not yet been completely assessed.

The American Medical Association's Data Panel stresses the experimental nature of the work, saying: "The clinical use of whole body hyperthermia in combination with radiation therapy or chemotherapy is still at an early stage of investigation." And some experts in the field, such as Bruce Chabner, director of cancer treatment at the National Cancer Institute, are pointedly skeptical: "[Presently] we don't have a specific disease we can point to that can be cured by it."

Nevertheless, many of the medical researchers



Dr. Padmaker Lele of MIT demonstrates his "sonic lens" ultrasound device, which he says can apply heat to tumors several centimeters below the surface.

involved have been greatly encouraged by recent results — data they contend augurs well for future cancer treatment.

"Many patients have died from cancerous tumors, despite available surgery, chemotherapy, and sophisticated radiation therapy," said one leading advocate, Dr. Padmaker Lele of MIT's Department of Mechanical Engineering. "Eighty

percent of cancer-related deaths are from tumor invasion. Decrease of localized tumors is essential."

One study by Lele, published in 1982 in the *British Journal of Cancer*, involved 43 terminally ill patients from four Boston hospitals who had not improved with use of traditional chemotherapy, radiation, and surgery. Six of them reported a 100 percent regression of the tumor treated with hyperthermia; in 20 patients there was more than 50 percent regression; in six there was less than 50 percent; and in four there was no regression. But even in some of the tumors that persisted, no cancer cells were found in biopsy after treatment. The malignant cells had been replaced by scar tissue.

Hyperthermia apparently works because of a combination of two factors. First, invasive tumors have a constricted blood flow because they compress the very vessels that nourish them, and heat treatment uses this trait against itself: the heat stays in the tumor longer because of its poor circulation, thereby increasing the chances of killing the tissue. Second, tumors die at temperatures 1 to 1½ degrees centigrade lower than that which would kill normal cells, so applying just the right amount of heat can kill cancer cells while leaving the surrounding tissue intact.

In addition, hyperthermia seems to increase

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Heat treatment

Hyperthermia tests are promising, but still highly experimental

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the body's own natural immune-system response, perhaps because of the accumulation of dead tumor tissue. This is in sharp contrast to most conventional therapies, such as radiation and chemotherapy, which suppress the immune response.

There are several different methods currently being used to produce the heating effect in experimental hyperthermia programs:

- Ultrasound, when set at frequencies ten times higher than that used to determine the shape of a fetus in the womb, produces heat. Normally, it does not penetrate far enough to deal with deep-seated tumors, but MIT's Lele has developed a way of focusing the heat in order to get deeper penetration.

- Radio waves can also be used to induce heat. In one such device, used for whole body hyperthermia, patients are put inside a specially-constructed chamber with their heads sticking out. They lie on top of a foam mattress that has a radio-wave induction coil running through it. According to Dr. H. Maddock Jones of New England Medical Center, "this setup warms the blood in the main vessels to "fever temperatures" of 102-103.

- Another method of producing whole body hyperthermia is by heating the blood externally and then returning it to the body. A tube, inserted in the thigh between the femoral vein and artery, is hooked up to the heating system. Blood flow passes from the artery to the heat exchanger, where it is warmed to 108 F. The blood is pumped back into the patient, where it warms the main vessels first, then the entire circulatory system.

- Another form of hyperthermia involves small microwave antennae inserted into a brain tumor. These "interstitial" antennae can heat a small tumor at microwave frequencies (about 900-1500 MHz). Since the heat is only produced within 5 millimeters of the antenna, which is about the size of a hypodermic needle, several are often used for larger tumors.

Combining methods

With all of these new techniques, if they are found to be effective it appears that they will be used primarily in concert with lower doses of chemotherapy and radiation, a synergistic partnership that could also help to alleviate such common side effects as nausea, bone marrow damage, even psychological stress.

As dramatic as these methods seem, it's important to realize that although ultrasound is new, heat treatment for tumors is not. As far back as 2000 B.C., healers reported the beneficial effects of elevated body temperature. Hippocrates tells of tumors that disappeared when he applied red-hot irons. Fifty years ago, doctors treated skin cancer with water bottles and inverted lamps.

But it wasn't until a decade ago that heat-therapy research began in earnest. Physicians found that when used in combination with chemotherapy or radiation, hyperthermia raised some cure rates sharply.

The key to the experimental ultrasound therapy used by MIT's Lele is a machine using a brass alloy "sonic lens" he designed, which focuses the ultrasonic waves from a transducer to achieve a high concentration of heat in a tumor

in much the way that light waves are converged by a magnifying glass. It can be applied accurately enough, says Lele, that the waves can be pinpointed on a tumor several centimeters below the surface without overflowing into healthy tissue.

Constant motion

His ultrasonic transducer looks like a high-tech Rube Goldberg device. About three times the size of a dentist's drill, it hovers over the patient's affected site, separated by a large polyethylene water bag. The bag cools the surrounding tissue and transmits the ultrasonic waves. Since ultrasound would produce too much heat if it remained in the same place for twenty minutes, Lele and his technicians use a computer to move the device through a programmed route around the area occupied by the tumor. Lele and his colleagues have determined and plotted the path the transducer will follow via a three dimensional "map" provided by CAT scans of the tumor. Lele refers to this procedure as "steered ultrasound." Thermal probes are inserted into the site to make sure the temperature does not exceed the desired 105.5 degree Fahrenheit temperature.

Although Lele has not discovered any significant side effects or toxicities from focused ultrasound, he has run into its limitations. It treats liver, pancreas, kidney, bladder, head, and neck tumors, but fails with bone and lung tumors, as it cannot pass through solid bone or porous organs, which tend to dissipate the vibrations. For these complicated tumors, hyperthermia can only be achieved by heating the whole body.

According to Dr. Frederic Gibbs of the University of Utah's Department of Radiation and Oncology, there are side effects from some forms of hyperthermia treatment, but they lie more with the individual machines than the treatment itself. For example, one electromagnetic prototype under investigation for lung and abdominal tumors is potentially dangerous. Some patients have received severe burns; a few have even gone into shock from this device, which surrounds the body.

Dr. Joan Bull of the University of Texas Health Science Center also points out hyperthermia's possible risks. Under some circumstances, the blood can coagulate, causing dangerous clots. Also, at high temperatures the veins dilate and the body is in a hypermetabolic state: it craves oxygen, its heart rate increases, and muscles get weak. Patients are often exhausted for days following treatment.

"I don't want this thing to sound like the greatest thing since mother's bread," Bull said. "But I would like to see it as a multi-pronged approach against very difficult solid tumors."

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