

News

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***Hyperthermia studies focus on advanced local tumors

DALLAS—Hyperthermia -- the use of heat to help kill cancer cells -- is the latest weapon researchers here will be using in their fight against the disease.

Researchers at The University of Texas Health Science Center at Dallas recently received Food and Drug Administration approval to begin using hyperthermia in combination with drugs in patients with advanced localized tumors. Studies will focus on head and neck tumors and other solid tumors which do not respond well to more conventional treatments such as surgery, chemotherapy or radiation.

Called the fourth modality of cancer therapy, hyperthermia research has become widespread throughout the country during the last decade. There is a strong biological rationale for its use, particularly in combination with other modalities, says UTHSCD physicist Dr. Peter Antich.

Extensive research has shown that combined with standard forms of treatment, hyperthermia is having a strong beneficial effect in some cancer patients. "Study upon study has shown that by adding hyperthermia to radiation you almost double the complete remission of a broad spectrum of tumors," says Antich. "As currently applied, it's a local form of treatment so you can't always talk about cures, but the tumor does disappear in a much larger proportion of patients."

Cancer specialists at the health science center hope their studies will bring out information regarding the proper application of hyperthermia with anti-cancer drugs -- an area that is still in the experimental stage. To do this they will be carefully measuring the effects of hyperthermia in all patients. "The clinical protocols were approved so we can study how best to use hyperthermia with radiation or chemotherapy or both to optimize control of these locally advanced tumors," says Radiation Oncology Director Dr. Daniel Flynn. "We don't know what dose and time sequence between hyperthermia and radiation will work best. We know there is an advantage and we want to maximize that advantage."

The radiation oncology group, consisting of Flynn, Antich and Dr. Phuc Nguyen, will be working with Ear, Nose and Throat surgeons Drs. Steven Schaefer and Lanny Close and Cancer Center Director Dr. Eugene Frenkel in the studies.

Flynn says many patients will come from Parkland Memorial Hospital, UTHSCD's teaching hospital. "At Parkland many patients have far locally advanced cancer at the time the diagnosis is made. Many times it is not operable so surgeons look for alternative treatment. Sometimes they have received chemotherapy and radiation to the maximum limit and there's still a lot of tumor left behind. So in the past there has been nothing else to offer," he says.

(Over)

Hyperthermia is not the preferred treatment for all kinds of cancer. To date it has been used mostly for solid tumors such as carcinoma, sarcoma and melanoma, according to Nguyen, who will be heading up the hyperthermia unit. Hematology (blood) tumors, which include leukemia, lymphoma and myeloma are more widespread in the body and thus more responsive to chemotherapy, drugs which work on the whole system versus a region.

"Most patients don't have locally far advanced cancers. For every 100 patients we treat in radiation oncology, I would say 10 would be candidates for the combined treatment with hyperthermia," says Flynn. For instance, with some advanced cases of breast cancer, the tumor is too big to remove surgically. Radiation may give an incomplete response, first shrinking the tumor down, allowing it to stay stationary and then it may start to grow again. Too much radiation can cause scar tissue and other damage to the body.

Hyperthermia would not be used for patients with small tumors whose cancer responds well to standard treatments. "With early tumors results with radiation or surgery are well established, we can't improve on that," says Nguyen.

"It would be foolish to look at patients with small tumors because those patients do well already," Flynn explains. "If there's a 90 percent chance of curing these patients with standard methods, it would be difficult to measure benefits from an added method. But if a patient only has a 10 or 20 percent chance of living or having a response, we would be able to offer a new modality. If there's a benefit we should be able to measure it because the response has been so traditionally poor."

Hyperthermia works on the premise that elevating the temperature of tumor cells makes them more sensitive to treatment that will kill them, relative to normal tissue. Because of inadequate blood flow, lack of oxygen, poor nourishment and a lower PH, tumor cells are more sensitive to heat than the surrounding normal tissue. Therefore after heating an area there is a quicker more noticeable response to subsequent doses of radiation.

Most testing so far has dealt with treatments combining hyperthermia and radiation since both are local treatments.

"Hyperthermia works not only with an additive effect, but with what is known as synergy -- they (hyperthermia and radiation) multiply each other," explains Antich. "This makes it very desirable from purely a biophysical point of view because by external means alone you can apply a combination of the two and that causes the tumor to be effected preferentially."

Another advantage of hyperthermia is that tumors tend to retain heat. Whereas normal tissue relies on blood circulation to take away the heat and cool the skin, tumors are not connected to the thermoregulatory system so they are not capable of cooling themselves.

"Many biological facts tend to conspire against tumors," observes Antich.

The hyperthermia unit at the health science center is one of few in the country capable of delivering heat in three ways: microwave, ultrasound and interstitial. Microwave heating is done using applicators applied to certain parts of the body; it is useful for relatively superficial tumors. Ultrasound uses sound waves of a certain type to generate enough energy to cause heating of tissue for deeper tumors. The third method, interstitial heating, works by implanting the heat source inside the patient using catheters containing small portable microwave antennae.

Doctors are still grappling with questions regarding the amount of heat to deliver to each patient and for how long. "How high do you elevate someone's temperature? Anyone can tolerate a one degree fever, but how high do you go up before there's a problem in someone who's 80 years old with heart disease and other problems," questions Flynn.

"Hyperthermia is not just a gentle form of treatment. It must be controlled with great accuracy to avoid damaging normal tissues," adds Antich.

To monitor the heat being given, catheters are attached to the patient. And a computer screen shows the exact rise in temperature and the temperature levels of each measuring point in each patient. "And the best thermometer of all are the patients," says Flynn. "They can tell us if they feel burning or uncomfortable in any way and no matter what the thermometer says we adjust accordingly."

Hyperthermia administered alone has shown a reduction in tumor size, but tumors usually recur. "My personal belief is that hyperthermia is most effective in conjunction with other forms of therapy where it modulates their effect locally. And that can be accomplished by applying a milder form of hyperthermia which is safer," says Antich.

Researchers here will also be exploring the validity of using the reaction of local tumors to hyperthermia as a model of a whole body response.

"To cure cancer it is not only necessary to kill the local tumor but a disease which in many cases is widespread. Metastatic (throughout the body) disease is what ultimately kills you. Regional and systemic hyperthermia is just now beginning to be technically feasible. This is the area in which hyperthermia has the greatest potential for a significant impact as a method for curing cancer," says Antich.

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