PIONS IN TUMOR THERAPY

A BEGINNING FOR THE PHOTON'S BIG BROTHER

Photons and pions play parallel roles in physics. Photons (X-rays, gamma rays) have long had a place in medicine. Pions may someday have a parallel role in medicine.

BY DIETRICK E. THOMSEN

Radiation has been used as therapy for tumors of various kinds almost since the discovery that certain atoms are naturally radioactive. Marie Curie is remembered as an ardent advocate of radium as a cure for cancer — too ardent, some people say. In modern times this business of using energetic subatomic particles to kill tumor cells — that, essentially is what radiation therapy is — has been aided substantially by the development of particle accelerators. Modern means of artificially providing energy have produced a variety of particles and a range of energies that were not available in the days when natural radioactivity had to be relied on. Some of these particles may prove more effective in treatment of certain tumors than are the traditional X-rays.

One such is the pion, a particle whose existence was totally unknown and unexpected in the early days of radiological research. It was not conceived as an aid to radiology. At about the time that Marie Curie was dying, Hideki Yukawa thought up the pion as part of a theory of what holds protons and neutrons together in an atomic nucleus. Pions are particles that embody the force that holds the nucleus together. A multitude of them has a virtual existence in every nucleus, and some of them can be materialized as free particles by striking a nucleus with a projectile, say a proton, with what is now fairly modest energy. Pions come in electrically neutral, positive and negative varieties with masses in the neighborhood of 273 million electron-volts.

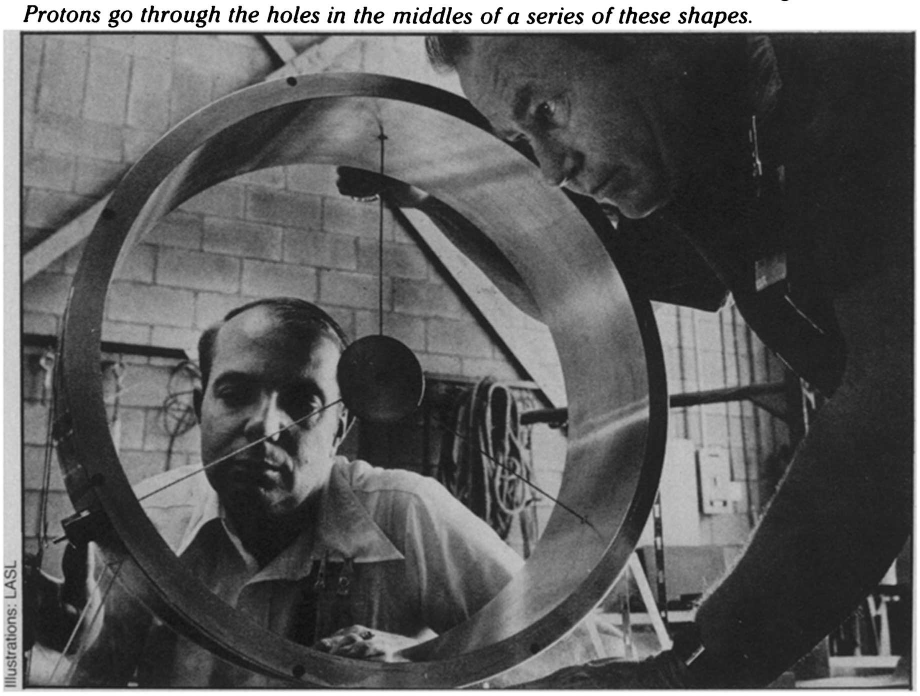
The characteristics of pions led to an expectation that they would be useful medically, and so, when an apparatus to study pions in large numbers, the Los Alamos Meson Physics Facility (LAMPF) was planned, a sizable section of the experimental facilities was earmarked for medical use. An experimental team directed by Morton Kligerman of the University of New Mexico has now completed treatment of the first human cancers ever to be subjected to pion bombardment. So encouraging is the result that larger clinical trials are beginning. At the same time, such facilities are being set up at a Canadian cyclotron in Vancouver and at a Swiss one near Zurich.

In reporting the Swiss development, NEW SCIENTIST pointed out that Kligerman had gone ahead with human trials in spite of the opinion of some (unnamed) European physicians that it was too early. But success convinces, and now the Swiss government is asking other European countries to contribute to a joint European laboratory of this sort to be set up at the Swiss Institute for Nuclear Research. The combination of the latest physics and the latest medicine is characteristic of the field, and it has more than once encountered conservatism in some physicians. Two early researchers in radioactivity, Marie Curie and Lise Meitner operated X-ray services (which were then rather experimental) in the field during World War I, Curie with the French army, Meitner with the Austro-Hungarian army in Poland. Both complained of old-fashioned military doctors who did not understand what they were trying to do.

Today the X-rays that were then so revolutionary are standard diagnostic and therapeutic agents for a large number of medical conditions. They are not, however, the most effective possible treatment for everything, and the experiments now underway at Los Alamos and soon to start at Zurich and Vancouver may lead to a medical practice in which pion therapy supersedes X-rays for some purposes and does things other forms of radiation therapy were never able to do.

The advantage of pions comes from the way they interact with human and other flesh. X-rays and gamma rays (which are the rays that come out of cobalt machines) are electrically neutral and thus are not easily stopped by matter, including living tissue. They go right through the body, depositing energy at a fairly even rate as they do. Thus, calculations of dosage have to take into account not only the destruction of tumorous tissue but the possibility of damage to surrounding tissue. To quote a statement of the UNM-Los Alamos group, "Damage to normal tissue frequently lim-

Lash Hansborough and Jerry Johnson consider the smallest drift tube design for PIGMI. Protons go through the holes in the middles of a series of these shapes.



Illustrations: LASL

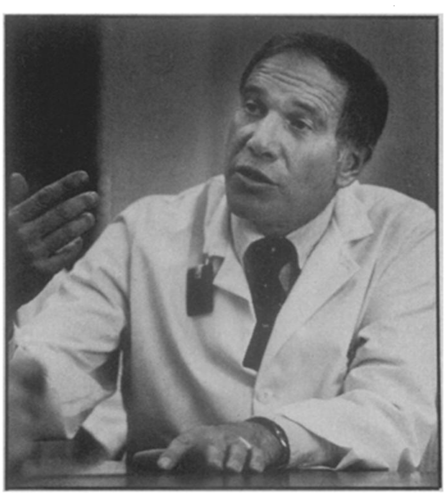
its the amount of conventional radiation which can be given to cancer patients, decreasing the chances for cure."

The hope for pions is that of targeting the tumor and delivering most of the energy there. Negative pions, which are the variety used in the medical experiments, are charged bodies, and therefore they will stop in the tissue. In particular, negative pions are captured by positively charged atomic nuclei. The nuclei explode, forming "pion stars." Pieces of the nucleus fly off in all directions, doing intense damage for very short distances. Although pions deposit energy on their way in and at an increasing rate as they slow down, most of their energy goes into the star at the end.

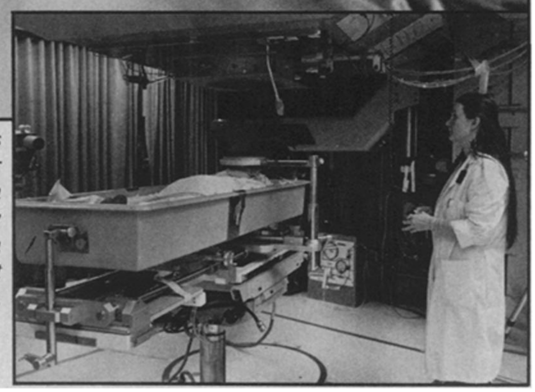
"Theoretically, pions should permit a higher radiation dose to the tumor, with relatively less damage to normal tissues, and improve the chances for local control and long-term survival in patients with large, solid tumors," the experimental group point out.

For experimentation to begin required a facility that provides energetic pions in copious amounts. The Clinton P. Anderson Meson Physics Facility (LAMPF's alternate name) is a linear accelerator half a mile long that delivers protons accelerated to 800 million electron-volts energy. Pions are produced when the protons strike nuclei in various targets. It was built at a cost of $100 million to study all aspects of pion behavior.

Proving out a new form of therapy for malignancies would certainly be a benefit. The research group quotes an estimate that 60,000 people die in the United States every year because their tumors can't be controlled at the primary site. The pion experiments are concentrating on the types of large tumors that are not managed well by other treatments or combinations of treatments in the hope of improving survival rates among these patients. Furthermore, if pion therapy reduces the masses of tumors, that will lessen the body's burden and improve the chances of other forms of therapy.



Kligerman: Optimism, no breakthrough.



A patient is prepared for pion irradiation by radiation technologist Carolyn Blies.

The testing of pions on tumors began between October and December 1974. It was interrupted for extensive refurbishing of the accelerator and resumed in June 1976. By the end of August 1978, 67 patients had had 136 tumors treated with pions. Thirty tumors were treated with X-rays for the purpose of comparing effects, and some received other therapies on pion-treated areas. These other therapies were applied because the long-term pion tolerance levels of healthy tissues around a tumor have not yet been determined, and the National Cancer Institute has therefore recommended low total dosages at the start of tests on any new kind of tissue.

Low though the dosage may be, it takes a while to get it. A patient will be under the pion beam for between 10 and 40 minutes at a time, two or more times a day, five days a week. The patient lies in a body mold to hold the body steady, and the pion beam is shaped to deliver the proper dosage to the proper place.

Some numbers are available from early studies. In a comparative study, seven patients underwent pion or X-ray irradiation of 65 metastatic tumor nodules in the skin, and the pions proved 1.42 times as effective as the X-rays in the short-term response of the skin. One patient, who had 16 nodules, could be followed for 346 days before additional treatment was found necessary. Data on the time required for tumor regrowth indicate that pions were 37 percent more effective than X-rays in suppressing tumor regrowth in that patient at 300 days.

Patient comfort is another aspect. Yoshiaki Tanaka, a physician from the University of Nagoya in Japan, who is visiting Los Alamos and observing the experiments, points out that "pion patients almost always have a good reaction to this therapy. It is different from cobalt and X-rays. There is less vomiting and diarrhea. If pion treatment shows better results we may go ahead with this in Japan." The hope for such a facility in Japan is also expressed by Yukawa, who heard about the early Los Alamos results after learning that he had cancer. He holds no hope that pion therapy may succeed in time to treat his disease, but he says, "this news brought me great pleasure to see that pion, which I imagined forty years ago by pure reason of theoretical physics, is turned out to be useful for rescuing people from the affliction of cancer."

Now that the accelerator intensity has been increased, the tests can proceed from skin nodules to larger and deeper tumors of the brain, neck and head, lung, abdomen and pelvis. Starting at low dosage levels, the tests gradually escalate. The results so far are still "anecdotal," as the researchers put it, but the surrounding tissues have shown no reaction to the radiation or only modest reaction, meaning that the upper tolerance levels for

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... Pions

normal tissue have not yet been reached, while the tumor responses have been "remarkably good. Many tumors have regressed two or three times faster with pion treatment than would be expected with ordinary X-rays," the UNM-Los Alamos group states. Full clinical trials for about 100 patients with advanced tumors of various kinds are about to begin.

But Kligerman cautions that pion therapy is still in its infancy. "We are just at the point where we feel we can continue, not to where we can prove our hypotheses."

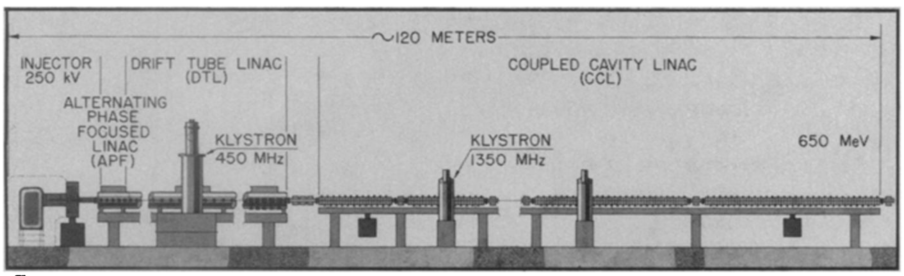
"It will take years to say whether pion therapy is superior to other treatments," says Malcolm Bagshaw, a radiation oncologist from Stanford University, who is visiting Los Alamos. "We are looking for local control where cancer has started. We probably can't do much about a cancer that has spread through the body."

Local control is important, because a large proportion of cancer patients die from continued growth of the primary tumor, and chemotherapy and immunotherapy are weak in their ability for local control. Nevertheless, pion therapy will have to show significant improvements over alternates to be worth the expense and effort.

Kligerman again: "If the cure rate for cancer of the lung is seven percent, and we increase that by 10 percent, we still only have a cure rate of 7.7 percent. But if we can increase the rate by 100 to 200 percent, we can show results." The written statement of the experimental group sees a 200 to 300 percent improvement in five-year survival rate as a sufficient basis to recommend government support of additional pion treatment facilities elsewhere in the country.

Already, however, a group of accelerator specialists under Donald Swenson, leader of the Linac Technology Group of Los Alamos's Accelerator Technology Division, is working on a pion source that may be applicable to such installations. It is called PIGMI (Pion Generator for Medical Irradiations), and it is designed to give somewhat less than LAMPF's total energy at much less cost and length. The hope is to get PIGMI to deliver 650-million-electron-volt protons in 120 meters (about the length of a football field). "We think PIGMI can be built for about $10 million, and a small neutron-producing version for less than $2 million [neutrons will also make pions when they hit nuclei]. Whether this will sell like hotcakes or not, we don't yet completely know," Swenson says.

Such an accelerator could be built in a chamber under a parking lot, especially if a design that includes a bending magnet to fold the length in half turns out to work, but the capital and operation costs mean that it would be for major medical centers only. Indeed, the price alone is likely to preclude the kind of rush to get one by neighborhood hospitals that greeted the introduction of computer assisted X-ray tomographs. □



Future pion medical facilities may use a PIGMI accelerator designed like this plan.

Gene Purkiss and Roy Slice operate the control room for the biomedical facility.

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