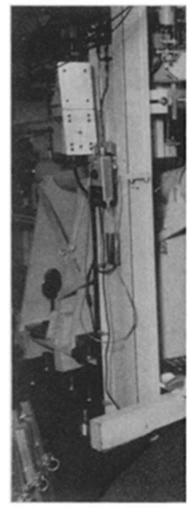
# Radiation Therapy: Beyond X-Rays



## While by no means a 'miracle cure,' neutrons, pions and ions show promise in therapy for several kinds of cancer

*Second of two articles*

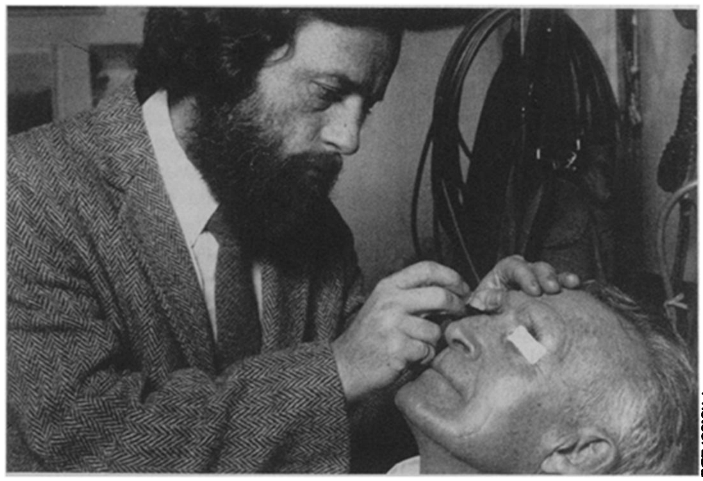
By DIETRICK E. THOMSEN

Radiation became a tool in medical therapy almost as soon as natural radioactivity was discovered. The beneficial effects of radiation on certain kinds of tumors led physicians to seek artificial as well as natural sources. Over the years of this century, artificially and naturally produced radioactive isotopes and machine-produced X-rays and gamma rays have come into common use.

In their search for better sources and more versatile forms of radiation, physicians are now experimenting with the products of modern accelerators: protons, neutrons, pions and ions. Laboratories for particle physics or nuclear physics nowadays often have medical adjuncts. Patients have been treated at such places as the Fermi National Accelerator Laboratory in Batavia, Ill., Los Alamos (N.M.) National Laboratory, the Harvard Cyclotron Laboratory, the Swiss Institute for Nuclear Research (SIN) in Villigen and the Lawrence Berkeley Laboratory (LBL) in Berkeley, Calif.

Physicians interested in treating patients with radiation heavier than X-rays and gamma rays met at LBL with biologists, biophysicists and biochemists interested in what these radiations do to individual cells (SN: 6/22/85, p. 394) for the recent Symposium on Heavy Charged Particles in Research and Medicine. About the future of these therapeutic efforts the consensus of the meeting seems to be guarded but optimistic.

When experiments with these heavy particles began, the investigators hoped they might find a treatment for the "radiation resistant" varieties of tumor, those on which X-rays and gamma rays have not been effective. So far no such treatment has turned up in trials of neutrons, pions, protons (hydrogen ions) and helium ions. Experimentation with ions heavier than helium is just starting. However, pions, protons and helium ions are finding an important place in the treatment of tumors that are located so as to be inoperable and for which X-rays or gamma rays are inadvisable.



*At LBL, physician and physicist William Saunders prepares a patient for treatment of choroidal melanoma with helium ions.*

Photos: LBL

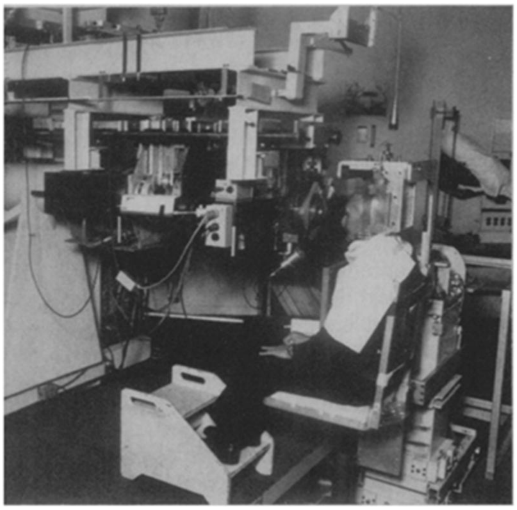
X-rays and gamma rays deliver energy fairly evenly to all the tissue they traverse from their entry into the body to their exit. The heavy particles give up most of their energy at the ends of their trajectories, and they can be manipulated so as to yield that in a fairly small volume. Thus the heavy particles are useful for tumors on or near vital organs, where X-rays might kill too much.

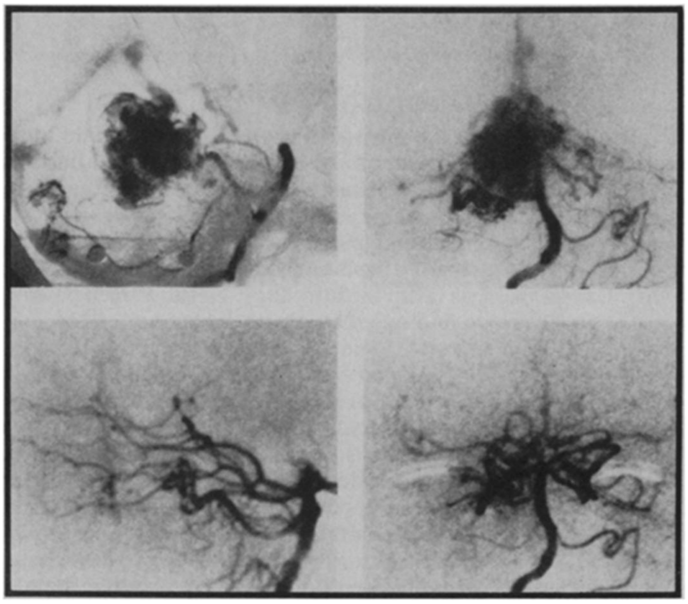
Neutrons, though not electrically charged, are included among the heavy particles. According to Thomas W. Griffin of the University of Washington in Seattle, over 6,000 patients have been treated with neutrons in several U.S. and European laboratories. Radiation with fast neutrons has shown a significant advantage in treatment of salivary gland tumors and prostate cancer, and some advantage against sarcomas of bone, cartilage and soft tissue. However, as Moshe H. Maor of the University of Texas M.D. Anderson Hospital and Tumor Institute in Houston points out, "there is only a slim likelihood to establish an advantage for neutrons in the majority of tumor sites."

He suggests a change in the way patients are chosen for neutron therapy. Therapists need to find a way to assay patients to decide which of them are likely to be cured by conventional radiation, he says. Only those who do not fall into this category should be considered for neutron therapy. "Are neutrons better than [X-rays or gamma rays]?" Maor asks. "You have to ask the question regarding each individual patient."

Pions, also known as pi mesons, are the lightest charged particles used in these radiation trials. Energetic protons striking various targets are the source of pions for medical application. Pions are intimately connected to the forces that hold atomic nuclei together and have a virtual or potential existence whithin nuclei. Energetic protons striking a nucleus can knock them out of the nucleus as independent particles. Three laboratories with accelerators specially built for the manufacture and study of pions and other mesons dominate medical experimentation with pions: Los Alamos National Laboratory, SIN and TRIUMF in Vancouver, British Columbia.

Los Alamos began pion treatment of tumors in 1974. Between then and 1981, researchers irradiated 227 patients with pions for a variety of tumors. Treatments at SIN lasted from 1982 to 1984 with a total of 126 patients. TRIUMF has treated the fewest humans, 80, mostly with brain and pelvic tumors, in what George B. Goodman of the Cancer Control Agency of British Co-





Helium ions also treat arteriovenous malformations, abnormalities of capillaries in the brain. Top photos show malformations of capillaries into tangled mess. Bottom photos show restoration of more normal appearance after treatment.

Far left, specially shaped polystyrene mask holds patient's face steady during irradiation.

lumbia in Vancouver calls preparatory clinical studies. TRIUMF has also irradiated 50 pigs in testing the effects of its pion beam. Lloyd D. Skarsgard of the British Columbia Cancer Research Centre in Vancouver says pigs were chosen because their flesh is most like human flesh from the radiation's point of view.

Of patients treated at Los Alamos, the largest group (59) had a brain tumor called malignant glioma. Some were treated with both pions and X-rays. Of 29 who received complete therapy with pions alone, only two had their tumors locally controlled without complications. (Sometimes tumors metastasize, spreading their cells to various locations in the body; these statistics concern control of the tumor's growth in its original location only.) On the other hand, of 20 patients with prostate cancer given doses between 26,500 rads (in 23 fractions) and 40,400 rads (in 38 fractions), the pions achieved local control in 18.

In Switzerland, pions show promise in local control of bladder cancer, with 19 "complete responses" in 22 cases treated. However, both SIN and Los Alamos report "discouraging" results with pancreatic cancer. "In no case was local control achieved," Schmitt says. He concludes that pion irradiation is a feasible treatment for specific cancers, particularly those of the head, neck, prostate and bladder, and deep-seated soft-tissue sarcomas.

Protons have been used for cancer treatment in Japan, Sweden and the United States. Hiroshi Tsunemoto of the National Institute of Radiological Sciences (NIRS) in Chiba-shi, Japan, reported that protons with 70 million electron-volts (70 MeV) energy from an accelerator at NIRS and protons with 250 MeV energy from an accelerator at Tsukuba University have treated a total of 50 patients with various cancers, both superficial and deep-seated. The patients' conditions included skin cancers, fibrosarcomas and breast, thyroid and tongue cancers. The technique concentrates the proton beam into a spot that scans a field 20 centimeters by 10 in area. The method seems to be of clinical value, Tsunemoto says, achieving very good results in local control of the cancers. The Japanese are so encouraged that they are planning a larger accelerator, which will provide ions with energies up to 600 MeV per proton and neutron and will have four treatment rooms for medical research.

In Cambridge, Mass., the Harvard Cyclotron Laboratory provides 160 MeV protons for a cancer irradiation program in cooperation with the Massachusetts General Hospital and the Massachusetts Eye and Ear Infirmary (both in Boston). Mary Austin-Seymour of Massachusetts General Hospital Cancer Center, Harvard Medical School, reported for the group that has been treating cancers experimentally since 1974. Up to the last day of 1984, a total of 965 patients had been treated with the proton beams, which can penetrate to a depth of 16 centimeters in tissue.

More than half of these patients (591) suffered from choroidal melanomas, cancers in the back of the eyeball (SN: 9/24/83, p. 204). Proton treatment achieved local control in 98 percent of the cases.

The Massachusetts group has also treated 67 patients with chordomas or chondrosarcomas of the base of the skull or cervical spine — a rather rare tumor, Austin-Seymour says. With a median follow-up time of 27 months, the local control rate is 89 percent. On the other hand, of seven patients with gliomas treated with protons, there is only one long-term survivor; six died between two and six months after treatment. Overall, however, the results are encouraging, Austin-Seymour reports, and the group plans to continue treating cancers.

Working somewhat in parallel with the Massachusetts group in that their major effort has been on choroidal melanomas, a group from LBL and the University of California at San Francisco uses helium ions, which consist of two protons and two neutrons. The ions come from the 184-inch cyclotron at LBL.

This work also began in 1974, when, according to William W. Saunders of LBL, "Joe Castro [of LBL] treated the first patient with helium." Saunders reports that for this group also, treatment of large tumors "traditionally felt to be radiation resistant," such as those of the pancreas, stomach and esophagus and advanced head and neck tumors, has not gone well. For example, of 25 patients with esophageal tumors, 21 died with tumors growing. Only one is alive.

The California group's successes have come with eye cancers and chondrosarcomas that envelop three sides of the spinal cord. Up to February 1985 they had treated 190 patients with eye tumors. Of these, 116 have been followed for periods from six to 67 months after treatment. Local control results have been very good, Saunders says. Only eight patients developed local recurrences of the tumor, and all of these were successfully treated, three with new irradiation and five with surgical excision of the eye. Eight patients (including two of the local-control failures) developed distant metastases. The most frequent treatment complication, Saunders says, is cataract. A total of 27 of the patients developed it.

The group has somewhat less experience with tumors adjacent to the spinal cord, having treated only 19 patients. Follow-up time ranges from two to 75 months, in which 15 patients have shown local control of their tumors. Saunders says the California group intends to continue treating these varieties of tumors with which they have had success, trying to improve their technique as they go. In the case of the eye tumors, they particularly want to do a comparative study of helium ion irradiation against one of the heretofore standard treatments of the condition, gamma radiation from plaques of iodine-125 surgically implanted behind the affected eye. □