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*W Stahl - RT
 M. Agnew*

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January 5, 1978

Mr. Jack Stahl
 c/o 200 Lomas, N.W.
 Suite 200
 Albuquerque, New Mexico 87102

Dear Mr. Stahl:

Attached is the project description you requested for use by your committee. I hope it is satisfactory for your needs. Please call me in Los Alamos (667-7392) if you have any questions or need any additional information. Thanks very much for your efforts on our behalf. We're looking forward to seeing you again soon.

Sincerely,

Stephany Wilson

Stephany Wilson
 Associate Administrator for
 Research and Communications

SW:ft
 attachment
 cc: L. Salazar, Office of Rep. Manuel Lujan
 Dr. M. M. Kligerman
 Dr. H. M. Agnew

N.B:
 Dear Dr. Agnew:
 Mr. Stahl is chairing a committee to attempt to obtain funds for the CAT scanner at Biomed, as a result of Rep. Lujan's efforts. Please call me if you have any questions.

Thanks.

Stephany

(SW)

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CLINICAL STUDIES OF
NEGATIVE PI MESON RADIOTHERAPY

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Progress in Experimental Cancer Treatment

A cooperative study to test a unique subnuclear particle, the negative pi meson, in radiation therapy for advanced cancer is being conducted by the University of New Mexico Cancer Research and Treatment Center (UNM CRIC), Albuquerque, and the Los Alamos Scientific Laboratory (LASL), Los Alamos, New Mexico.

Scientists are studying negative pi mesons, or "pions," because of their theoretical advantages in cancer therapy over conventional radiation, such as high-energy x-rays produced by linear accelerators or gamma rays produced by cobalt machines. Unlike x-rays or gamma rays, pions are particles which can be stopped at a predetermined point. Pions deposit relatively sparse radiation as they travel through the body tissue, and their path is called the "plateau region." As each pion slows, it is pulled into the nucleus of an atom. This makes the nucleus unstable and it explodes, releasing large subnuclear fragments that deposit dense radiation. This process is referred to as the creation of a "pion star," and the stopping region is called the "peak region." By adjusting the "peak region" to that of a tumor area, scientists hope to seriously damage tumors, while sparing normal surrounding tissues in the plateau region from high doses of radiation.

The tests are being conducted at the Los Alamos Meson Physics Facility (LAMPF). The 800 million electron volt (MeV) proton accelerator at LAMPF is the only such machine in the world now capable of producing pions in sufficient quantities for medical tests. Support for physics, biological, and clinical studies is provided by grants from the National Cancer Institute, Division of Research Resources and Centers, to the UNM CRIC. The U.S. Department of

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Energy provides funds for accelerator operations.

Tests with patients having multiple metastatic tumor nodules in or near the skin have been conducted to establish tolerance of skin to pions.

Results indicate that peak pions are 1.4 times more effective than x-rays on the skin surface, and 37 percent more effective than x-rays in preventing tumor regrowth, for equivalent normal skin injury.

A new series of tests is now underway to assess tumor reaction and normal tissue reaction in patients with a variety of locally advanced or recurrent tumors. After preliminary work is complete, full clinical trials will begin for tumors of the brain, head and neck, esophagus, lung, bladder, stomach, pancreas, prostate, rectum, and uterine cervix. Such trials are expected to begin for some sites as early as February 1978.

As of December 31, 1977, a total of 41 patients with a total of 83 tumors had been treated with pions at LAMPF. In addition, 30 tumors in the total patient population have been treated with x-rays to assess comparative effects, and 7 patients have received additive x-ray therapy to pion-treated portals. Additive therapy is needed on occasion because doses are still being slowly increased to determine normal tissue tolerances to pions. Therefore, doses may not be large enough to completely eliminate the localized tumor. When, three to four weeks after the end of pion therapy, marked but incomplete regression of a localized tumor and minimal normal tissue reaction are observed, conventional radiation is added for the patient's benefit.

Although patient data is still anecdotal for sites other than skin, it should be noted that remarkable tumor regression is now being seen, for relatively mild normal tissue injury, in patients with deep-seated lesions being treated with pion doses approaching tolerance. This implies that a therapeutic gain may soon be demonstrated for sites in addition to skin. Doses are being escalated gradually in each general anatomic site (for example,

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head and neck, pelvis, abdomen, brain, etc.) until acute reactions are adequately assessed. However, substantially more patients need to be treated and followed for periods of up to five years before definitive results become available.

The Need for a Pion-Dedicated CAT Scanner

The principal theoretical advantage of pions is that the major radiation damage they incur can be confined to a precisely controlled area, corresponding with the tumor volume, while at the same time surrounding normal tissues can be spared, thus improving chances for cure. Matching the peak dose region with the tumor volume is possible, however, only with accurate localization of the tumor, intervening body inhomogeneities, and nearby critical structures. With pions, the presence of inhomogeneities (bone, air-filled cavities, soft tissue and lung) significantly alters the stopping location of the pions. Dense structures, such as bone, cause the pions to stop short, while air and lung cause the pions to overshoot their target stopping area. Thus, the shape of the planned pion stopping region can be significantly changed, causing the pions to miss portions of the tumor or to unduly damage nearby critical organs (such as heart, spinal cord or liver).

This phenomenon can be overcome by scanning the patient under the beam and changing the energy with which the pions are delivered to each section of the treatment area or by adding absorbent material above the patient's skin surface, provided the material can be constructed to correspond precisely with the dimensions of the internal structures of the body. With ordinary x-ray pictures and isotopic or ultrasound scans, it is not possible to precisely define the dimensions of these structures because there is little discrimination among various types of soft tissue. However, new technology has recently been developed which represents a significant advance in visualizing interior sections of the body. The device is a computer-assisted tomographic (CAT) scanner. The

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ability of this system to discriminate between tissue densities of less than .5% makes possible cross-sectional visualization of the body, with plotter output showing remarkable details of the several soft tissues and bony structures. Within these, the extent of the tumor can be precisely identified, and the shapes and sizes of sections of bone, air, and other normal tissues lying between the body surface and the tumor target can be measured, so that the pions will reach their planned stopping destination.

Experience at LAMPF in the treatment of tumors deep to the skin surface demonstrates a critical need for a whole-body CAT system to provide adequate information on the location of tumors and the position of body inhomogeneities. Not only is the CAT scanner the most sophisticated equipment available for tumor/inhomogeneity localization, it can be used repeatedly, unlike isotopic scans, to follow the changing distribution of the tumor during treatment, allowing greater sparing of normal tissue.

While it was thought possible to utilize diagnostic CAT scanners at locations other than Los Alamos (and this is presently being accomplished) for initial treatment planning, experience now indicates that a CAT scanner directly on-site at LAMPF is necessary, for the following reasons:

- (1) Patients treated at LAMPF must undergo stringent immobilization and positioning to ensure correct placement of the radiation field. They must hold this position, absolutely immobile, for treatment times of 10 minutes at minimum. This requires the construction of individual patient immobilization casts. The patient and cast are then placed in a module, with all alignments and positioning done outside the treatment room. The patient is then transported by stretcher into the treatment room in his module, which is transferred to the treatment table. This procedure has been implemented to conserve valuable beam time and maximize the number of patients that can be treated at LAMPF. By fabricating the patient module of radioluscent materials, the patients' tumors could be delineated by the CAT scanner in the same position as that in which

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they will be treated, thus ensuring correct position of tumor tissue and internal organs for treatment planning calculations.

(2) The patients need to be periodically checked during treatment (over 5-10 weeks) so that the radiation field can be altered as the tumor regresses, and to see if the beam is missing or delivering an inadequate dose to portions of the tumor (as evidenced by lack of regression). The treatment plan can then be changed to correct this situation (which has occurred on a number of occasions).

(3) The preparation of a patient for treatment at LAMPF (i.e., completion of all diagnostic tests, cast construction, CAT scanning, treatment planning, etc.) can take one to three weeks. During this time, the tumor continues to grow, or patients sometimes develop problems which preclude their treatment in the position originally planned (e.g., the tumor may begin pressing on internal structures, making it impossible for a patient to lie for long periods on his back, stomach, or side). The patient needs to be rescanned just before treatment as a final check that all identifiable tumor is still in the treatment field and that any last-minute alterations in the patient's position or treatment plan still retain adequate dose to the tumor and sparing of nearby structures.

(4) The design of compensating material to overcome problems in dose delivery due to intervening bone, muscle, air, or lung, requires cross-sectional views of the internal body structure at 1-cm intervals across the treatment field. If the patient is to be treated with two portals to improve dose uniformity, as is usually the case (from the front and back or from both sides), these views are required in both treatment positions, with the patient in his immobilizing casts. This means, for the average patient, about 30 planes or slices of information in the initial treatment-planning series. With the stringent immobilization, reference marking, localization films, and

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other procedures required at this time, the average time per patient for the initial series of scans is 6 to 8 hours, at a cost of approximately \$1800. Additional time is then needed to physically transport the data tape produced by the CAT scanner computer to LAMPF and to input the data to the treatment planning computer which performs dose calculations and designs the bolus. Follow-up scans are much less extensive in the number of planes required (and are usually taken in only one position), ranging in time from 2 to 4 hours and in price from \$200 to \$600. Transporting patients to the CAT scan site remote from Los Alamos adds to the cost (approximately \$60 to and from Albuquerque and approximately \$400 to and from cities out of state, as has been the case to date, since no CAT scanner will be operational in New Mexico until April 1978).

(5) It is conservatively estimated that 80 patients will be treated in Fiscal Year 1979 (July 1, 1978 to June 30, 1979), 20 per treatment cycle of 6 to 10 weeks, 4 treatment cycles per year. Total CAT scanner utilization, as currently practiced, is estimated at 13 hours per patient (7 for the initial series and 3 hours each for two follow-up scans, one during and one after treatment) at a total cost per patient of \$2,700 excluding travel costs, for a grand total of 1040 CAT scanner hours at \$216,00. For the following year, this is expected to increase by a factor of approximately 50 to 75 percent, and by an additional 50 to 70 percent the following year, as the LAMPF accelerator reaches its design intensity of 1000 milliamps (thus delivering more particles per second and increasing by a factor of about 2.5 the number of patients who can be treated each year). At the rate of approximately \$200,000 to \$450,000 per year in CAT scanner costs and 1000 to 2500 CAT scanner hours per year projected for the coming three years, it is not economically feasible to consider other than a pion-dedicated CAT scanner, nor feasible to believe that the diagnostic CAT units presently planned for installation in Albuquerque (three) could handle such a load, particularly on the short time frames required because of the cyclic operation of the LAMPF accelerator.

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At present, the CAT scanning requirements for pion patients are most difficult to meet without a dedicated scanner on-site at LAMPF, and are accomplished only marginally at considerable discomfort and inconvenience to patients, stress on our staff, and frequently delay in the start of patients' treatments. Since the LAMPF accelerator operates on cycles (presently of approximately six weeks in length), delays can compromise our ability to deliver an optimum course of radiation treatments to the tumor, thus jeopardizing recovery of normal tissues (if daily doses are pushed to the maximum) or total destruction of the tumor (if sufficient total dose cannot be delivered in daily doses tolerable to normal tissues).

Approximately \$1.1 million is needed to pay for a CAT scanner and associated equipment and an addition of approximately 2100 square feet to the LAMPF Biomedical Facility to house the scanner. Of this amount, \$200,000 is presently available from the National Cancer Institute, leaving a balance still needed of \$900,000.

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