714537

# PROPOSAL
for the
CONTINUATION
of the
NEGATIVE PION THERAPY PROGRAM

## STUDIES OF THE PION BEAM FOR RADIOTHERAPY

for Calendar Years 1974 and 1975

To be performed by
The Los Alamos Scientific Laboratory (LASL)
under AEC Contract (W-7405-ENG-36)
for the
American Cancer Society


Prepared by: Chaim Richman
Chaim Richman, Ph. D., LASL

Approved by: George L. Voelz
George L. Voelz, M. D., LASL
Health Division Leader

A. D. McGuire
A. D. McGuire - LASL
Special Projects Office



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LASL No. P-184

March 1973



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# COST ESTIMATE

Project Term - Begin - January 1, 1974

Project Term - End - December 31, 1975

| | FY 74 (6 mo) | FY 75 | FY 76 (6 mo) | Total |
|---|---|---|---|---|
| **Man-Years** | | | | |
| Scientific | .5 | 1.0 | .5 | 2.0 |
| **Costs ($1,000)** | | | | |
| A. Direct Salaries | 10.8 | 22.8 | 12.1 | 45.7 |
| B. Materials & Services | 18.0 | 27.0 | 9.0 | 54.0 |
| C. Other Direct Charges | | | | |
| 1. Travel | 1.0 | 2.0 | 1.0 | 4.0 |
| 2. Consultants | 1.5 | 3.0 | 1.5 | 6.0 |
| 3. Visiting SM's | 3.0 | 6.0 | 3.0 | 12.0 |
| Total Direct Costs | 34.3 | 60.8 | 26.6 | 121.7 |
| D. Indirect Costs | 5.5 | 11.6 | 6.2 | 23.3 |
| Total Costs | 39.8 | 72.4 | 32.8 | 145.0 |
| **Equipment Costs ($1,000)** | | | | |
| A. Obligation | 30.0 | 27.0 | 3.0 | 60.0 |
| B. Cost | 30.0 | 27.0 | 3.0 | 60.0 |
| | 69.8 | 99.4 | 35.8 | 205.0 |

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# APPLICATION FOR A RESEARCH OR CLINICAL INVESTIGATION GRANT



(Please read carefully the attached "Policies Governing Research and Clinical Investigation Grants" and the instructions on all pages of this form, before completing this application.)

TO: American Cancer Society, Inc.
219 East 42nd Street
New York, New York 10017

Date March 10, 1973

Application is hereby made for a grant* in the amount of $ 205,000
for the period from Jan. 1, 1974 to Dec. 31, 1975 inclusive.

Title "Studies of the Pion Beam for Radiotherapy"

FROM:

Chaim Richman
Name of Investigator

Chaim Richman
Signature

Staff Member, H-10
Title

(505) 667-4915
Telephone No.

Biophysics and Instrumentation
Department

Health Division
Division of Institution

Los Alamos Scientific Laboratory
P. O. Box 1663
Street and Number

Los Alamos, New Mexico 87544
City, State, Zip Code

Official Name of Institution

Street and Number

City, State, Zip Code

Name of Official Authorized to Sign for Above Institution

Signature

Title

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Checks to be Made Payable to

Street and Number

City, State, Zip Code

*It is understood that each applicant, by the act of applying for a grant, agrees, if the grant is made, to abide by the Society's POLICIES GOVERNING RESEARCH AND CLINICAL INVESTIGATION GRANTS.

No. 0059.02-10/70

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Units = $1,000

| 1. BUDGET PROPOSED* | Calendar 1974 1st Year | Calendar 1975 2nd Year |
|---|---|---|
| A) PERSONNEL ..... *(Itemize all positions; indicate per cent of time on project and names of personnel, if selected)* | | |
| C. Richman (100%) | 0 | 0 |
| Research Scientist (100%), Vacancy | 20.4 | 21.6 |
| *Retirement or other security benefits (Total)* ..... | 1.8 | 1.9 |
| **CATEGORY TOTAL** | 22.2 | 23.5 |
| B) PERMANENT EQUIPMENT *(ITEMIZE)* ..... | | |
| Magnetic Tape Unit and Interfaces | 8.0 | 8.0 |
| Amplifiers and Timing Units | 3.0 | 3.0 |
| Two Parameter Analyzer | 16.0 | 16.0 |
| Programmable Calculator | 6.0 | 0 |
| **CATEGORY TOTAL** | 33.0 | 27.0 |
| C) CONSUMABLE SUPPLIES *(GROUP IN MAJOR CATEGORIES)* ..... | | |
| Scanner Unit | 8 | 8 |
| Phantoms | 4 | 4 |
| Silicon Detectors | 6 | 6 |
| Germanium Detectors | 4 | 4 |
| Detector Holders and Electronic Parts | 2 | 2 |
| Cold Probe Assembly | 3 | 3 |
| **CATEGORY TOTAL** | 27 | 27 |
| D) MISCELLANEOUS *(LIST SPECIFIC AMOUNT FOR EACH ITEM)* ..... | | |
| Travel | 2 | 2 |
| Consultants | 3 | 3 |
| Visiting Staff Members | 6 | 6 |
| **CATEGORY TOTAL** | 11.0 | 11.0 |
| **SUBTOTAL** | 93.2 | 88.5 |
| E) INDIRECT COSTS ..... | 11.3 | 12.0 |
| **GRAND TOTAL** | 104.5 | 100.5 |

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See POLICES GOVERNING RESEARCH AND CLINICAL INVESTIGATION GRANTS

*If more space is needed prepare budget using above format.*



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# APPLICATION FOR A RESEARCH OR CLINICAL INVESTIGATION GRANT

| ESTIMATE OF BUDGET REQUIRED FOR: | 3rd Year | 4th Year | 5th Year |
|---|---|---|---|
| A) PERSONNEL | | | |
| RETIREMENT *(TOTAL)* | | | |
| CATEGORY TOTAL | | | |
| B) PERMANENT EQUIPMENT | | | |
| CATEGORY TOTAL | | | |
| C) CONSUMABLE SUPPLIES | | | |
| CATEGORY TOTAL | | | |
| D) MISCELLANEOUS | | | |
| CATEGORY TOTAL | | | |
| SUBTOTAL | | | |
| E) INDIRECT COSTS | | | |
| GRAND TOTAL | | | |

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# APPLICATION FOR A RESEARCH OR CLINICAL INVESTIGATION GRANT

## SUMMARY OF RESEARCH PROPOSED

Name and Official Title of Principal Investigator

Chaim Richman, Staff Member H-10

Name and Address of Applicant Organization

Los Alamos Scientific Laboratory
P. O. Box 1663
Los Alamos, New Mexico 87544

Title of Project

Studies of the Pion Beam for Radiotherapy

Use this space to summarize concisely your proposed research. Outline objectives and methods. Underscore the Key words (not to exceed 10) in your abstract.

The present proposal describes research to be conducted during calendar years 1974 and 1975, the third and fourth years of an American Cancer Society sponsored project at the Los Alamos Scientific Laboratory of the U. S. AEC. The general goal of the project is to develop and demonstrate methods of treatment of human malignant tumors by irradiation with negative pi-mesons. Treatment of patients is planned using apparatus presently under construction as part of the U. S. AEC's Clinton P. Anderson Meson Physics Facility, Los Alamos, New Mexico. Patient treatment is planned as a joint activity of the U. S. AEC and the University of New Mexico Medical School.

From January 1971 to the present, grant support from the American Cancer Society has been used at Los Alamos to develop instrumentation necessary in patient treatment for:

1) Assuring that the pi-meson beam entering a patient is not unduly contaminated with undesirable particles (i.e. electrons, mu-mesons, and neutrons).
2) By direct dosimetry measurements in a phantom, prepare the pi-meson beam in both energy and spatial distributions optimum for the irradiation of particular tumors.

At present, an instrumentation system consisting of several solid-state radiation detectors and electronics to present a spatial distribution of dose delivered in a variety of phantoms is being assembled. Availability of a pi-meson beam is anticipated in the fall of 1973. Observations and measurements using the pi-meson beam entering phantoms will begin when the beam is available. During 1974 I propose to construct and operate a complete instrumentation system as required to prepare and monitor the pi-meson beam in human therapy. Clinical trials of pi-meson therapeutic efficacy can presently be anticipated in the 1976 to 1979 time frame.

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APPLICATION F A RESEARCH OR CLINICAL INVES ATION GRANT

## BIOGRAPHICAL INFORMATION

*(Give the following information for all professional personnel listed on page 2, beginning with the Principal Investigator. Use continuation pages and follow the same general format for each person.)*

| NAME | TITLE | BIRTHDATE (Mo., Day, Yr.) |
|---|---|---|
| Chaim Richman | Staff Member, H-10 | [redacted] |

| PLACE OF BIRTH (City, State, Country) | PRESENT NATIONALITY (If non-U.S. citizen, indicate kind of visa and expiration date) | SEX |
|---|---|---|
| [redacted] | U. S. A. | ☒ Male ☐ Female |

**EDUCATION** (Begin with baccalaureate training and include postdoctoral)

| INSTITUTION AND LOCATION | DEGREE | YEAR CONFERRED | SCIENTIFIC FIELD |
|---|---|---|---|
| [redacted] | B.A. | [redacted] | Mathematics |
| | M.A. | | Mathematics and Physics |
| | Ph. D. | | Physics |

**HONORS** [redacted] Sigma Xi; American Physical Society, Fellow
Ethel M. Rubelson Lecturer, Department of Radiology,
University of Minnesota Medical School
Chairman CPAMF Biomedical Users Steering Committee 1970-1972

| MAJOR RESEARCH INTEREST | ROLE IN PROPOSED PROJECT |
|---|---|
| Pion Physics and Treatment Planning | Principal Investigator |

**RESEARCH SUPPORT** (See instructions)

none

**RESEARCH AND/OR PROFESSIONAL EXPERIENCE** (Starting with present position, list training and experience relevant to area of project, including teaching and clinical responsibilities. List all or most representative publications.)

Staff Research Scientist, Los Alamos Scientific Laboratory
Lecturer, Assistant Professor and Associate Professor, [redacted]
Staff Member, [redacted]
Director of Research, [redacted]
Professor of Physics, [redacted]
Professor of Physics, [redacted]

Dr. Richman started work on pions at the [redacted] synchrocyclotron in 1949. From 1961-1971 he directed a program on radiotherapy with pions at [redacted] from the [redacted] This program involved various experiments on the dosimetry and radiobiology of negative pions. Since 1971 he has been at the Los Alamos Scientific Laboratory.

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Deuteron Disintegration by Electrons, with B. Peters, Physical Review, 59, 804 (1941)

Angular Distribution in Deuteron Disintegration by Electrons, (A), Physical Review, 61, 203 (1942)

The Production of Slow Neutrons in a Carbon Block, with T. Snyder and R.W. Williams, U. S. Atomic Energy Commission Report MDDC-302, Sept. (1946)

Drift Tubes for Linear Proton Accelerator, (A), with F. Oppenheimer and L. H. Johnston, Physical Review, 70, 447 (1946)

Initial Performance of a 32 MeV Proton Linear Accelerator, (A) with L. V. Alvarez, H. Bradner, H. Gordon, L. C. Marshall, F. Oppenheimer, W.K.H. Panofsky, R. Serber, C. Turner, and J. R. Woodyard, Science, 106, 506 (1947)

On the Neutron-Proton Scattering Cross Section, with D. Bohm, Physical Review, 71, 567 (1947)

Resonant Cavities, Electronic Lecture Series, BP-94, September 17 (1947)

Control of the Field Distribution in the Linear Accelerator Cavity, with W.K.H. Panofsky, Physical Review, 73, 535 (1948)

Apparatus for Measuring Proton-Proton Scattering at 32 MeV Using Proportional Counters, (A), with B. Cork and L. Johnston, Bulletin of the American Physical Society, 24, 214 (1949)

Berkeley Proton Linear Accelerator, with L. Alvarez and others, UCRL-236 (1949)

An Experiment for Measuring Heavy Meson Production by High Energy Particles, (A), with H. Wilcox, presented at the December 29-30, 1949 meeting of the American Physical Society at Stanford University, Physical Review, 78, 85 (1950)

Measurement of the Production of Positive and Negative Mesons by 345 MeV Protons on Carbon, (A), with H. A. Wilcox, presented at the December 20-30, 1949 meeting of the Americal Physical Society at Stanford University, Physical Review, 78, 85 (1950), also Classified Document No. LA-38, Lawrence Radiation Laboratory

Production Cross-Sections for $\pi^+$ and $\pi^-$ Mesons by 345 MeV Protons on Carbon at 90° to the Beam, (L), with H. A. Wilcox, Physical Review, 78, 496 (1950)

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PUBLICATIONS (Continued)

The Production of $\pi^+$ Mesons by Protons on Protons in the Direction of the Beam, (L), with F. Cartwright, M. Whitehead, and H. A. Wilcox, Physical Review, 78, 823 (1950)

Proton-Proton Scattering at 31.8 MeV Proportional Counter Methods, with B. Cork and L. Johnston, Physical Review, 79, 71 (1950)

Production of a $\pi^+$ Meson Beam Using the Deflected Proton Beam of the 184-inch Synchrocyclotron, (L), with M. Skinner, J. Merritt, and B. Youtz, Physical Review, 80, 900 (1950)

Scattering of $\pi^+$ Mesons on Carbon, (A), with M. Skinner, Physical Review, 83, 217 (1951)

On the Angular Distribution of the $\pi^+$ Mesons from 341 MeV Protons on Protons, (L), with M. Whitehead, Physical Review, 83, 855 (1951)

On the Angular Distribution and the Polarization of the Deuteron in the Reaction $p + p - d + \pi^+$, with K. M. Watson, Physical Review, 83, 1256 (1951)

The Production of $\pi^+$ and $\pi^-$ Mesons by 340 MeV Protons at 90° to the Beam from Carbon and Lead, with M. Weissbluth and H. A. Wilcox, Physical Review, 85, 161 (1952)

The Production of Positive Pions by 341 MeV Protons on Protons, with W. F. Cartwright, M. Whitehead, and H. A. Wilcox, Physical Review, 91, 677 (1953)

The Berkeley Proton Linear Accelerator, with L. W. Alvarez, H. Bradner, J. F. Finch, H. Gordon, J. Gow, L. C. Marshall, F. Oppenheimer, W. K. H. Panofsky, and J. R. Woodyard, Rev. Sci. Insti., 26, 2, 111 (1955)

On the Dosimetry of Negative Pions with a View Toward Their Use in Cancer Therapy, with H. Aceto, M. R. Raju, B. Schwartz, and M. Weissbluth, Spring 1964, Semiannual Report Biology and Medicine, 114, Donner Lab, University of California, Berkeley, California

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Pion Studies with Silicon Detectors, with M. R. Raju and H. Aceto, Nuclear Instruments and Methods, 37, 152-158 (1965)

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PUBLICATIONS (Continued)

Lithium-Drifted Silicon Detector Used as a Pulse Dosimeter, with M. R. Raju, E. J. Lampo, S. B. Curtis, and J. M. Sperinde, UCRL-16924 (delivered at the 13th Nuclear Science Symposium on Instrumentation in Space and Laboratory, Boston, Massachusetts) (1966)

$\pi^-$ Mesons, Radiobiology, and Cancer Therapy, C. Richman, Proceedings of the First International Symposium on the Biological Interpretation of Dose from Accelerator-Produced Radiation, 346-348 (1967)

A Review of the Physical Characteristics of Pions Beams, with M. R. Raju and S. B. Curtis, Proceeding of the First International Symposium on the Biological Interpretation of Dose from Accelerator-Produced Radiation, 349-367 (1967)

Studies of Vicia Root Meristems Irradiated with $\pi^-$ Beam, with S. P. Richman, M. R. Raju, and B. Schwartz, Radiation Research, 7, 182-189 (1967)

Effect of Negative Pions on the Proliferative Capacity of Ascites Tumor Cells (lymphoma) in Vivo, with J. M. Feola, M. R. Raju, S. B. Curtis, and J. H. Lawrence, Radiation Research, 34, 70-78 (1968)

Physical and Radiobiological Aspects of Negative Pions with Reference to Radiotherapy, with M. R. Raju. Presented at the XII International Congress of Radiology, October 6-11, Tokyo, Japan. GANN Monograph on Radiology of Cancer, No. 9, 105 (1970)

The RBE of Negative Pions in 2-day-old Ascites Tumors, with J. M. Feola, M. R. Raju, and J. H. Lawrence, Radiation Research, 44, 637 (1970)

The Oxygen Effect of $\pi^-$ Mesons in Vicia Faba, with M. R. Raju, N. Amer, and M. Gnanapurani, UCRL-18644, Radiation Research, 41, 135-144 (1970)

The Pion Radiobiology Program at Berkeley and the Biomedical Plans at the Los Alamos Proceedings of the Planning Meeting on Biomedical Applications of the Pion Beam from the 590 MeV Isochronous Syclotron Zurich, Switzerland, 1-17 (1971)

Negative Pion Radiotherapy: Physical and Radiobiological Aspects, with M. R. Raju, Currents Topics in Radiation Research Quarterly, 8, 159-233 (1972)

Recommendations for Implementing Radiotherapy with Negative Pions at LAMPF, LAMPF Biomedical Steering Committee, Chaim Richman, Los Alamos, LA Report 1973 (in preparation)

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## 1. AIM and METHOD of STUDY

At this time an accelerator, the Clinton P. Anderson Meson Physics Facility, is being completed in our laboratory, which will produce a beam of negative pions of sufficient intensity so that human neoplasms can be treated for cure. This will be the first time that negative pions will be brought to bear on the treatment of human cancer.

Many years of studies with weak beams, in this country and in Europe, have led to the opinion and the expectation that negative pions should be useful in improving radiotherapy. The physical advantages of pions are very clear and there is no doubt on this score. Pions are lightly ionizing particles which can be directed in a well-defined beam and stop at a finite range. Wherever the pions stop they cause the breakup of nuclei with the emission of short range alpha particles, protons, and recoil nuclei. (The pion produced nuclear breakup is often called a "star".) The stopping region should be the treatment volume. The energies of the pions are chosen properly for each tumor and for each patient by means of the magnet settings and the slit openings in a magnetic system called the beam line or beam channel. The traversal and stopping of pions is very much sharper and better defined than for Co-60 or neutrons or electrons.

The breakup of the nucleus results in radiation being produced of a character entirely different from the pion. Up to now the pion in traversing the healthy tissue has been a lightly ionizing radiation (for much of its path it is near minimum ionization); thus the healthy tissue in front of the tumor experiences low dosage. The release of the short range nuclear fragments gives a higher dose in the tumor region. From the radiobiological standpoint, a profound change has taken place: From a radiation with an RBE of about 1.0 like Co-60 or electrons, in the healthy tissue, a dose is now given to the tumor region with an RBE of about 1.5 to 3.0. This greatly enhances the effectiveness of pions in the tumor region. Another effect is that the plateau region of the dose distribution has an OER of $\sim 3$, however the peak region has an OER of 1.5 to 2. Consequently much of the protection that anoxic cells have had with low LET radiations will be removed and the chances of tumor cells regrowing will be lessened.

Because of the phenomenon of reoxygenation the advantages of pions against anoxic cells may not be as clear as has been postulated; nevertheless a localized high LET dose is being invoked here which in principle could be much more effective than low LET radiations.

The accelerator produces 800 MeV protons which impinge on a target and produce negative pions. To collect and focus the pions properly a series of focusing and bending magnets will be used to bring the particles to the biological test object or the patient. This beam has now gone through a number of designs, and it is expected that it will be ready this fall.

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The objectives of this work are to characterize the physical parameters of the pion beam for radiobiology and then continue to fashion various configurations for therapy.

The specific aims are the following:

1) To measure the numbers and dosage of electrons, muons, and pions in the beam.

2) To measure the fractions and distributions of low LET and high LET dosage in the beam.

3) To study attenuation and scattering in different materials, especially mock-ups of lung, bone, muscle etc.

4) To obtain beam configurations using bolus, wedges, and various phantoms which are appropriate for the irradiation of different neoplasms at different anatomical sites guided by our experience with supervoltage therapy and especially electron beam therapy.

The main technique used in this work is the semi-conductor silicon and germanium detectors which are versatile and linear detectors. Their range of response is well known to be from minimum ionizing particles to heavy charged particles so that they can detect electrons, muons and pions, and with a proper converter, even neutrons.

At a recent meeting of our dosimetry advisory subcommittee, there was a strong expression of the fact that on several occasions when new machines were brought into therapeutic use, the work was rushed and the machines were used in therapy before sufficient experience and knowledge was obtained. We want to avoid this in every way at the Meson Facility. A basic need, both for radiobiology and for therapy, is the full and detailed knowledge of the beam.

In preparation for therapy, data will be obtained in radiobiological experiments on the RBE for different tissues and this will be folded into the dose measurements. Silicon detectors also give a good measure of the LET distributions in the beam; therefore correlations will be possible with the values of RBE, and a sensible picture will be obtained of the various beams that can be fashioned.

A cutaway view of the treatment room now in construction is shown in Figure 1. The shielding around the primary beam can be seen as well as the beam line. Figure 2 is a detailed drawing of optical paths that the pions will travel. (The actions of quadrupole and bending magnets on particles is similar to the actions of lenses on light; therefore optical language is frequently used in describing the paths of pions in the beam line.)

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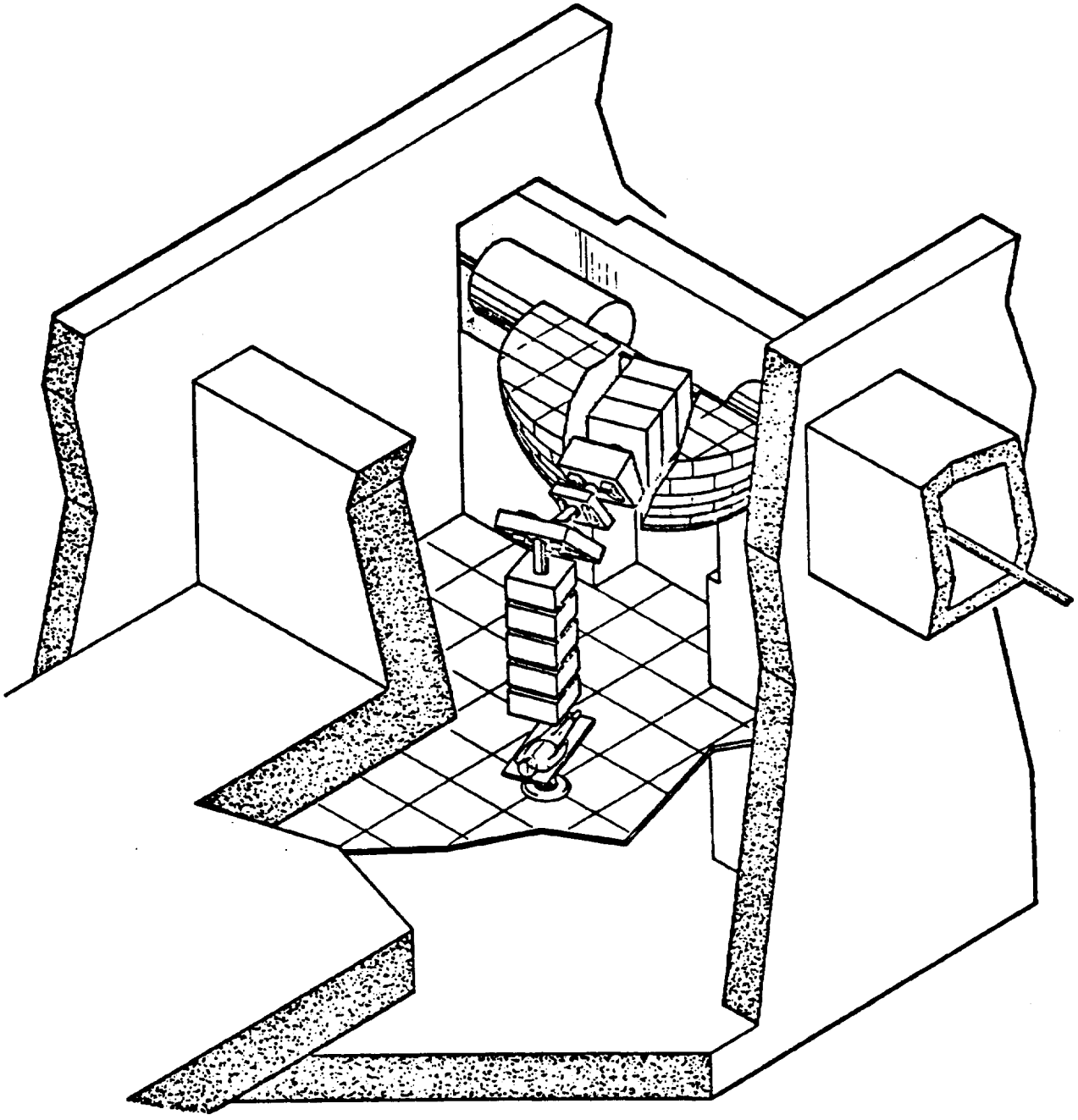

CUTAWAY VIEW OF THE TREATMENT ROOM

Figure 1.

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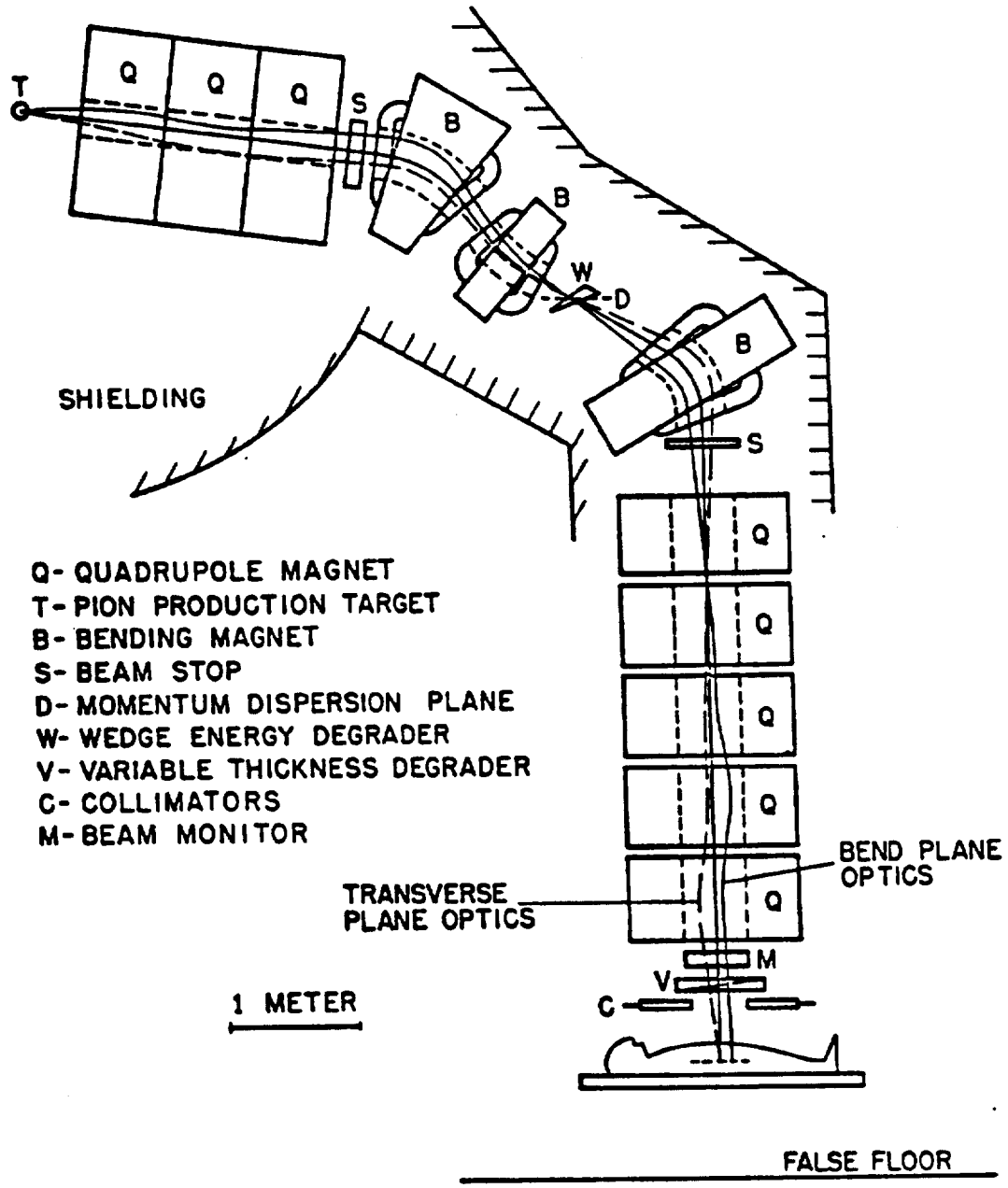


THE LOS ALAMOS MESON PHYSICS FACILITY
BIOMEDICAL PION CHANNEL

STUBOUT FLOOR

Figure 2.

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More Detailed Treatment Considerations and Planning for Treatment

The therapeutic channel has been designed to produce an essentially parallel beam of emerging pions. The parallel character of the beam is of great advantage whenever one is irradiating an extended target volume and adjacent fields need to be used. With $\gamma$-rays from point sources (e.g. Co-60), the beam is cone shaped and one can therefore get hot spots and cold spots in using adjacent fields.

The channel gives a narrow distribution around a single pion energy of 90 MeV. This results in the well-known entrance plateau and a peak dosage at a depth in unit density tissue of about 25 cm. The scheme being worked out now is a scanning technique whereby a variable absorber will be used to vary this range in a specified way so that the treatment volume is covered. Because the plateau region of the dose is low LET and the peak contains the high LET dosage, it is necessary that the detection scheme check out the ratio at every point in a phantom so that treatment is given in a specified way corresponding to the radiobiological test data.

The total dosage (of low and high LET) will also be measured with standard ionization chambers.

There is of course so far no practical experience of the behavior of this radiation in lung, bone, fat, etc. So we are now making, in our plastics shop, tissue-equivalent materials in sheets that will go into the phantom and the practical distributions in these various tissue-like materials will be investigated.

Good lessons and good experience is available from electron beam therapy. The electron and the pion have equal negative charge; they are both particles and have finite ranges. In a limited area the particles are similar.

The fact that there is little exit dose beyond a range that is chosen makes pions similar but better than electron beam therapy, and we can be guided by the problems that have been found in this field: It has been observed that lung inhomogeneities may result in complications from overdosage or recurrences from underdosage. Chest radiographs have shown radiation pneumonitis and pulmonary fibrosis in electron beam therapy of the chest wall. Theoretical calculations are being made using a Monte-Carlo code available at Oak Ridge, and subsequently phantom measurements will be made of the behavior of pions in and around inhomogeneities.

In treating with electron beams behind bone, there is evidence that the dose is significantly decreased. This comes about because the scattering in calcium is much higher than in surrounding tissue and it therefore depletes the beam. Workers at M. D. Anderson Hospital and Tumor

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Institute have observed several recurrences of oral cavity and oropharingeal lesions located immediately behind the mandible. Electrons are comparatively light particles and they scatter easily in the Coulomb fields of nuclei. The pion is about 275 times heavier than the electron and is much less prone to this kind of scattering. The behavior of pions in bone will also be calculated by the codes mentioned earlier and will also be studied in phantoms.

It is expected that the pion beam can be shaped to almost any desired region of tissue wherein a high dose or a "boost" dose is required. If such shaping is indeed possible, pions may be expected to replace interstitial insertion of radioactive sources (as for floor of mouth and tongue lesions). This could be used then to treat the floor of the mouth with good control of the total volume brought to a high dose. Such a technique would lead to a greater dose homogeneity than is achievable with interstitial sources and should produce better results. This shaping will be studied in a phantom to see how far this can be accomplished by control of the beam. Special controls for this shaping are being included in the machine now.

The region of stopping of pions in a phantom is determined by the momentum distribution of the beam. This distribution is basic to the work with variable absorbers and bolus. We will use thin silicon detectors of about 50 $\mu$ for this purpose. In such a detector a large pulse of the order of 5 MeV or more means that a pion has stopped and a heavily ionizing fragment has been produced. Passing electrons, muons and pions give much smaller pulses, of the order of kilovolts. Consequently this method separated the high and low LET components.

In thicker detectors of the order of millimeters electrons and pions can be separated by their energy loss, at least for energies from 70 MeV down. Therefore these detectors with the associated electronics provide a basic picture of the beam as needed for radiotherapy.

Treatment planning with pions will be developed and it promises to be simpler in nature than planning with X-rays because in general fewer fields are necessary to achieve a good distribution. First, good isodose distributions will be generated theoretically and will be measured experimentally. Then the superposition of two fields can be done even without computers to study good treatment plans. At the present time most electron beam treatment planning is done by hand for the same reason.

There is available a compilation of preferred treatment plans for many types of lesions. The work will begin here with seeing what pions can do for different lesions.

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Electron beams are now used primarily for head and neck lesions and breast cancer; the reason for this is that the cut-off for electrons is a sharp one only for the lower energy electrons and therefore for limited penetration. For energies of something like 30 MeV, electron depth doses begin to look like X-ray distributions. With pions this is not true: The range cut-off remains intact even for high energies. Consequently a new range of treatment plans can now be considered, that is a sharp cut-off radiation for deep-seated tumors. Here we will arrive at new possibilities of irradiation of different lesions, with greater comfort for the patient and with far fewer undesirable sequelae than with present modalities.

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## 2. WORK ACCOMPLISHED

### Progress on the Machine and the Beam Line

In July of 1972 the Accelerator produced a beam of protons of the maximum design energy of 800 MeV. The currents so far have been low, ~1 microampere. In the immediate future accelerator development will be devoted to achieving high currents. To do this one must understand and overcome the problems of radioactivation of the accelerator structure by possible "spill" of beam at high currents.

Construction of the biomedical treatment room is progressing. The basic design of the magnets for the biomedical beam line has been completed. Most of the detailed drawings have been completed. Iron and copper for the magnets have been ordered and testing of assembled magnets is scheduled to begin in the summer of 1973 at Los Alamos. Detailed design of the beam line support structure is progressing, and it is anticipated that the pion beam will be available in August of 1973. The intensity will be sufficient so that dosimetry can begin.

### Instrumentation to Measure the Electrons, Muons, Pions and Pion Stars Simultaneously

The pion beam will come off at an angle of 70° to the proton beam, and this large angle insures that the electron contamination will be at a low level, not more than 10% of the pions. We have set up silicon detectors followed by the necessary electronics and readouts which makes it possible to identify and count all the particles. Radioactive sources of low and high energy electrons and of $\alpha$ -particles have been used to test the system.

Bismuth-207 is a radioactive bismuth isotope (with a half-life of 28 years) which emits a number of photons and four strong monoenergetic conversion electrons of 0.482, 0.554, 0.972 and 1.044 MeV. The spectrum of these lines obtained with our detection system is shown in Figure 3. The two highest energy electron lines are both around 1 MeV and are minimum ionizing particles. They can therefore be used to approximate the 200 MeV electrons that will occur in the pion beam, since these will also be at minimum ionization.

The electrons from the bismuth source go through a thin ($\Delta$E) detector and then stop in the thick (E) detector. The single channel analyzer in the E channel is set to choose only the highest energy electrons and the energy loss in the $\Delta$E detector is studied for these electrons. The spectrum

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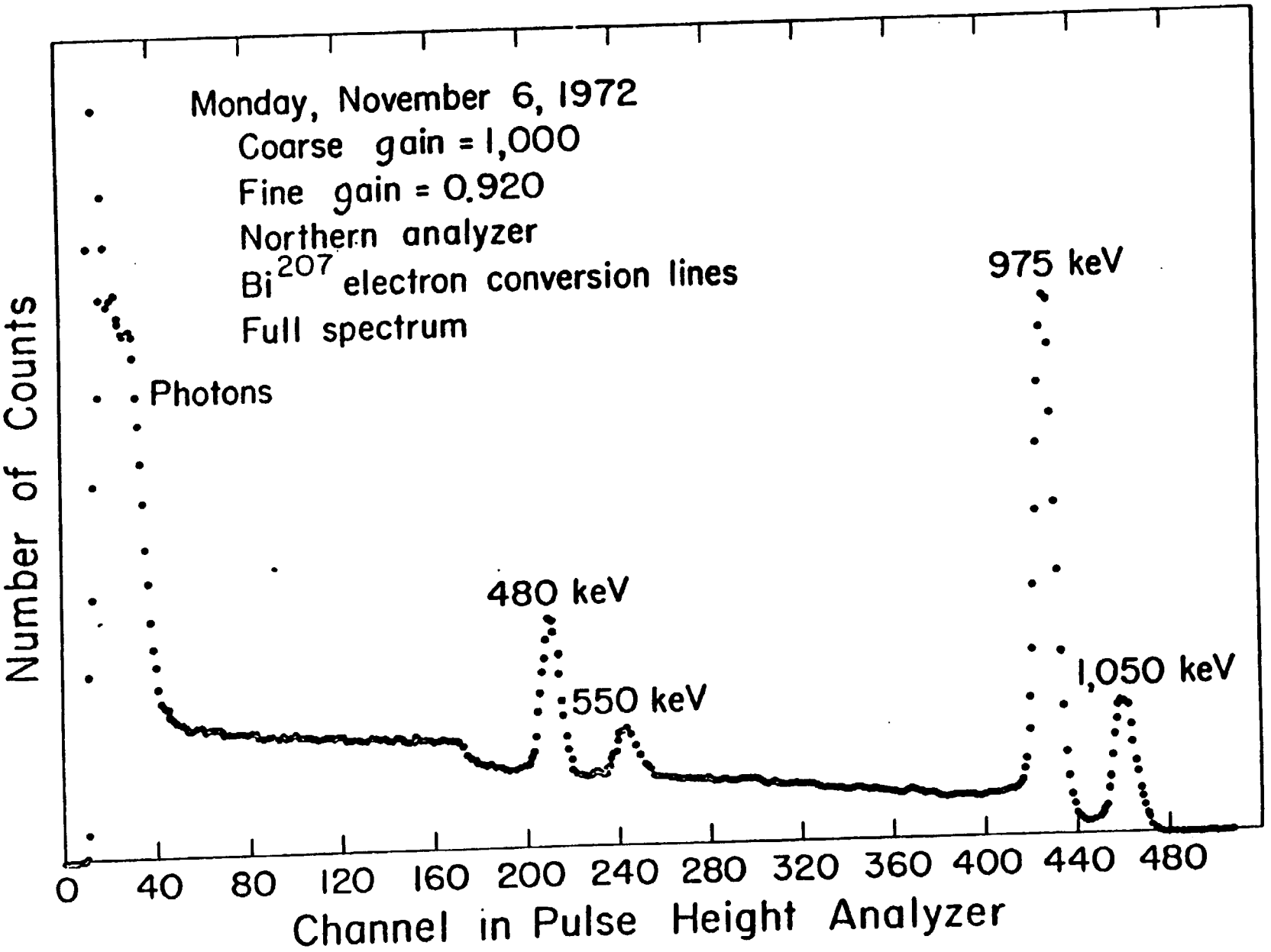
Figure 3.

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of energy losses is then obtained and this is shown in Figure 4. We have also studied the $\alpha$-particles from Am-241 and Pu-239 to check the techniques for measuring the heavily ionizing fragments from the pion star. It is clear therefore that the detectors can detect both light and heavily ionizing particles and count them. The integrals under the peaks shown weighted by the appropriate energies are the relative doses. A certain amount of theory is necessary to arrive at the absolute doses in tissue.

To improve the resolution, the detectors have been cooled down to -20°C; and in this way, the noise limitations of the detector and the electronics have been approached.

To further identify the electrons a Čerenkov counter has been built and will be installed above the phantom. The Čerenkov counter is a large counter and covers the entire beam. It gives a fast pulse whenever an electron enters the phantom and can therefore be used to gate the electronics for subsequent differentiation between the electrons and the other particles.

A scanner has been designed for solid phantoms and is in the shops now. Also phantoms are being built to study the distributions for therapy.

We are beginning to get some insight into how treatment planning will be done with pions: Since experimentally we can separate the high and low LET dose, it makes sense to give the therapist the isodose distributions of these two components. These two components behave biologically quite differently in terms of OER and RBE. Now, can one vary the relative amounts of these two contributions in a treatment volume? At first hand one would be inclined to say no, because the peak to plateau ratio is fixed. However, our beam is essentially monoenergetic and a treatment volume is covered by scanning. By using multiple ports to scan from different directions, the time spent by the peak and plateau in a given region can be changed. Therefore to a certain extent we may be able to vary the relative amount of low and high LET dosage in the tumor.

A recent paper summarizing our work at Berkeley on pion radiotherapy is appended.

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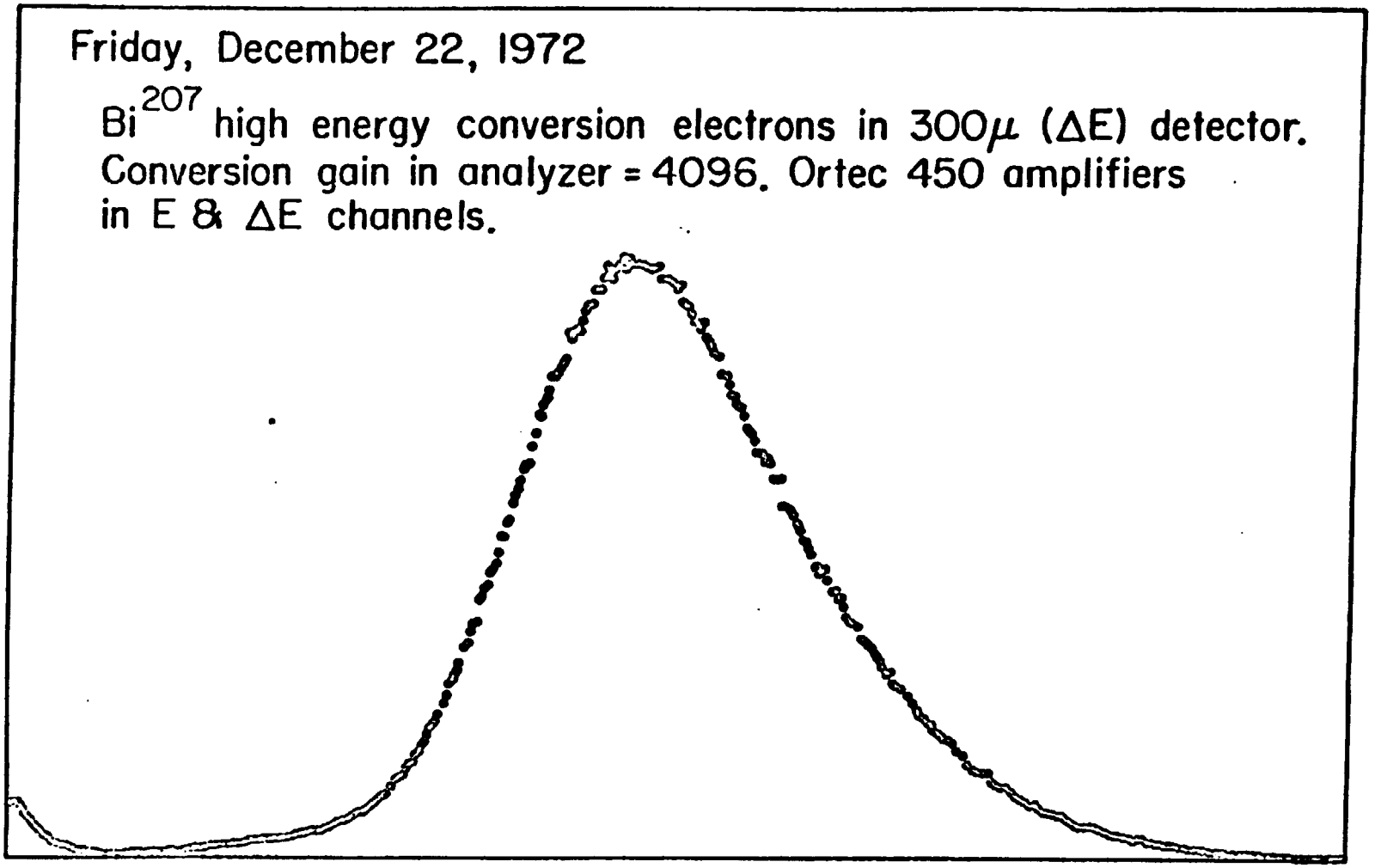
Figure 4.

Note: The run shown here was uncalibrated. A run was made on March 7, 1973 with a 50$\mu$ silicon detector cooled to 5° F. It was calibrated with the two conversion electrons from Cd-109 of energies 62.2 kev and 84.2 kev. The average energy loss for 1 MeV electrons was ~23 kev with a FWHM of ~13 kev. These typically asymmetric energy loss distributions are known as Landau distributions.

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## 3. FACILITIES AVAILABLE

The meson facility is now being completed in our laboratory and it has already attained its design energy of 800 MeV. The biomedical channel is well underway and will be completed this fall. A radiobiology and treatment facility is now on the drawing boards which will adjoin the treatment room. If all goes well, construction should start on this building this summer.

We have tested and built our electronics for these experiments over the last few years, and we have the support of the Electronics Division for maintenance and advice. We have the machine shops to build the scanning equipment and a plastics shop for the tissue mock-up materials.

It is a fair statement to say that we have or are building everything needed to do the work.

## 4. TIME to ACCOMPLISH the WORK

The schedule that can be foreseen at this time is something like this: The beam will be available this fall at fairly low intensity but at full energy. The beam diagnostics work and dosimetry can begin right away. As the intensity is increased and we learn more about the operation of the beam line, radiobiology will begin and continue for many years. Around 1976 or so a program of human trials will be inaugurated that will show what real advantages pions can effect over the other radiations.

This phase of the work, of studying, characterizing and fashioning the beam for different treatment situations will continue through the clinical trials.

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