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18.20PRODUCTION OF NEGATIVE PIONS AND
THEIR INTERACTIONS IN TISSUE

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A number of articles on the possible uses of negative pi mesons in radiotherapy are available (Bond, 1971; Boyd, 1971; Fowler and Perkins, 1961; Kaplan, 1969; Raju and Richman, 1972). The intense beams of negative pi mesons required for radiotherapeutic application are produced by causing either energetic protons or electrons to impinge on a target. It is possible to use a wide variety of target materials; beryllium or a higher Z metal have been employed. Although pions are produced at lesser energies, usually particles of 500 or more MeV are used in order to obtain the intense pion beams required. The cross-section for pion production with an electron beam is of the order of 30 times less than for a proton beam; however, this varies with projectile energy, pion energy, pion angle, target material, etc. Greater pion yields can be obtained with higher energy protons if thicker targets are used. Electrons with the same momentum as the pions are produced in the target and are initially present in the beam. These can be removed almost quantitatively by electromagnetic means, before the beam impinges on tissue.

The negative pi meson has a mass 273 times that of the electron, or approximately 15% of that of the proton. Pions are unstable particles with a charge of minus one that decay with a mean life of 2.6×10^{-8} seconds (rest frame), to form a muon and a neutrino. Practically, some 5 to 10 meters minimal distance from the target to the experimental area is required because of the need for shielding and for beam optics equipment. There is a considerable loss of pions over this distance due to decay as well as capture and scattering of the pions if shielding or other absorber is introduced into the beam. Muons and electrons are produced, which are retained as contamination of the beam if their momentum is equal to that of the pions. Muon contamination should be a minor problem; electrons can be removed either by electromagnetic means or by the use of absorbers.

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In tissue, pions give up their kinetic energy in interactions with atomic electrons. Thus along most of the path of a pi meson in matter, they behave somewhat like an electron as regards rate of energy loss, or dE/dx (however, the values of dE/dx for electrons and pions of the same energy are different). Because its mass is intermediate, it scatters less than does the electron but more than the proton. The degree of scattering depends on energy. Near the end of its range the slowed down meson is captured in atomic electron orbits to form a 'pi mesic atom', which then disintegrates. Near the end of the particle track, the pi meson undergoes reactions with the nuclei of atoms, principally with carbon and oxygen. Of the remaining mass of 140 MeV, approximately 96 MeV is converted to energy of emitted particles, and approximately 44 MeV is used in overcoming the binding energy of the nucleus.

The cross-section for pion capture increases linearly with Z. In soft tissue, about 73% of the pions are captured in oxygen, 20% in carbon, 3% in nitrogen and 4% in heavier ions. Results of measurements (Raju and Richman, 1972) to determine the types of particles produced

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TABLE 1

Particles produced at the end of pi minus tracks in water

Particle	Average energy per pion star (MeV)	Average no. of particles per pion star
Protons	15	0.95
Alpha particles	8	0.99
Neutrons	69	2.7
Recoil nuclei	4.4	0.8

by pion-nuclear interactions in water, and the energy carried off by each type of particle, are shown in Table 1. For a beam of negative pions with an energy of 96 MeV, a momentum of 190 MeV/c, the range in tissue is approximately 25.5 cm.

The negative pi meson beam thus, by undergoing dE/dx losses much as beams of other particles, produces a Bragg curve in tissue or other matter. In addition, because of nuclear disintegrations confined largely to the end of the range of the negative pi meson, additional energy in the form of high LET radiation is liberated in the region of the peak of the Bragg curve of the negative pi mesons. Such a primary Bragg peak of the negative pi mesons, and the added energy from star formation at the end of the range is shown in Figure 1 (Bond, 1971). The curve is for a pure negative pi meson beam with an energy of 96 MeV, a momentum of 190 MeV/c, and a momentum spread of 5%. The peak to plateau ratio is approximately 3 to 1, and the full width at half maximum is about 4 cm.

Because the plateau region of the depth-dose curve results mainly from dE/dx losses of the negative pions, the LET is low, similar to that of energetic electron beams. In the peak region, however, because of the liberation of charged particles and neutrons, the LET is higher. The range of LET's is quite broad, extending from a fraction of 1 keV/ μ due to electrons and muons, to values approaching 1000 keV/ μ due to recoil nuclei such as carbon.

Fig. 1. Depth-dose curve in tissue for a beam of pure pi minus mesons. Momentum 190 MeV/c $\pm$ 5%. (Calculated by S. Curtis, personal communication.)

The mean LET has been shown to be comparable to that of fast neutron beams with mean energies of several MeV.

The peak region of the depth-dose curve shown in Figure 1 is too narrow for most purposes in radiotherapy. Thus usually the peak would be widened by increasing the momentum spread of the beam. In doing so, however, the peak to plateau ratio of the depth-dose curve is reduced. However, with the peak region covering a 10 cm span, the peak to plateau ratio is still of the order of 1.5 or 2, to 1. Because the high LET region of the beam has a higher RBE than does the plateau region, the ratio of 'effective dose' (dose $\times$ RBE) in the peak to plateau region is of the order of 2 to 3 times these values. LS

With the use of a proton beam to generate pions, the beams of pions can be very intense and yield dose rates of the order of 80 rads/min due to pion stars over a tumor volume of 1000 cm³. With this intensity and dose rate a single pion beam, directed horizontally, vertically, or either as desired, can be used for radiotherapy.

If electrons are used to generate pions, then because of the relatively small cross-section for pion production, a much larger solid angle of pion beam must be accepted in order to obtain the necessary intensity and dose rate. This approach is being investigated at the Stanford facility, in which a beam of 500 MeV electrons with a current of one milliamperere is allowed to impinge on a metallic target. Pions emitted over a 360° sector are then entrained into 60 separate beams emerging at roughly a 90° angle to the electron beam path. These beams are then bent electromagnetically to form a large 'cylinder' of beams, which are then again bent through 90° to allow them to enter, potentially from the full 360° expanse, normal to the surface of the patient placed horizontally partially within the 'cylinder' of beams. Exposure of a tumor volume is achieved by horizontal translation of the patient. Each beam must be controlled separately with respect to momentum and momentum spread.

The above properties of a pi meson beam lead to the two presumed advantages of such beams for radiotherapy. First is that one can obtain good dose distributions, both laterally and in depth. This results in maximum energy deposition in the target tissues with minimal energy deposition in normal tissues. Also, the fact that the beam has a well defined range allows one to stop the beam just short of vital structures. A second advantage is the high LET radiation confined to the terminal structures. ~~A second advantage is the high LET radiation confined to the terminal parts of the charged particle beam.~~ This leads to a high RBE with a correspondingly greater peak to plateau ratio of 'effective dose' (dose $\times$ RBE), and a low OER that has the potential for partially overcoming the problem encountered with conventional radiations, namely hypoxic but viable cells that are believed to be present in many tumors and which are resistant to killing by low-LET radiations. = }

As the negative pi meson cascades down the atomic electron levels to be captured by the nucleus, characteristic X-rays are emitted. These are termed π -mesic X-rays. Most energetic and most easily detected are the 160 keV X-rays emitted when the negative pion interacts with an oxygen nucleus. Efforts have been made, by detecting either π -mesic X-rays or gamma rays produced in the course of pion capture, to locate the stopping region of the pion beam in tissue-equivalent material.

No pion generators are as yet available for radiotherapeutic trials. Beams to date have been of low intensity, and frequently contaminated with electrons. They have been suitable for dosimetry. A number of radiobiological experiments have been done; however, the low dose rates available have created problems in obtaining quantitative evaluations.

Several large pion facilities are being prepared for radiobiological and radiotherapeutic evaluations. These include the Los Alamos meson production facility (LAMPF), the Stanford University pion generator, the Tri-university meson facility (TRIUMF) machine in Vancouver, Canada and a facility in Zurich, Switzerland.

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