

[ca. 1981]

NASA FACILITIES CONFERENCE

INTRODUCTION

When major facilities become underutilized as a result of program changes, the management faces the decision of whether or not to shut them down. Because there is usually a base level of manpower required to maintain and operate a facility, there is often no large savings in manpower if a facility is dropped to occasional use, a fact which leads management to consider closing lightly used facilities. This situation prevailed for the Lewis Research Center cyclotron in 1973 when NASA dropped all nuclear energy programs. The cyclotron had been heavily used in both basic and applied research related to the nuclear programs. There had been a 15- to 20-percent utilization of the cyclotron for other research, such as calibration of particle detectors for spacecraft, radiation damage to solar cells, and some collaborative research with the Food and Drug Administration. When all nuclear work was terminated the management decision in this case was to keep the facility operational and to expand the operation in non-NASA activities in order to achieve a high-use rate. My purpose today is to describe the expanded program.

DESCRIPTION OF THE CYCLOTRON FACILITY

The LeRC has had an operational cyclotron since 1956 when the General Electric Company completed a "turn-key" installation of a 60-inch machine and research area. This cyclotron could accelerate heavy hydrogen (deuterons) to 21 MeV and helium nuclei (alpha particles) to 42 MeV.

In 1971 the original cyclotron was shut down and disposed of, except for the 300-ton steel yoke, the copper coils that excite the magnetic field, and some power supplies. The replacement cyclotron was of a new design referred to as AVF (azimuthally varying field), which provides for detailed adjustment of the magnetic field for acceleration of all the isotopes of hydrogen and helium to any final energy up to some maximum limit.

updated version of the cyclotron at Michigan State (MSU), which was copied at Princeton. Complete engineering drawings from Princeton were obtained and a minimal amount of engineering was done by the Facilities Engineering Division to adapt the reclaimed components of the old cyclotron to the new facility. Also, the radio frequency power amplifiers which provide 200 kw of voltage regulated power were redesigned, because there were some obvious deficiencies in the MSU and Princeton designs.

A budgetary limitation of \$250K per year forced the modification to extend over a three-year period and allowed a reasonable period for the procurements and installation. The old cyclotron was operated for the first two years of this period; therefore, the Center was without a cyclotron for only one year. The installation was accomplished with NASA personnel, some of whom are now in operation and maintenance and have had the benefit of the installation experience.

MEDICAL APPLICATIONS OF A CYCLOTRON

Early in the pioneer days of cyclotrons (mid 1930's), the medical applications were investigated. This was probably in part because the cyclotron's inventor, E. O. Lawrence, had a brother, John, who was a medical doctor. The most significant work of those early days was the making of radioactive iodine and the recognition of its specific absorption by the thyroid gland. This was the birth of the field of nuclear medicine. Another use of the pioneer cyclotron was to generate fast neutrons which were used to irradiate cancerous tumors. These experiments were not encouraging because there was more damage done to the skin than in conventional x-ray treatment. It is now known that these patients were overexposed, producing clinical symptoms of fibrosis and necrosis of the skin. These problems often arose months after the treatment and were termed "late effects." This put an end to neutron therapy until twenty-five years later when, at Hammersmith Hospital in London, a careful study established the correct radiation exposure for fast neutrons and produced encouraging results for this means of treating cancer.

At the time the LeRC cyclotron was being considered for termination of operation, there were three cyclotrons in the United States receiving funding from the National Cancer Institute (NCI) to continue the work started at Hammersmith Hospital. These institutions are listed on the third slide.

CLEVELAND CLINIC (CCF) - LeRC THERAPY PROGRAM

The Cleveland Clinic, after learning of the availability of the LeRC cyclotron, made a proposal to NCI, a division of the National Institutes of Health (NIH), for support to join the ongoing clinical trials. The requested NCI support was primarily to pay for the salaries of LeRC personnel and the operating costs of the cyclotron. The Clinic proposed to put their money into the construction of therapy-related facilities. The support of the cancer therapy program by another federal agency, the NIH, was a legal simplification, in that patient treatment did fall within the charter of that organization.

A legal agreement between CCF and LeRC was approved by the NCI. The agreement calls for LeRC to perform as a subcontractor of the CCF under the Clinic's grant from NCI. The LeRC agrees to supply neutrons four days a week for eight hours a day for a two-year period; the agreement is renewable for five years.

DESCRIPTION OF THE NEUTRON THERAPY FACILITY

A. Cyclotron

The cyclotron required no modification for the cancer therapy program. It was decided to produce the fast neutrons by bombarding beryllium with 25 MeV deuterons. With a 20 microampere current of deuterons, a radiation dose of 40 rads per minute would be obtained at the patient position, 125cm from the beryllium target.

B. Beam Delivery System

The cyclotron area is shown schematically in Figure 4. The deuteron beam emerges from the cyclotron as a horizontal beam 48 inches from the floor and is bent by three magnets to strike a beryllium target located in a large assembly of neutron shielding material.

It is also possible, as shown on the fifth slide, to insert a 21° bending magnet in the deuteron beam so that the beam is bent upward out of the horizontal plane and into a 111° magnet located in a house above the treatment room. The deuterons are then bent vertically down upon a beryllium target located in a large neutron shield a few feet below the ceiling. The result is a vertical neutron beam, the first in this country. This offers the possibility of treating patients in the supine and prone positions, which are the usual treatment positions for x-ray machines; therapists prefer these to the standing or sitting positions because the patient can be better immobilized and the internal organs are not shifted by

gravity.

C. Shielding and Collimator

In the vertical and horizontal modes, the shielding, target, and collimators are identical. The overall construction of the horizontal neutron beam assembly is shown in Figure 6. The bulk shielding consists of a minimum of 30 inches of benelex in every direction from the beryllium target. For the vertical beam the benelex is suspended from the treatment room ceiling and consists of a block of benelex approximately 6 feet by 6 feet by 6 feet. The horizontal shield is slightly less massive. For each beam the collimator and target assembly is located within a 14-inch diameter hole through the benelex shield. The collimator consists of a hollow steel cylinder, filled with a mixture of tungsten powder and paraffin, and an inner collimator, constructed of water-extended polyester to which iron and boron have been added. This inner collimator defines the treatment field and is interchangeable from patient to patient. The target assembly is shown in more detail in Figure 7. It consists of a water-cooled beryllium disk 1/8-inch thick. Directly in front of the beryllium there is a four-sector aperture equipped with current readout to insure that the deuteron beam is always properly positioned on the target. Immediately after the target a dual parallel plate ion chamber is located. All the neutrons that strike the patient must pass through these monitor chambers; thus, by collecting and measuring all of the charge from these chambers during a treatment, a measure of the patient's exposure is obtained.

DOSIMETRY

Prior to treatment of patients the radiation field in tissue equivalent liquid must be measured relative to the charge collected in the monitor ion chambers. A 30-gallon container of a liquid having the same number of carbon, oxygen, nitrogen, and hydrogen atoms as does muscle tissue was placed in front of various size collimators and the radiation field was measured as a function of depth. From these data the Cleveland Clinic physicist can plan the treatment. Figure 8 shows the radiation field at various depths in the liquid. Particular attention has been given to the first centimeter of depth because this represents the skin of the patient and it is very important that the radiation field increase with depth as shown in Figure 9. This means that the skin receives a lower radiation exposure than the deeper tissue. Skin is more sensitive to radiation and can become necrotic if the exposure is too large. The lack of "skin sparing" was one of the problems in the very early neutron therapy studies.

RATIONALE FOR NEUTRON THERAPY

The Hammersmith Hospital group has obtained encouraging results in their

fast neutron studies. They started by treating terminally ill patients and in this way established the exposure necessary to cause regression or disappearance of a tumor. They now treat patients they hope to cure and according to Dr. Mary Catterall, the project leader, the results with neutrons are often better than would have been expected with conventional gamma radiation therapy. Biologists have an explanation as to why fast neutrons are superior to gamma radiation, although it is generally agreed that their understanding of the process is not complete.

Gamma rays interact only with the electrons of atoms. At the energies used in therapy (.25 to 25 MeV), the gamma rays act like particles and collide with electrons, transferring some of their energy to the electrons which then travel as charged particles causing ionization of the molecules along their paths.

The fast neutron, on the other hand, does not interact with electrons at all, but moves through tissue until it strikes the nucleus of an atom. At this point a nuclear reaction occurs and the struck nucleus moves off at high speed causing a high density of ionization along its path of travel. The basic difference in the two radiations is that the secondary particles that cause ionization are lightly ionizing in one case (gamma radiation) and densely ionizing in the other (fast neutron radiation). Biologists believe that the more densely ionizing particle is more likely to cause damage to the DNA molecule, which cannot be repaired, than is the lightly ionizing electron. Experimental evidence for this is shown in the next slide which shows the fraction of cells surviving a given dose of radiation. After receiving 400 rads, the radiation was terminated and 24 hours was allowed for the surviving cells to recover. When the radiation was resumed, the cells exposed to gamma radiation behaved as though they were an untreated group of cells, whereas the neutron group continued to show the same steep slope in the survival curve as they had shown at the end of the first radiation period.

The effect on cell recovery in laboratory animals is just one of the differences observed between gamma radiation and fast neutron radiation. the extrapolation from animals to man is uncertain; thus the importance of these effects in therapy is a question the NCI program is seeking to answer. It is significant to note that the densely ionizing radiations are promising enough for cancer therapy to warrant investigation of other sources of densely ionization radiation. Pi mesons and heavy ion beams of carbon, neon, and even argon, of billions of electron volt energy are being studied at the Lawrence Radiation Laboratory in Berkeley.

USE OF LeRC CYCLOTRON IN NUCLEAR MEDICINE

Fast neutron therapy, as you see, has the complication of requiring that patients be brought to the laboratory for treatment. For the cyclotron to be used in nuclear medicine, this problem need not arise, since radioisotopes can be made at the cyclotron and then shipped to the hospital for use there.

Radioactive iodine, first made many years ago, is enormously effective in treating thyroid cancer. In this use the radioisotope goes to thyroid tissue and there undergoes radioactive decay where the radiations emitted can act locally on the cancer. However, most of the radioisotopes used in nuclear medicine are for diagnostic purposes where the objective is to use a radioisotope with radiation that can be easily detected outside the body; that means a gamma ray with an energy between 0.1 and 0.2 MeV and no electron emission, because the charged particle contributes to a patient's radiation exposure. Cyclotron-produced radioisotopes are more likely to meet these conditions than are nuclear reactor-produced isotopes. For this reason there are a number of commercially owned cyclotrons producing radioisotopes for diagnostic nuclear medicine.

The fact that there are commercial suppliers of radioisotopes can cause a problem for a government owned cyclotron that produces and distributes the isotopes to other than government funded work. Commercial suppliers can claim unfair competition. For this reason we have concentrated our work in nuclear medicine research on new radioisotopes of which there is no commercial production.

One very successful effort was the discovery that very pure iodine 123 could be made by producing radioactive xenon-123. Xenon is a chemically non-reacting gas and is easily removed from a target. After a waiting period of several hours, the xenon-123 has decayed into radioactive iodine-123. The purity of this radioactive iodine is such that the patient's radiation exposure is just 25 percent of that of commercially produced iodine-123 and the images of organs that have taken up the radioactivity are more clearly defined. The commercial producers have only small cyclotrons and, therefore, cannot make xenon-123.

A target that produces xenon-123 by bombardment of liquid cesium is being developed at the cyclotron in Vancouver, B.C., called TRIUMF (Tri University Meson Facility). This target system shown in slide 11 will stand up to the high currents of 500 MeV protons and requires a minimum of processing of the radioactive materials. This is important in keeping the patient cost low.

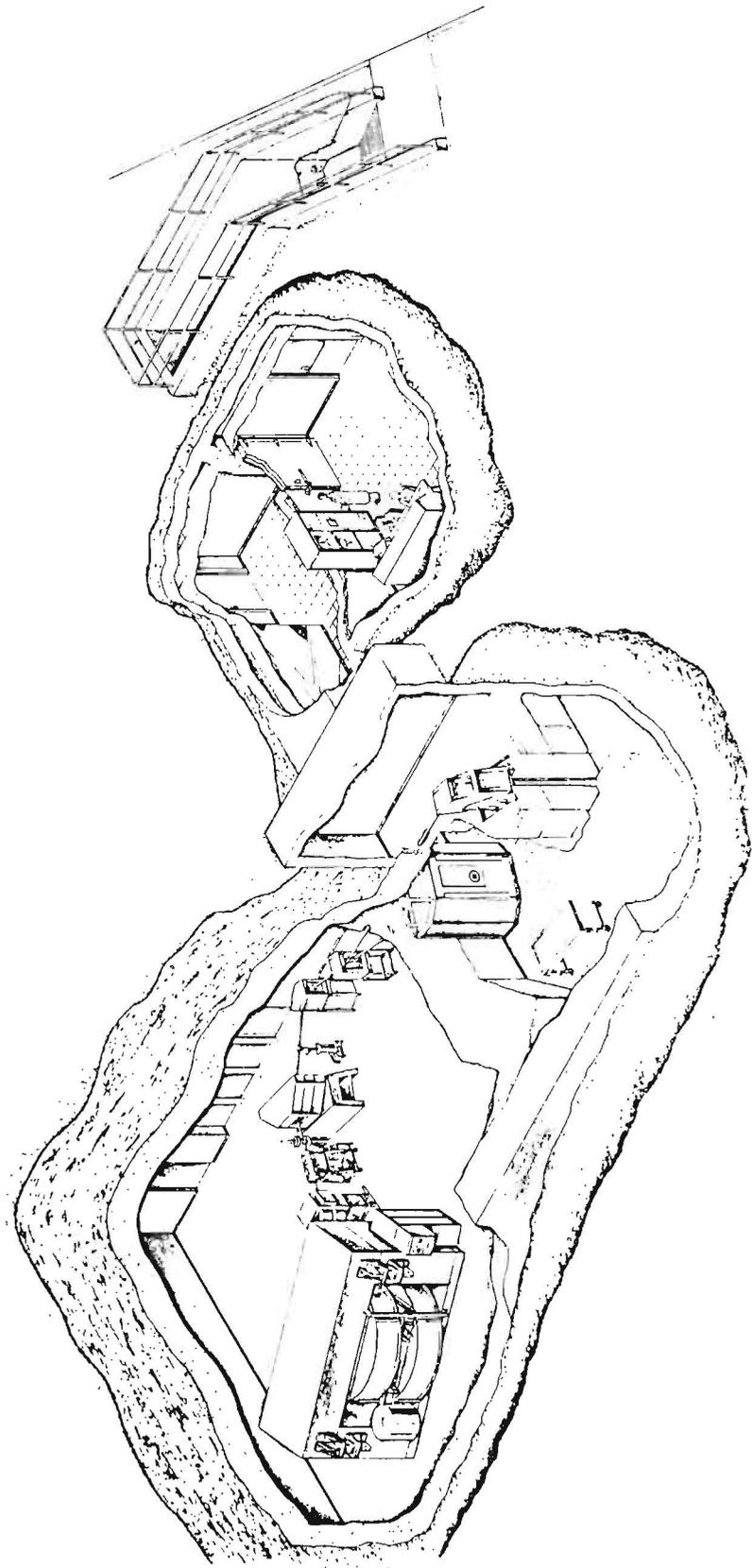
Radioactive iodine-123 is the best radioisotope to use for thyroid studies but is also very useful in studies in which it is chemically

attached to a pharmaceutical compound that is specifically taken up by a particular organ. The next slide shows an image of the liver of a child who has been given iodine-123 tagged rose bengal. This radioisotope should have gone to the liver and the bile duct should have been apparent in two hours. In this case, twenty-one hours were required. This condition was found to be caused by a rare choledochus cyst.

The LeRC cyclotron is currently producing on a routine basis one radioisotope which is being used on patients. The radioisotope is thallium-201 which goes to healthy heart muscle and does not go to tissue that is infarcted (dead) or poorly supplied with blood (ischemic). Thallium-201 appears to be valuable in developing a prognosis for a patient who has had an acute myocardial incident.

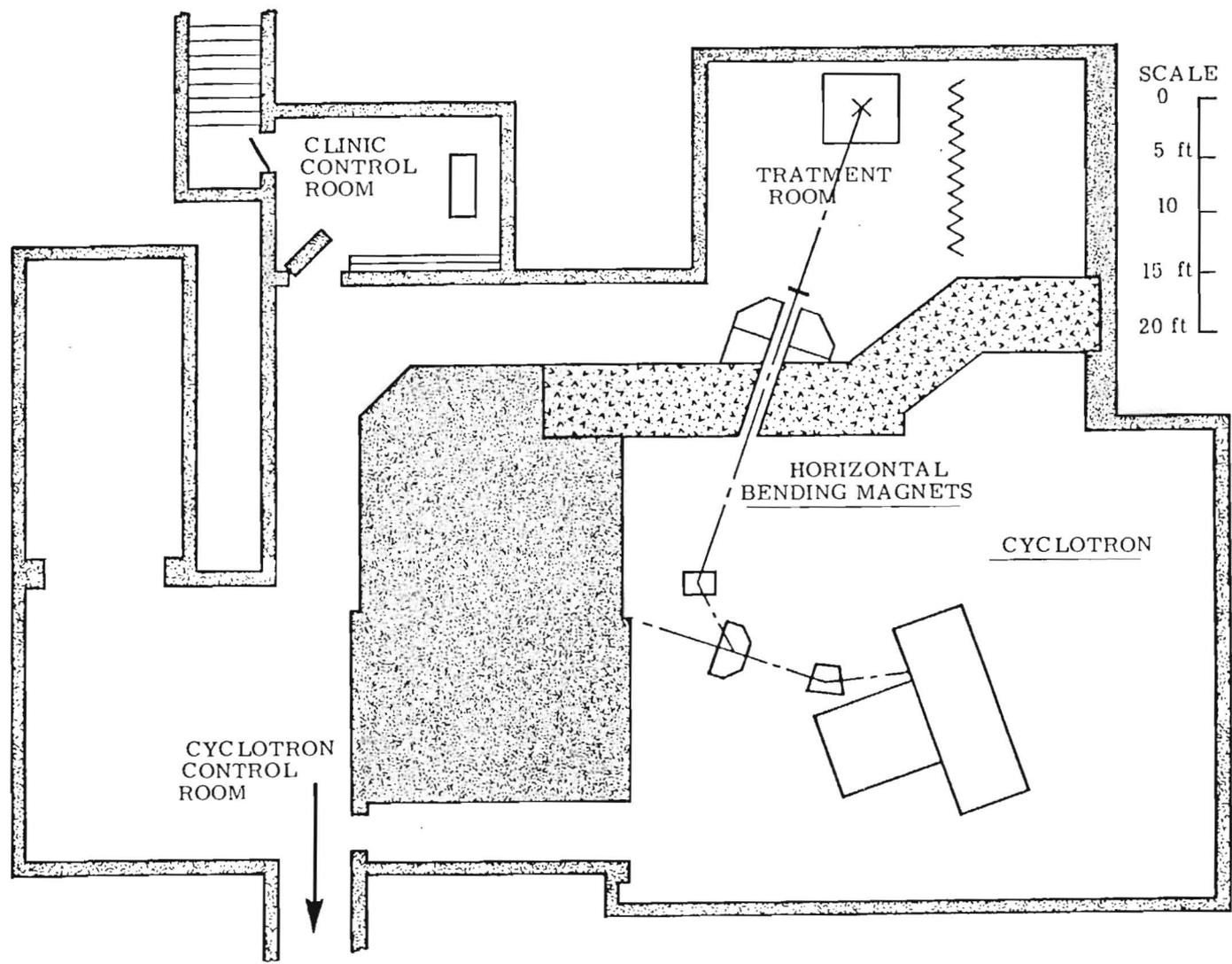
PARTICLES ACCELERATED BY LEWIS CYCLOTRON

<u>TYPE</u>	<u>MAXIMUM ENERGY</u>
PROTON	50 MeV
DEUTERON	28 MeV
HELIUM-3	87 MeV
HELIUM-4	56 MeV



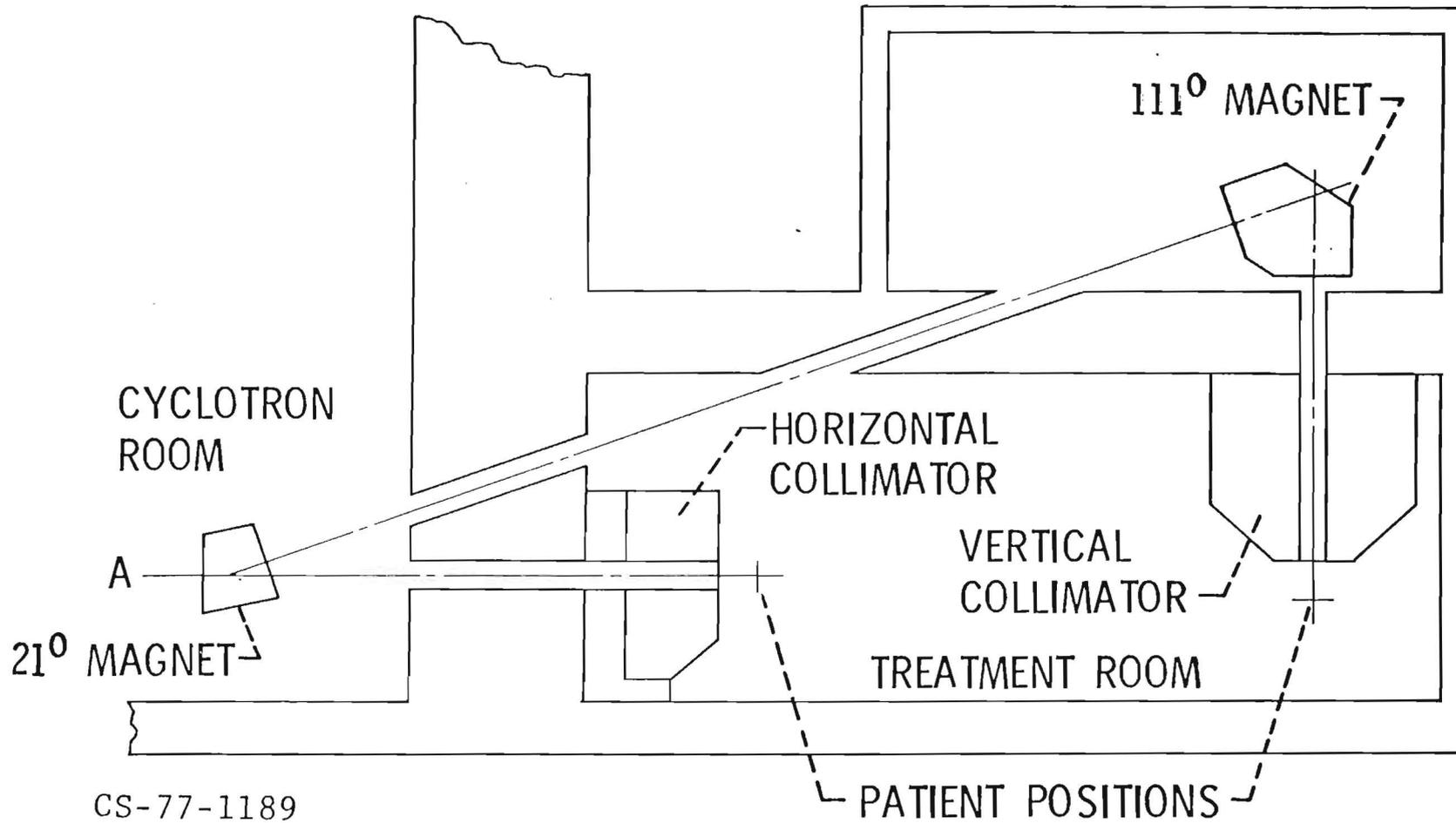
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<u>CYCLOTRON LOCATION</u>	<u>MEDICAL INS TITUTION</u>	<u>DEUTERON ENERGY</u>
UNIVERSITY OF WASHINGTON SEATTLE	U. of W. MEDICAL SCHOOL	21 MeV
NAVAL RESEARCH LABORATORY WASHINGTON, D. C,	GEORGE WASHINGTON UNIV. MEDICAL SCHOOL	35 MeV
TEXAS A & M UNIV. COLLEGE STATION, TX	M. D. ANDERSON CANCER CENTER HOUSTON, TX	50 MeV

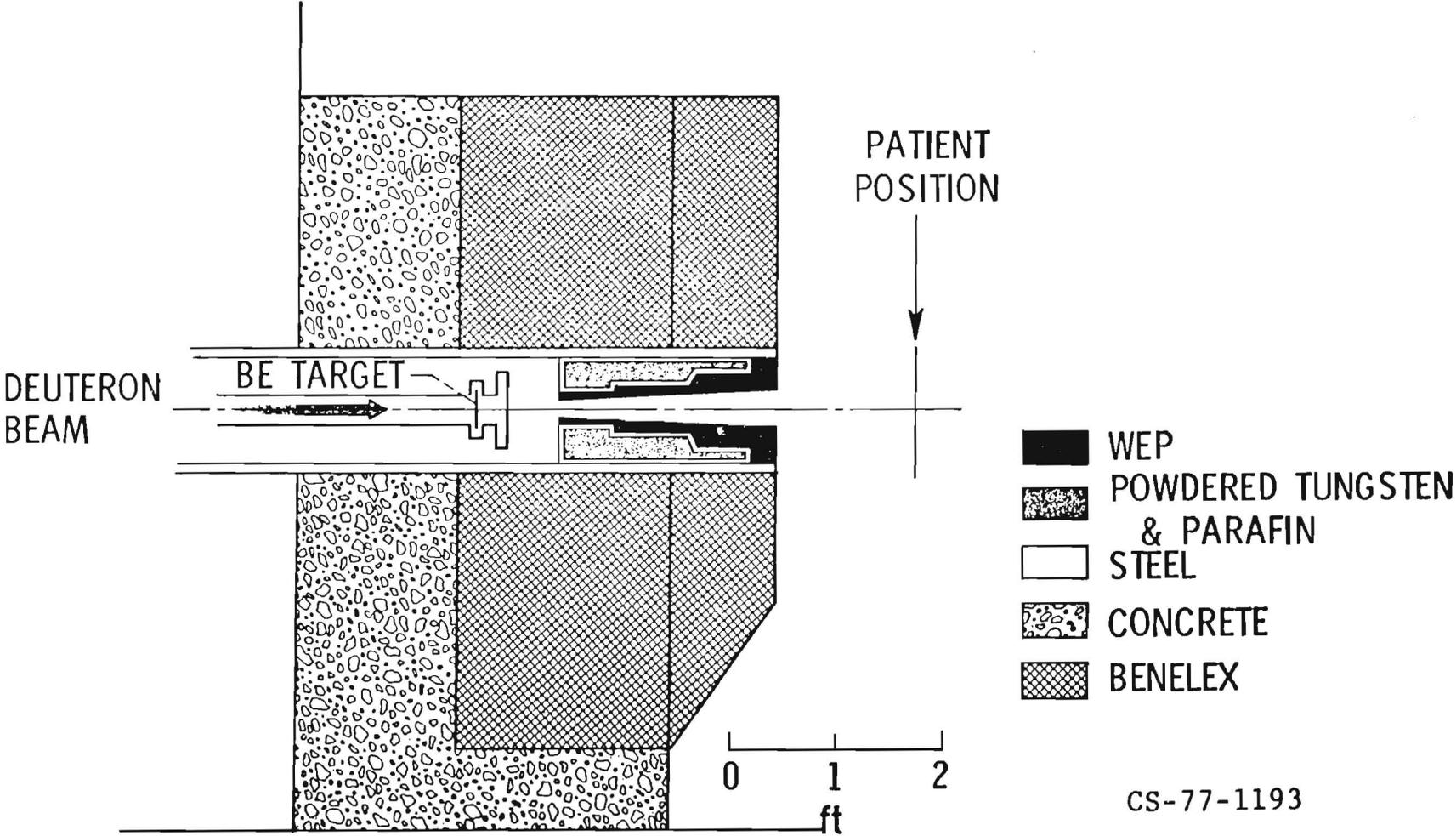


LEWIS RESEARCH CENTER CYCLOTRON AND CLEVELAND CLINIC
NEUTRON TREATMENT AREA

VERTICAL CROSS SECTION OF BEAM TRANSPORT SYSTEM

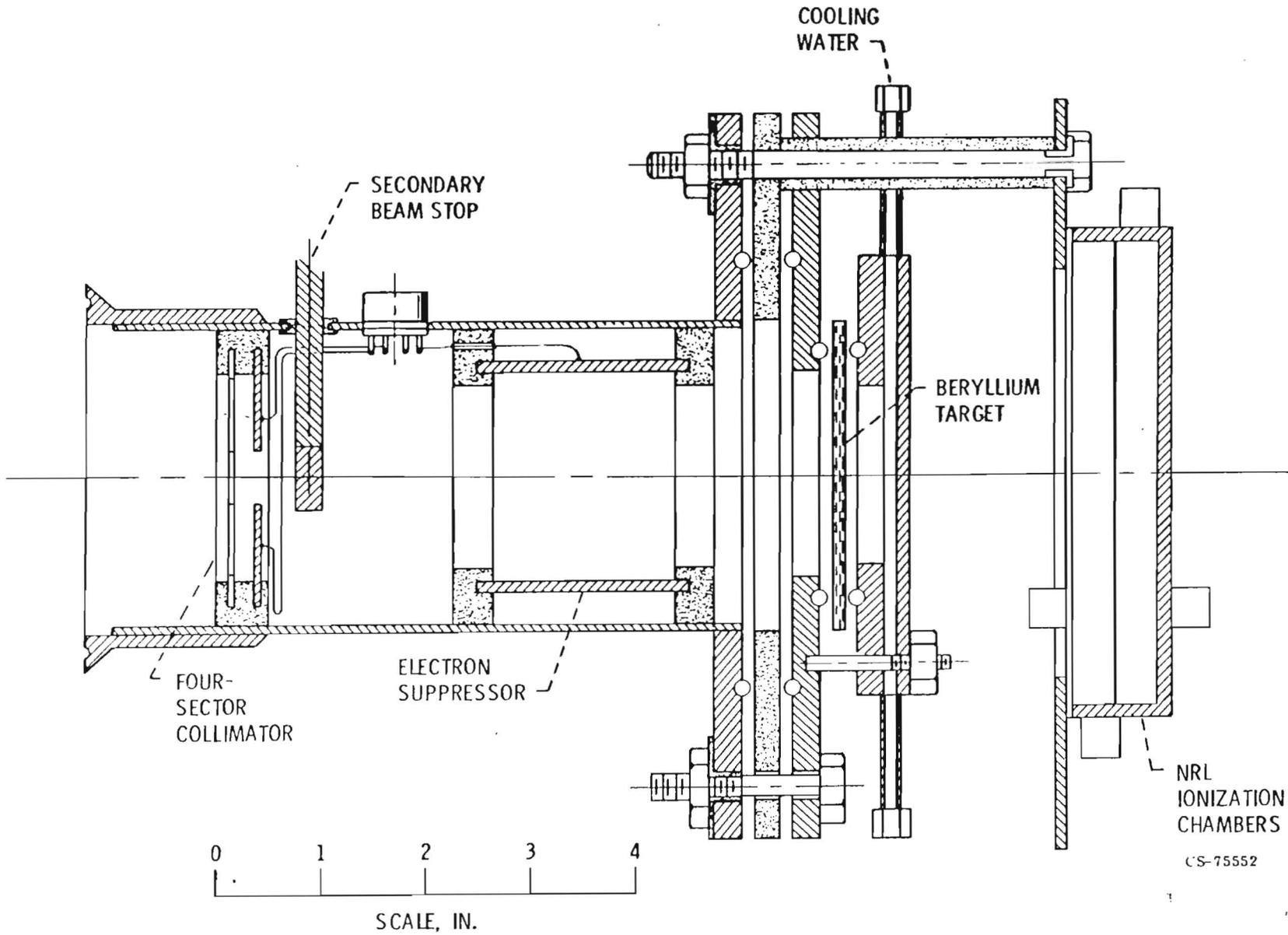


SHIELDING AND COLLIMATOR CONSTRUCTION

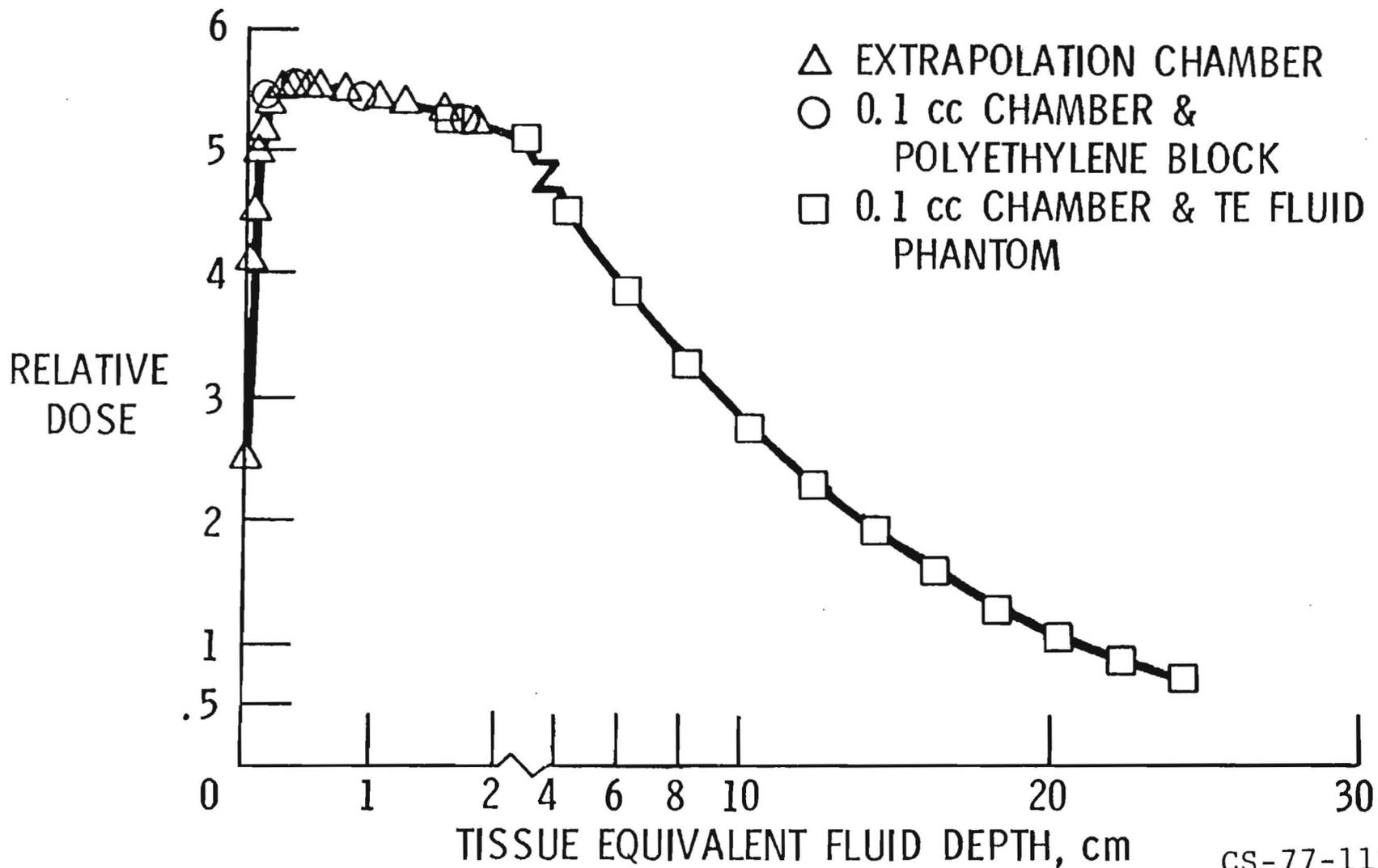


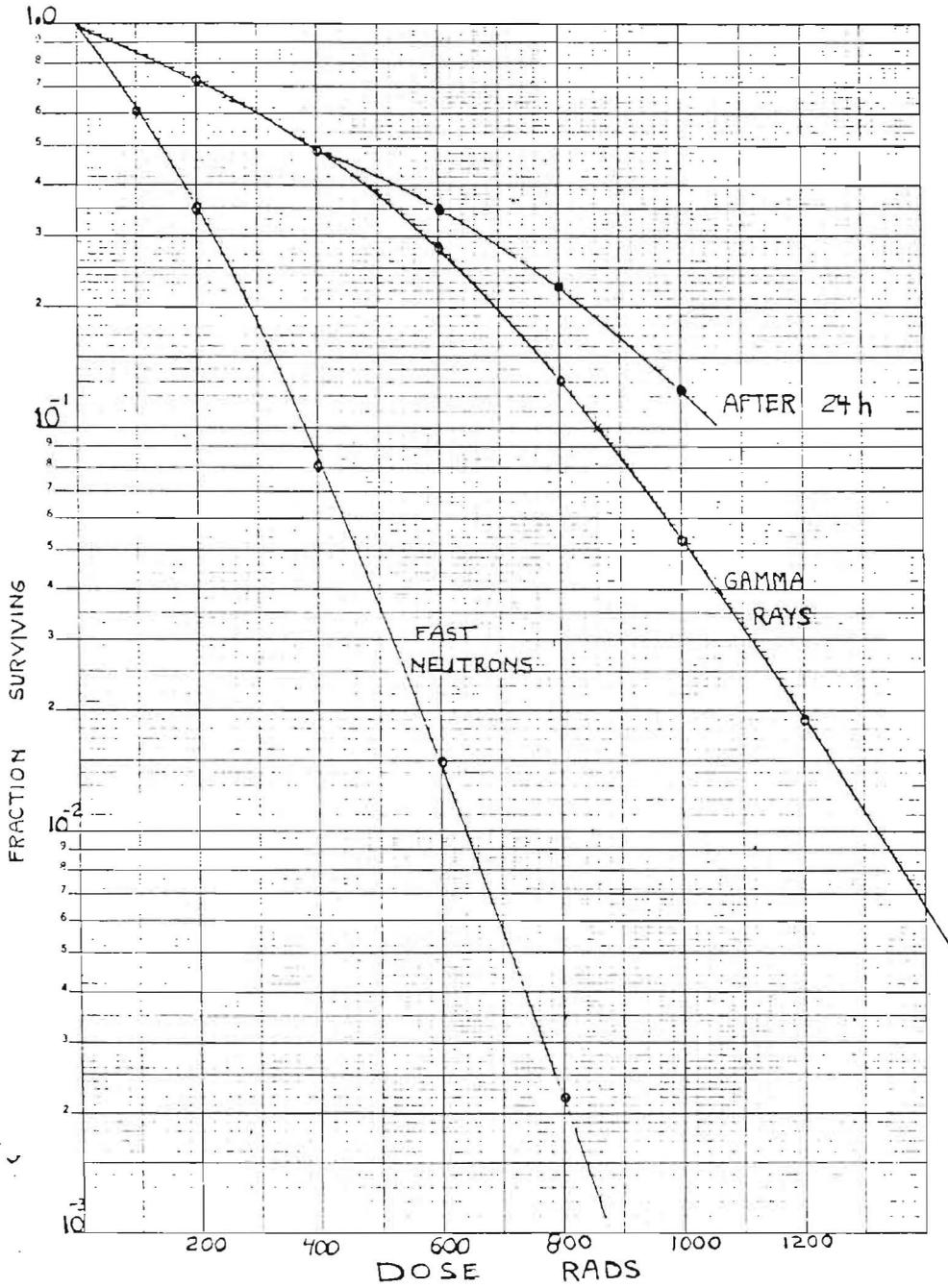
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TARGET ASSEMBLY

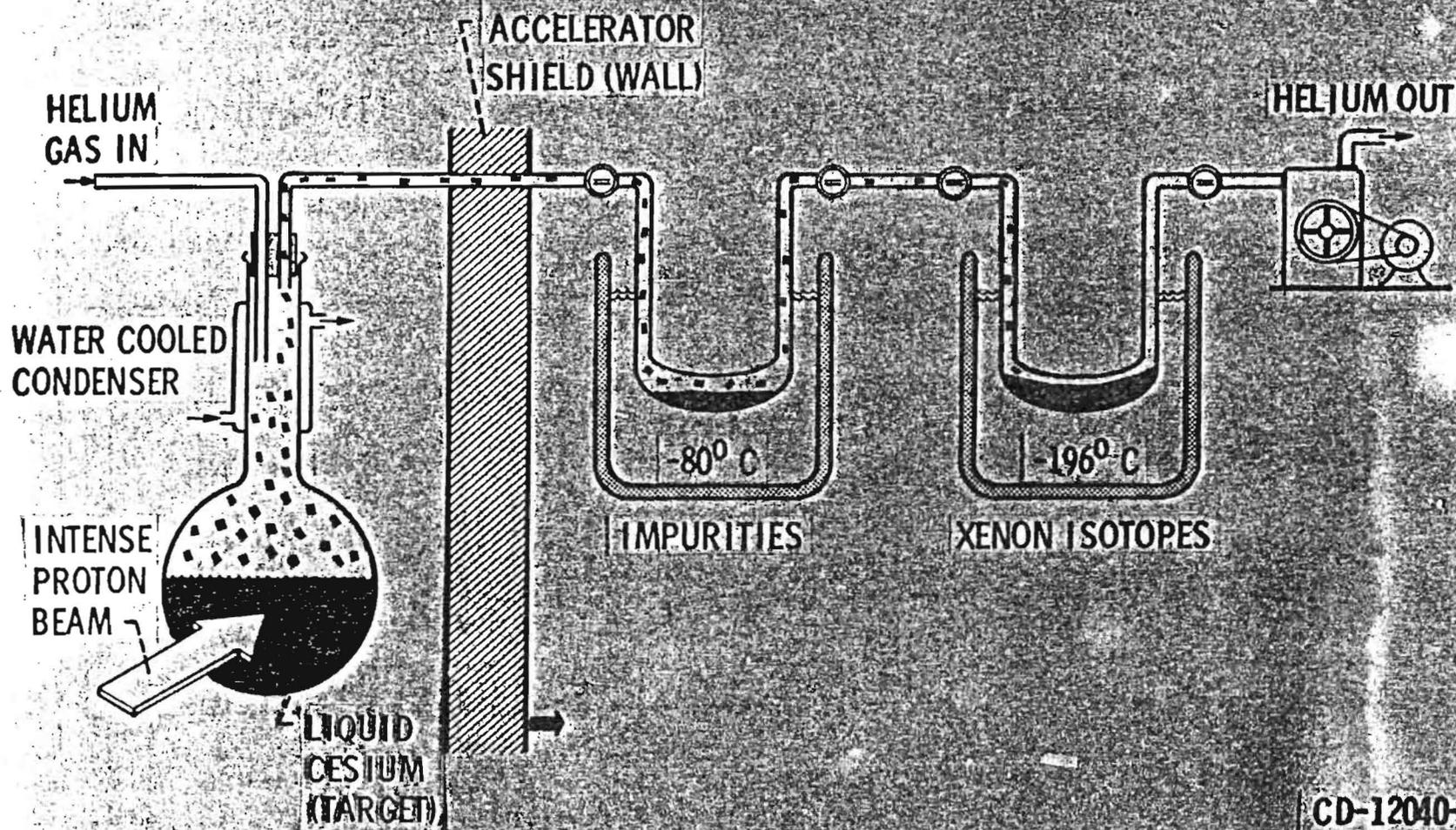


RELATIVE AXIAL DOSE

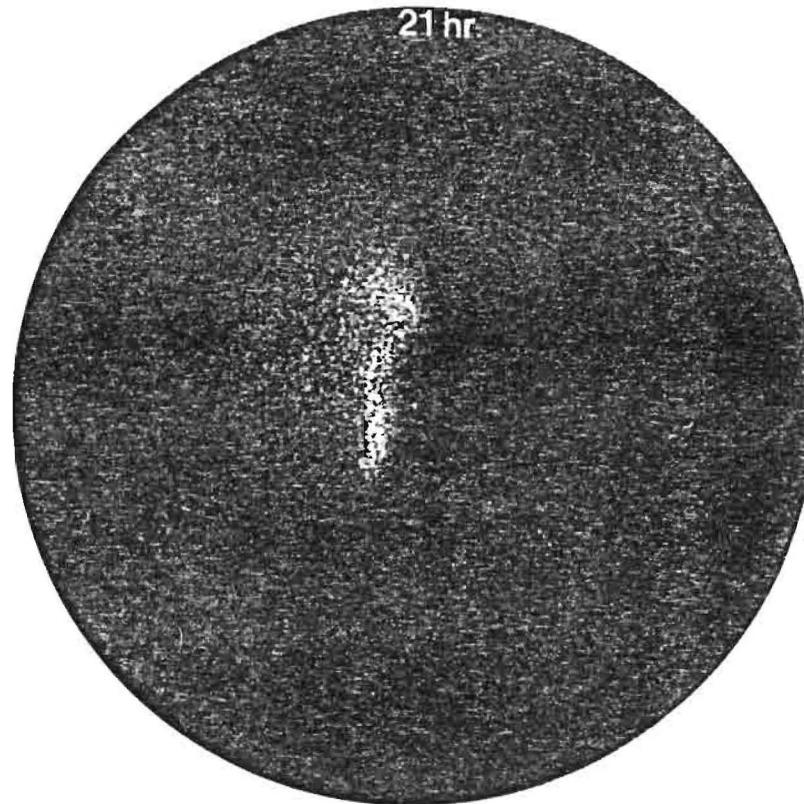
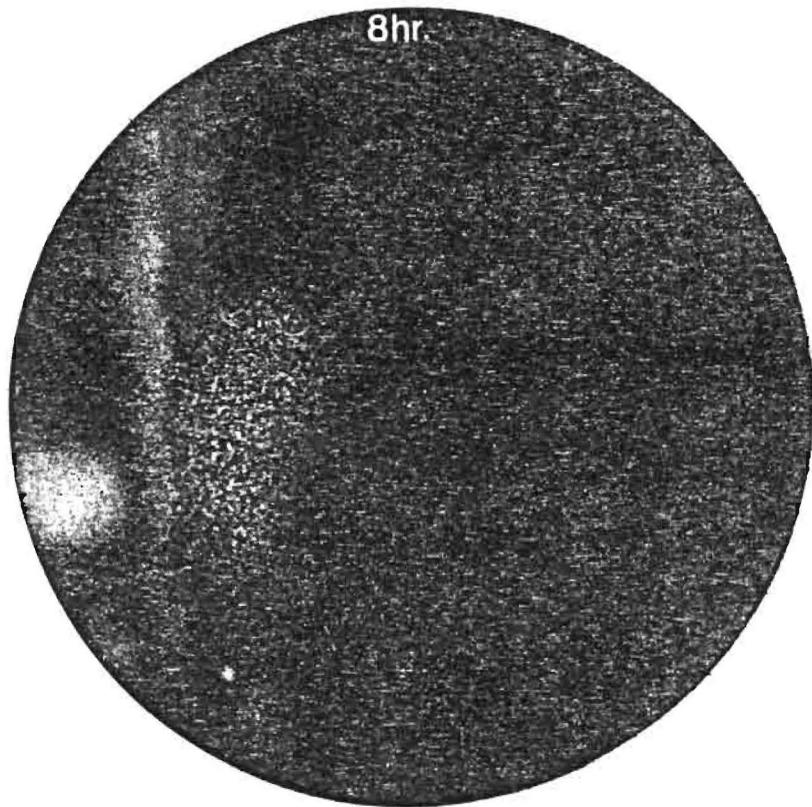




CONTINUOUS PRODUCTION CYCLOTRON TARGET



CD-12040-31



DISTRIBUTION OF IODINE-123 ROSE BENGAL
AT 8 HOURS AND 21 HOURS POST INJECTION