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## Accelerator & Fusion
## Research Division

Presented at the conference on "Biological Imaging:
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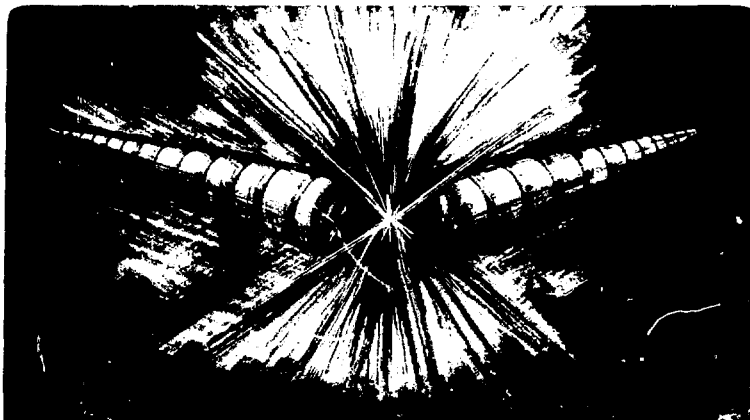
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# Developments in Accelerators and Instrumentation

## Relevant to Imaging with Charged Particles

### and Positron Emitters[1]

Jose R. Alonso

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## Introduction

In past years particle accelerators have become increasingly important tools for the advancement of medical science.[1,2,3] From the pace of advancing technology and current directions in medical research, it is clear that this relationship between accelerators and medicine will only grow stronger in future years. In view of this importance, we shall investigate this relationship in some detail, with an eye not so much towards the medical uses of the beams produced, but more towards the technology associated with these accelerators and the criteria which make for succesful incorporation of these machines into the clinical environment. In order to lay the necessary groundwork, we shall first explore the different kinds of accelerators found in medical use today, briefly discussing salient points of each.

## Accelerators

A list of the accelerated beams presently used in medical research is given in Table I, listed by increasing energy. Primary applications of these beams are given, along with the beam energy range which is considered best suited for that application. Energy requirements depend on the particular applications. In the case of charged particle therapy the energy is determined by the treatment depth, since the beam must penetrate the proper distance into the body to reach the tumor. In cases where nuclear reactions are required, such as for isotope production or the generation of neutrons and pions for therapy, the optimum energy is determined by the nuclear reaction energy thresholds and yield characteristics.

The accelerator type used most frequently to produce each beam is given in the last column. The size of the required accelerator is most easily characterized by the total beam energy in the case of linear accelerators, or by the magnetic rigidity of the highest energy beam produced, in the case of circular accelerators. Linear accelerator energy gain values range typically from 2 to 10 megavolts per meter depending on the accelerator structure; the electron linacs (the first line of Table I) are all a few meters or less in length, while the Los Alamos LAMPF pion generator is several hundred meters long. Magnetic rigidity relates to the magnetic field strength required to bend the particle beam, and is measured in kiloGauss-meters (kG-m). As an example, a beam with a rigidity of 50 kG-m passing through a magnet with a maximum field of 20 kG will be bent in a circle of 2.5 m radius. Thus to contain the beam in a closed circular orbit the magnet would have to be 5 meters in diameter. One sees in Table I that light ion beams up to a few hundred MeV in energy have magnetic rigidities which are low enough that single-magnet accelerators are quite practical. Heavy ion rigidities are much higher, making the synchrotron the accelerator of choice for these beams. This machine consists of a string of smaller magnets enclosing the large-diameter particle orbit. The magnetic field is increased in synchrony with the particle energy, keeping the particles in the same orbit. This configuration greatly reduces the magnetic field volume required and hence the construction and power costs.

A word is in order about beam intensities. For cases where the primary beam is used for radiotherapy, the beam intensity requirements from the accelerator are quite modest, and thus present no technological challenge to reach. However, when the primary beam is run into a target to produce the secondary beam actually used in treatment, which is the case with neutrons and pi mesons, extremely high beam currents are needed since the conversion efficiency from primary to secondary beam is quite low. The ion source, beam extraction (in the case of circular machines), target shielding and cooling, and general accelerator component activation all become severe problems.

Let us now run down the list in Table I.

Electron beams serve either as primary beams or for producing x-ray beams for diagnostics or therapy use. In past years betatrons were used, but more recently small high-gradient linear accelerators have been employed to produce these beams.[4] The energy of the electron beam is determined by the desire for the most favorable depth-dose distribution, in other words that the normal-tissue to tumor dose-ratio be as favorable as possible. This last requirement has pushed the desired electron energies to 30 MeV and higher.

Table II gives a representative but by no means thorough list of radioisotopes used in medicine today, with the production reaction and beam energy required for each.[5] The magnetic rigidities of the required beams are low enough that small cyclotrons can meet many of the isotope-production needs. There are several commercial suppliers of such machines which are compact, efficient and specifically designed for the hospital environment.[6]

Neutrons for radiotherapy are produced by the (p,n) reaction of protons of at least 40 MeV, or by the (d,n) reaction of deuterons of at least 50 MeV, on a beryllium target.[7,8] These energies require more substantial cyclotrons, with high intensity requirements since the neutrons are a secondary beam. The d-t generator producing 14 MeV neutrons requires only a very modest acceleration of the deuterons (performed electrostatically).[9] However, the very unfavorable depth-dose characteristics of these low energy neutrons has precluded the widespread use of these devices.

Using protons or alpha particles directly for radiotherapy requires a beam of around 250 MeV per atomic mass unit (i.e. 250 MeV protons, or 1 GeV alpha particles) to give a penetration distance of 30 cm in tissue. The rigidity of these particles, 25 kG-m and 50 kG-m respectively, is still within reason for a single-magnet accelerator, such as a large cyclotron or synchrocyclotron.[10,11] A variant of the cyclotron which has recently become quite popular is the split-pole cyclotron, in which the magnetic field is generated by four or more pie-shaped magnets. Examples of this machine can be found in Berlin (VICKSI), France (GANIL), and in the Indiana Cyclotron.[3] For large accelerators this approach is somewhat more economical, and avoids some of the vertical focusing problems inherent with large single-magnet cyclotrons.

Production of pi mesons for radiotherapy requires a very high current source of primary particles of energies greater than 600 MeV. Although medical pion channels have been built or are operating on electron linacs (Stanford)[12] and very large cyclotrons (TRIUMF[13] and SIN[14]), the most promising medical pion generator is the proton linac. Linear accelerators, such as the LAMPF machine[15], are more easily capable of the very high beam intensities needed for producing adequate dose rates of the secondary (pion) treatment beam. An extensive study effort at Los Alamos has led to the development of the PIGMI concept[16], a variant of the LAMPF accelerator, which is somewhat reduced in size and highly optimized for the clinical environment.

The final entry in Table I is for heavy ions.[18] The medical use of primary beams of carbon, neon or other ions up to argon for radiotherapy and diagnostic applications will be discussed later.[17,18] The energy required for these beams to achieve 30 cm penetration in tissue varies with the ion species, from 400 MeV/nucleon for carbon to almost 825 MeV/nucleon for argon. The rigidity of this argon beam is around 110 kG-m, indicating that a circular heavy ion accelerator must be a synchrotron ring with a radius of about 15 meters. Although such a machine is quite spread out, it need not be massive since the beam enclosure can be a tube of cross sectional dimensions around 5 cm x 10 cm, with the accelerator magnets being of similarly modest proportions.[19]

## Technology

Of the accelerator categories listed in able I, only the electron linacs and small cyclotrons are presently found in the hospital environment. The medical work done on other accelerators is in most cases an adjunct to more extensive nuclear science programs conducted at large laboratories. It is perhaps desirable that the early phases of a biomedical research effort with a new modality be performed in such an atmosphere, where physics technology and support facilities are generally available to develop necessary instrumentation and techniques for the biophysical characterizations of the beam. However, when the early phases are completed and the clinician is interested in treating patients, difficulties arise. Beam scheduling, machine availability and the overall atmosphere are generally less than ideal for such clinical work. It is the general experience at such facilities that radiotherapy and nuclear science programs coexist only with the greatest of difficulty. Note that the emphasis should be laid on the problems of sharing a machine between research programs, not on the incompatibility of a large machine with a purely biomedical objective. It is certainly true that the large machines which are presently used for medical research with what we shall for now call exotic beams are not suitable for transfer to a hospital environment, but these are not the machines one would build for a hospital anyway. Once the basic work is done on these accelerators, and the desirability of having such a beam in a clinical environment is established, then one designs an accelerator

specifically tailored to medical needs and builds it in a hospital. This is precisely the developmental history of the small electron linacs and cyclotrons which one now finds in so many hospitals.

Let us examine now some guidelines to be kept in mind in adapting accelerator technology for a hospital-based operation. The basic requirements for a piece of hardware in a hospital can be summarized in the following three points.

1. Reliability.
2. Low maintenance and reliability...
3. Ease of operation and reliability!

The machine must be available, hopefully, at the turn of a key; it should not break down, or if it does it must be back up in a few minutes; and it must be operable by the technical staff normally available in the hospital.

This may seem like asking for a lot from a device as complex as a large particle accelerator, but in fact our experience indicates that we have already met these requirements with some existing machines. Designing new accelerators with these ideas in mind is by no means unthinkable, the accelerator community as a whole is quite convinced that the task is well within present technological capability.

There are certain general concepts one must keep in mind which will most greatly enhance chances for a reliable design.

1. One must stay with mature technology. Techniques which have been used extensively are in general well understood, permitting one to design confidently for reliability and efficiency. Unpleasant surprises rarely happen in these areas.

At this point let us digress briefly to discuss the question of superconductivity. Superconducting magnets have been hailed as the panacea for reducing both power bills and magnet sizes to the point where both are considered manageable. Some words of caution are in order. Power is saved when running such magnets in a DC mode, but this is partially offset by refrigeration costs. A convenient rule of thumb is that every watt of power consumed at $4.2^{0}K$ requires about one kilowatt of refrigeration power at room temperature. Presently available cryostats are generally delicate, and refrigeration equipment is costly and requires high maintenance. One must also consider cool-down times, generally measured in hours, and magnet energizing times which can be as long as tens of minutes.

On the other hand, conventional magnets are more rugged, easier to maintain, can be turned on or off easily, and may not cost that much more to run. Superconducting technology is not yet to be considered "mature", and from our present viewpoint will not become so in the next five years. We feel that the benefit-to-risk ratio for the clinical use of superconductivity is not favorable at this time.

2. The second consideration for designing reliable hardware is to design for a <u>dedicated function</u>. Most large physics research facilities require the utmost in flexibility, and every conceivable application of the accelerator must be planned for. Such flexibility greatly increases the complexity of design, and also increases the difficulty in tuning all the independent parameters. Such design complexity generally compromises reliability--to some extent in added risk of component failure, but to a larger extent in the required stability in tuning and control functions. A machine built for a single purpose is much simpler, stabler, and more dependable.

3. One must keep to very <u>conservative designs</u>. Allowing ample safety margins for normal operating parameters greatly decreases component failures.

4. Great care must be taken in the <u>human interface</u>. Easy self-explanatory controls, good operator prompting, consistency checks to guard against operator error, system diagnostics and monitoring to pinpoint problem areas are all features that a good control system must have.

There are some excellent examples which reinforce these points, particularly the second and third ones. Two older accelerators, the synchrocyclotrons at Harvard[10] and Berkeley[11], have been dedicated solely for medical use for the past several years. In so doing, they are running in one prescribed mode with ample safety margins. Their reliability records are truly enviable. Presented in Table III is an evaluation of the failures at the LBL 184" synchrocyclotron. In the past three years, availability averaged 99%, most failures were repaired in less than an hour or two, and not one patient treatment was lost because of an accelerator-related failure. The operating staff of this machine consists of one BS level crew chief and two operator-technicians.

The lesson to be learned from this is that the size of a machine does not determine its reliability. Reliability comes from good engineering practices and conservative operating modes. Furthermore all aspects of the technology for large conventional accelerators can be considered to be "mature", so there is no reason to doubt that such accelerators are ready for the clinical environment. We shall return to this point at the end of this paper.

Now we shall discuss some of the applications for such large accelerators, and why one might want to consider placing machines of this size in a hospital. Emphasis will be placed on high energy heavy ions, and on the ongoing work at the Berkeley Bevalac facility.

## Heavy Ions - the Bevalac

The Bevalac complex is shown in Figure 1. It includes the Bevatron, a proton machine for its first 20 years, but now a heavy ion accelerator following completion of the Transfer Line from the SuperHILAC in

1975.[20] Flexibility is the watchword for the operations of this facility. Time sharing of different ion species from two injectors (soon to be three) allows for continuation of simultaneous research programs at the SuperHILAC as well as for injection into the Bevatron for shared medical and nuclear science programs. This highly complex machine, with its operating staff of 200, is not to be taken as a model for a clinical machine.

However, the groundbreaking biomedical work being performed is quite exciting.[17,18] The cause of most of the excitement is illustrated in Figure 2. This curve, called the Bragg curve, shows the energy deposition profile of a heavy ion beam as it slows down and stops in tissue. The beam loses most of its energy right at the stopping point, leading to a very high concentration of dose at the end of the particle range. Placing this dose in a tumor offers the potential for a substantial amount of normal tissue sparing. Before performing actual treatments the beam must be modified; its range must be modulated to cover the entire tumor thickness,[21,22] since few tumors presented for radiotherapy have the few mm depth of the unmodified peak. This spreading of the Bragg peak dilutes the dose distribution somewhat, as shown in Figure 3,[23] but the biological effectiveness of the stopping particles is still seen to be very high.

The Biomedical division at LBL, headed by Dr. Edward Alpen is now conducting pilot large-field radiotherapy studies at the Bevalac with carbon, neon and argon beams, with radiotherapy direction from Dr. Joseph Castro.[24] The same radiotherapy team is conducting similar pilot studies and clinical trials at the 184" synchrocyclotron with 225 MeV/nucleon alpha particle beams which have similar depth-dose characteristics to those of the heavier ions.[24] Small field treatments have been performed at the 184" for many years now. Since 1958 over 800 patients have received pituitary irradiations for treatment of acromegaly, Cushing's disease and other conditions, with an excellent degree of success.[25] More recently a highly successful ocular melanoma program has been instituted, with over 20 patients treated in the last year.[24]

In addition to radiotherapy applications, the sharpness of the Bragg peak can also be exploited for diagnostic applications.[26] Figure 4 illustrates that because of the rapid falloff of the back side of this curve a very small change in the range of the beam can result in a very large difference in ionization at a particular point. With a suitable detector this can be translated into a highly sensitive indicator of soft tissue density differences. It should be pointed out that charged-particle slowing down is most sensitive to the electron density in the stopping medium, unlike x-rays, where the nuclear charge dominates the beam attenuation. Thus in principle soft-tissue density differences should be more easily discernable with charged particles.

This radiography work is being very actively pursued by Dr. Tobias and his group[27,28]. Questions of optimum detection techniques, and ultimate resolution and image quality, are being researched.

There is one application we shall dwell on for a few minutes, because it utilizes an instrument built several years ago by Dr. Tobias and the author in a rather novel 3-D imaging technique. The instrument, called Medusa (for MEdical Dose Uniformity SAmpler) is shown in Figure 5.[29] It is a 16 plane multi-wire proportional chamber designed and used to monitor the uniformity of large-field radiotherapy beams. Each plane of wires measures a projection of the beam at a different angle. The 16 projections are then reconstructed with fairly standard back-projection algorithms to produce a 2-D picture of the beam intensity distribution. Figure 6 shows the reconstructed image of a 20 cm diameter beam in the final tuning stages before therapy. A 10% hot spot at the upper left indicates that some beam steering is required on the beam-shaping apparatus upstream of the patient.

Dr. William Chu of our laboratory, who has done all of the software for this project, has recently developed a new use for Medusa: the imaging of objects placed in the beam in front of the chamber.[30,31] Figure 7 shows some early exploratory work. One can clearly see the modification of the beam caused by the C clamp and screwdriver used as test objects. It is noteworthy too that dimensions substantially smaller than the 4 mm spacing of the signal wires are faithfully reconstructed. From these studies one sees that each pixel in the 2-D Medusa image contains information about the beam ionization intensity, which is related through the Bragg curve to how the range of the beam was modified before reaching the chamber. One can use this to obtain a full 3-D reconstruction of an object by rotating the object in front of Medusa and reconstructing the beam range modifications at each pixel for each orientation of the sample. Note that only one set of measurements needs to be made to reconstruct the entire object since all slices are accumulated at the same time. Figures 8, 9 and 10 show a very recent reconstruction of a lucite model of a human thorax. Easily discernable are the lung spaces, cut out from the lucite, and the Teflon spinal column. At this point this work is still very exploratory. Questions of resolution limits are currently being explored by Dr. Chu, and may eventually lead to the fabrication of a new chamber more suited to such imaging applications. Even if the ultimate instrumental resolution proves not to be of the best diagnostic quality, these imaging efforts still are most valuable as an adjunct to the therapy program, since they provide position verification information for a patient just prior to treatment.

One final application of relativistic heavy ions to be mentioned is the production of radioactive beams.[32,33] Because the energy of the beam is so high a type of nuclear reaction seen very frequently is one in which nuclei graze past each other exchanging energy, then breaking up in their respective rest frames. Figure 11 shows such a reaction seen in nuclear emulsion.[34] The beam particle going from left to right breaks up into the fragments all shown going forward with the initial beam momentum. Note that the target nucleus fragments are isotropic in the target frame. The logical extension of this phenomenon is that one can bring a beam into a target, transmute it to a different nuclear species,

and then, since it still retains the momentum of the primary beam, one can transport it, remove unwanted contaminants and deliver it to the user. Production efficiencies can be quite high. Almost 2% of an incident $^{12}C$ beam can be and in fact has been converted to $^{11}C$. The transport efficiency of the $^{11}C$ is only something like 10% for the present Bevalac Biomed beam line, and much higher efficiency would be possible for a line designed for this function. Figure 12 shows a Bragg curve for the $^{11}C$ beam delivered to the biomedical area. The beam is free of $^{12}C$ contamination, which would have about a 1 cm longer range were it present. With $10^{10}$ $^{12}C$ ions per second striking the production target, and our measured efficiencies of about one part in 500, the activity deposition rate is of the order of several hundred nanocuries per second. Beams of other positron emitters are also easily obtained. $^{19}Ne$ beams have been produced with slightly greater efficiencies, and because of the shorter halflife have significantly higher specific activities. $^{13}N$ and $^{15}O$ are other beams which could be produced with no difficulty. Figure 13 shows the first generation positron camera system being used to detect this beam, as designed by Drs. Alpen, Chatterjee, Tobias and Llacer at our lab.[35]

The present applications of these radioactive beams are in two areas. First is the localization of the Bragg peak to confirm treatment plans in the presence of heterodense stopping tissue. Bragg peak localizations to about 1 mm accuracy have been observed to date. With suitable advances in instrumentation it may even be possible to image the treatment volume with these beams as a further measurement of treatment delivery accuracy. A second application is in tracer implantation studies. The beam can be focused to a spot of a few millimeters in diameter and deposited in any area of the body desired. Since the Bragg peak itself is only a few mm thick all of the radioactive nuclei can be placed into a volume measuring a few mm on a side. The experimental possibilities with this kind of an implantation technique are quite extensive. Needless to say, interest in using these beams is running very high.

## Dedicated Medical Heavy Ion Accelerator

The indications from the work at the Bevalac are that indeed heavy ions are a tool the medical community will eventually want to see in a clinical environment. As alluded to earlier, an accelerator for heavy ions is a large machine, but since it can be designed from very mature technologies, no heroic efforts are required in any of the major subsystems (conventional magnets, RF, or vacuum and control systems). Studies performed over the past five years at LBL[19] and in Edmonton, Alberta[36] have confirmed this maturity, and have established the technological feasibility for building such an accelerator in a hospital-based environment.

Figure 14, taken from the 1977 LBL/Arizona Medical Accelerator Design Study report[37], gives an example of what a heavy ion treatment center might look like. The figure shows an accelerator designed for 500

MeV/nucleon carbon and three treatment rooms each with horizontal and vertical beams. Although the machine we would build today would be somewhat larger than this, with the capability for silicon or argon, and would probably be injected with a linac instead of a cyclotron, one can still get a good picture of the scope of the facility. Even though the accelerator is of large diameter, it is made from modestly sized components. Note that beams can be brought into numerous treatment rooms. The three rooms shown here were dictated more by patient load than accelerator capabilities. At least six or eight rooms could be serviced by the same machine.

Plans for building such accelerators are maturing rapidly. A set of workshops in Edmonton this fall has reviewed design parameters for an accelerator, to be sited at the Cross Cancer Institute in Edmonton. Full funding for this project is expected by next February, and their goal is to have beam within five years.

At LBL a grant application has been recently submitted to NCI to perform a detailed engineering design study for a dedicated medical heavy ion accelerator. Thus during the next few years we expect to proceed with specific design and construction plans for a fully optimized medical facility. It is expected that with a favorable funding climate we could start construction of this machine in as little as three years. With these plans now on the horizon, it is anticipated that these dedicated accelerator facilities will fully realize the exciting potential for the clinical use of heavy ions.

## References

1. See for example, proceedings from Conferences on Applications of Small Acceleratrors at Denton, Texas, 1974, 1978, 1980.

2. Also, proceedings from International Conferences on Particles and Radiation Therapy, 1972, 1976.

3. Also, 8th Conference on Cyclotrons and their Applications, IEEE NS-26, 1979, pp 2219-2299.

4. G. Oliver, J. Purdy, 3rd Conf. on Appl. of Small Accel., Denton, Texas, 19   CONF 741040-P2, p 310.

5. For a more complete list of accelerator-produced isotopes see M. Anwar Chaudhri, 8th Conf. Cycl. & Appl. IEEE NS-26, 1979, p 2281.

6. a) The Cyclotron Corporation, Berkeley, Calif. 94710,
   b) Scanditronix, Uppsala, Sweden.

7. J.L. Tom, 8th Conf. Cycl. & Appl. IEEE NS-26, 1979, p 2294.

8. J. Smathers, V. Otte, P. Almond, A. Smith, D. Hussey, 3rd Conf. Appl. of Small Accel. CONF 741040-P2, 1974, p 324.

9. Various papers in PART II (Particles and Radiation Therapy), Int. J. Radn. Oncol. Biol. Phys., 1977, V3, pp 359-401.

10. A.M. Koehler, K. Johnson, 8th Conf. Cycl & Appl. IEEE NS-26, 1979, p 2253.

11. C.A. Tobias, H.O. Anger, J.H. Lawrence, Am. J. Roentgenol. Rad. Ther. Nucl. Med. 68, 1952, pp 1-27.

12. D. Boyd, H.A. Schwettman, J. Simpson, Nucl. Instrum. Meth. III, 1973, p 315.

13. R.M. Henkelman, L.D. Skarsgard, K.Y. Lam, R.W. Harrison, B. Palcic, Int. J. Radiat. Oncol. Biol. Phys., 1976.

14. W. Jolio, 1975 Particle Accelerator Conf., IEEE NS-22, 1975, p 1397.

15. M.M. Kligerman, E.A. Knapp, D.R. Petersen, Cancer 36, 1975, p 1675.

16. J. Stovall, 1979 Particle Accelerator Conf., IEEE NS-26, 1979, p 3767.

17. Biol. and Med. Research with Accel. Heavy Ions at the Bevalac 1974-1977, Lawrence Berkeley Laboratory Report LBL-5610, April 1977.

18. Biol. and Med. Research with Accel. Heavy Ions at the Bevalac 1977-1980, Lawrence Berkeley Laboratory Report LBL-11220, November 1980.

19. Dedicated Medical Ion Accelerator Design Study, Lawrence Berkeley Laboratory/Arizona Medical Center Joint Study, Lawrence Berkeley Lab Report LBL-7230, December 1977.

20. A. Ghiorso et al, 1972 Particle Accelerator Conf., IEEE NS-20, 1973, p 155.

21. B.G. Karlsson, Strahlentherapie 124, 1964, p 481.

22. J. Lyman, J. Howard, L. Kanstein, J.R. Alonso, LBL-11220 (ref 18), 1980, p 319.

23. M. Raju, E. Blakely, J. Howard, J. Lyman, D. Kalofoncs, B. Martins, T. Yang, Radiat. Res. 65, 1976, p 191.

24. J.R. Castro et al, LBL-11220 (ref 18), 1980, p 305.

25. J.H. Lawrence, C.A. Tobias, J.T. Lyman, J.A. Linfoot, Nucl. Medicine, 2nd Ed., W.H. Blahd editor, McGraw Hill 1971, Chapter 32, pp 806-820.

26. see Ref. 18, LBL-11220, Part VI, Section B, Heavy Ion Radiography and Microscopy, pp 335-388.

27. C.A. Tobias, J.I. Fabrikant, E.V. Benton, W.R. Holley, LBL-11220 (ref 18), 1980, p 335.

28. C.A. Tobias, E.V. Benton, M.P. Capp, Recent Advances in Nucl. Med. 5, 1978, p 71.

29. J.R. Alonso, C.A. Tobias, W.T. Chu, 1979 Particle Accelerator Conf., IEEE NS-26, 1979, p 3077.

30. J. Llacer, W.T. Chu, C.A. Tobias, J.I. Fabrikant, J.R. Alonso, LBL-11220 (ref 18), 1980, p 367.

31. W.T. Chu, J.R. Alonso, C.A. Tobias, LBL-11718, Oct. 1980, to be presented at 1981 Particle Accel. Conf., March 1981.

32. A. Chatterjee, E.A. Alpen, J.R. Alonso, J. Llacer, C.A. Tobias, in press, Jnl. Rad. Onc.

33. J.R. Alonso, A. Chatterjee, C.A. Tobias, 1979 Particle Accel. Conf., IEEE NS-26, 1979, p 3003.

34. H.H. Heckman, D E, Greiner, P.J. Lindstrom, F.S. Bieser, Science 174, 1971, p 1130.

35. J. Llacer, A. Chatterjee, B. Jackson, J. Lin, V. Zunzunegui, IEEE NS-26, 1979, p 634.

36. MARIA Workshop III, Edmonton, Alberta, October 1980. Proceedings to be published by University of Alberta Press.

37. LBL/Arizona Study (ref 19), LBL-7230, Dec 1977, p 65a.

## Figure Captions

1. Plan view of the Bevalac, showing the SuperHILAC injector, the Transfer Line passing the heavy ion beam down the hill to the Bevatron, where it is accelerated to relativistic energies. In operation in this mode since 1975, beams as heavy as iron are routinely accelerated. An upgrading project to be completed by December 1981 will allow acceleration of any ion species, to uranium or heavier. Beams of greatest interest in biomedical work are carbon, neon, silicon and argon.

2. Bragg ionization curve for a carbon beam. This curve is a measure of the energy deposition of the beam in a thin ion chamber as a function of thickness of a water absorber placed just upstream of the ion chamber. The rate of energy deposition is seen to increase as the beam slows down, reaching a maximum at the stopping point of the beam. Ionization beyond the Bragg peak is caused by beam fragments of longer range which have been produced by nuclear reactions in the water absorber.

3. Spread-out Bragg peak; the range of the beam has been modulated by a brass spiral ridge filter to place stopping particles over a 4 cm depth. Even though the sharp peak in the ionization curve has been largely attenuated, the biological effectiveness of the stopping particles is still quite evident. Such ridge filters are used to tailor the heavy-ion beam to cover the full treatment volume with stopping particles.

4. The advantage of using charged particles for diagnostic imaging is demonstrated here. Unmodified x-ray and heavy ion beams are shown in solid lines (a), while beams having passed through some material are shown by dashed lines (b). A detector placed in the very sharp fall-off at the distal edge of the Bragg peak will record a much larger ionization difference for heavy ions than for x-rays, thus indicating substantially enhanced resolution for small variations in tissue density with heavy ion beams.

5. The Medical Dose Uniformity Sampler (MEDUSA) wire chamber, with sixteen planes of 64 signal wires, planes spaced at 11 1/4° intervals. Charge collected on each wire from beam passing through the chamber is stored on a capacitor, providing a line integral of beam intensity along this wire. The voltages on the 64 capacitors for each plane provide a projection of the beam profile along the orientation of that plane. These projections at the 16 different plane angles are combined in a standard back-projection reconstruction algorithm to produce a 2-dimensional picture of the beam intensity profile.

6. Picture of a beam profile in the radiotherapy beam line taken with MEDUSA. The full-color display alerts the operators to non-uniformities in the field, and serves as an aid in tuning the

beam in preparation for the day's therapy. The lighter area at 10 o'clock represents a "hot spot" with about 10% higher intensity in the 20 cm-diameter beam. This information, available within a few seconds, allows the operator to adjust tuning magnets and see directly the effect on the therapy field.

7. Use of MEDUSA as an imaging device. The range of the highly-uniform therapy beam is adjusted so that the region of rapidly-changing ionization near the Bragg peak passes through the chamber. Material objects placed in the beam modulate the beam range and significantly change the ionization observed in the detector, which is then converted into an image of the sampled object. Note that each pixel in the reconstructed image contains information about the beam range at the particular $(x,y)$ coordinates.

8. Lucite and teflon phantom designed to simulate the human thorax, used in the 3-D reconstruction efforts with MEDUSA. Sections have been removed to show lung-space cutouts.

9. Preliminary results of 3-D reconstruction of the phantom shown in Figure 8. Transmission images were reconstructed for each of 16 different orientations of the phantom in the beam. Electron density (range shortening) information extracted from each pixel at each phantom orientation was used to reconstruct the phantom. Shown are 64 horizontal cuts through the phantom, one clearly sees the teflon "spinal column" and lung spaces. Note that data for all slices are collected simultaneously, providing true 3-dimensional imaging.

10. 3-D display of the same data shown in Figure 9. Although the clarity and resolution of this image is not of diagnostic quality, it is a significant first step in the right direction. Advancements in beam preparation and data handling should see substantial improvements in the image quality in the coming months.

11. Nuclear emulsion tracks of a high-energy heavy-ion peripheral fragmentation reaction. The incident beam ion, on the left, grazes by a nucleus in the emulsion, exchanging enough energy to cause breakup of both target and projectile nuclei. However, the momentum of the individual projectile nucleons is hardly affected by the collision, the beam fragments are seen to travel forward in a very narrow cone. This mechanism has been used to transmute beams of carbon and neon ions to radioactive species (positron emitting $^{11}C$ and $^{19}Ne$) suitable for diagnostic applications. Passing the primary beam through a 2.5 cm beryllium block causes almost 2% of the beam to emerge as the desired radioactive product. Magnetic analysis of the emerging beam allows for isolation of the desired species, so that a highly purified, well focused beam of the positron emitting isotope can be delivered into the sample to be studied. Activity levels approaching one microcurie per second have been deposited into a volume element measuring a few millimeters on a side.

12. Bragg curve for a $^{11}C$ beam delivered to the experimental area. The sharpness of the peak, and the absence of other peaks at different ranges attests to the purity of the beam.

13. PEBA (Positron Emitting Beam Analyzer) used in experiments with radioactive beams. The beam, running along the axis of the lucite cylinder stops within this cylinder, and subsequently decays. The array of sodium iodide crystals detects the annihilation radiation and localizes the stopping point of the beam to within one millimeter. Primary applications of these beams include Bragg peak localization for radiotherapy treatment planning and dose-delivery confirmation, and biological function studies facilitated by being able to implant the tracer directly in the organ or system to be studied.

14. Example of a possible layout for a facility for clinical use of heavy ions. Three treatment rooms are shown in this example, but in fact the beam intensity from modern accelerators is high enough that many more rooms can be serviced simultaneously using beam switching and sharing techniques. The decision of the number of treatment rooms to be included need be driven only by the projected patient load. Similarly, beam orientations can be selected by therapy planning considerations, static horizontal, vertical or oblique beams can be easily provided. Today's technology of accelerator components and control systems is mature enough that such a clinical facility can be constructed and operated for reasonable costs with the level of availability and reliability expected of a modern instrument in the hospital environment.

Table I

# **Accelerated Beams for Medical Use**

| Particle | Application | Energy | Rigidity | Accelerator |
|---|---|---|---|---|
| Electrons | Photon Radiotherapy | 5-30 MeV | .2-1 kG-m | Linac Betatron |
| Light Ions (p,d,$\alpha$,...) | Isotope Production | 15-70 MeV | 6-12 kG-m | Cyclotron |
| Protons/ Deuterons | Neutron Therapy | 40-80 MeV | 9-16 kG-m | Cyclotron |
| Protons/ Alphas | Therapy | 250 MeV/nucleon | 24-48 kG-m | Synchrocyclotron |
| Protons | Pi meson Therapy | 800 MeV | 50 kG-m | Linac |
| Heavy Ions (C,Ne,Ar,...) | Therapy & Diagnostics | 825 MeV/nucleon | 110 kG-m | Synchrotron |

## Table II

## Partial list of Accelerator-Produced Radioisotopes

| Radionuclide | Half-life | Production Reaction | Energy(MeV) | | | |
|---|---|---|---|---|---|---|
| | | | p | d | $^3$He | $\alpha$ |
| $^{11}$C | 20.3 min | $^{11}$B(p,n) | 10 | | | |
| | | $^{12}$C(p,pn) | 34 | | | |
| $^{13}$N | 10.0 min | $^{12}$C(d,n) | | 8 | | |
| $^{15}$O | 123 sec | $^{14}$N(d,n) | | 13 | | |
| $^{18}$F | 109.7 min | $^{19}$F(p,pn) | 25 | | | |
| | | $^{16}$O($^3$He,p) | | | 12 | |
| $^{43}$K | 22.4 hr | $^{40}$Ar($\alpha$,p) | | | | 18 |
| $^{52}$Fe | 8.2 hr | $^{50}$Cr($\alpha$,2n) | | | | 28 |
| | | $^{55}$Mn(p,4n) | 53 | | | |
| $^{67}$Ga | 78.3 hr | $^{66}$Zn(d,n) | | 10 | | |
| $^{81}$Rb | 4.7 hr | $^{79}$Br($\alpha$,2n) | | | | 27 |
| $^{99}$Mo | 66.7 hr | $^{100}$Mo(p,pn) | 25 | | | |
| $^{99}$Tc | 6.1 hr | $^{100}$Mo(p,2n) | 20 | | | |
| $^{111}$In | 2.8 days | $^{111}$Cd(p,n) | 9 | | | |
| $^{123}$I | 13.3 hr | $^{122}$Te(d,n) | | 10 | | |
| $^{157}$Dy | 8.1 hr | $^{159}$Tb(p,3n) | 29 | | | |
| $^{203}$Pb | 52.1 hr | $^{203}$Tl(p,n) | 9 | | | |
| | | $^{203}$Tl(d,2n) | 14 | | | |
| Maximum Rigidity (kG-m) | | | 11 | 8 | 4 | 8 |

# Table III

## 184" FAILURE MODE ANALYSIS

|  | Failures | (#) | MTBF | MTTR | Total Down Time | % Down Time |
|---|---|---|---|---|---|---|
| 1. | July 1977 - June 1978 | | (1018.5 operating hours) | | | |
| | Mechanical | (5) | 204 hrs | 0.40 hrs | 2.00 hrs | 5.3/1018.5 |
| | Electrical | (8) | 127 hrs | 0.40 hrs | 3.25 hrs | = 0.52% |
| 2. | July 1978 - June 1979 | | (1144.5 operating hours) | | | |
| | Mechanical | (7) | 164 hrs | 0.93 hrs | 6.50 hrs | 11.5/1144.5 |
| | Electrical | (8) | 143 hrs | 0.63 hrs | 5.00 hrs | = 1.0% |
| 3. | July 1979 - June 1980 | | (976.3 operating hours) | | | |
| | Mechanical | (3) | 325 hrs | 1.25 hrs | 3.75 hrs | 13.3/976.3 |
| | Electrical | (6) | 163 hrs | 1.60 hrs | 9.50 hrs | = 1.4% |
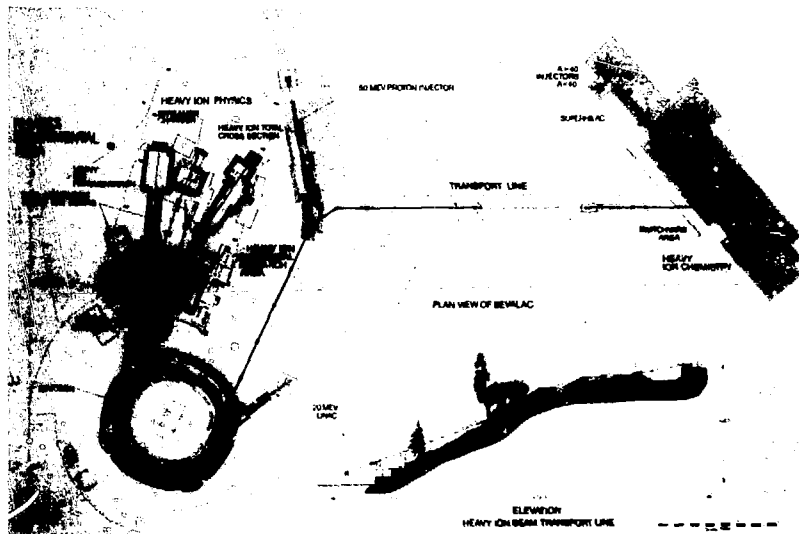
Figure 1

CBB 740-7911

CARBON
400 MeV/amu
22 Oct. 1977
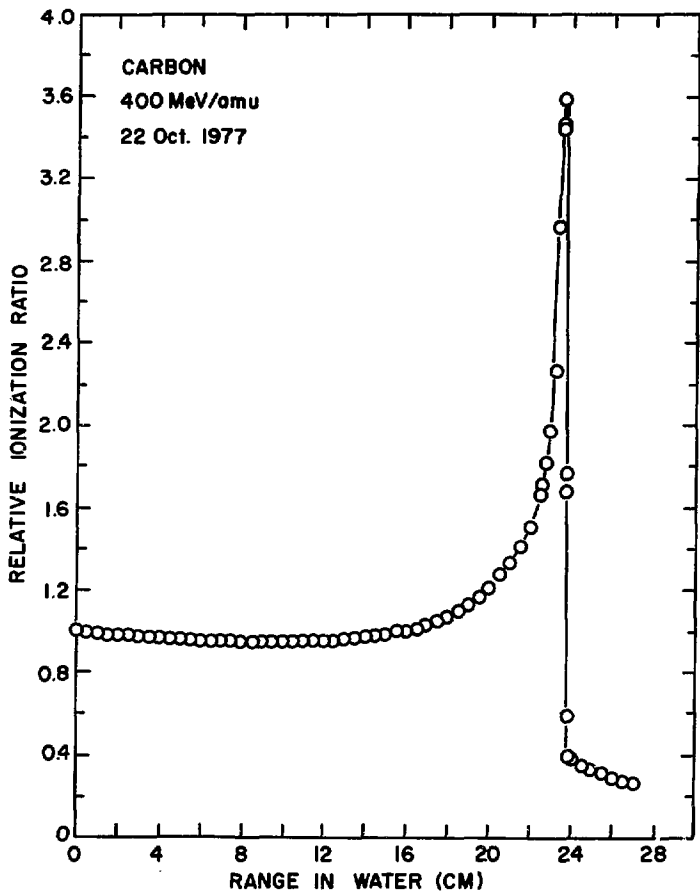
Figure 2

XBL 785-8447
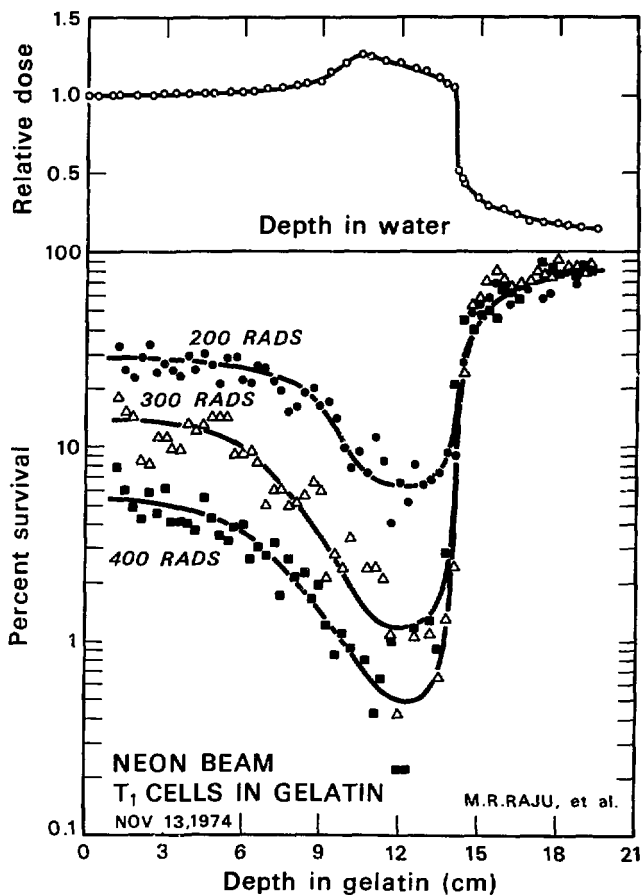
Figure 3
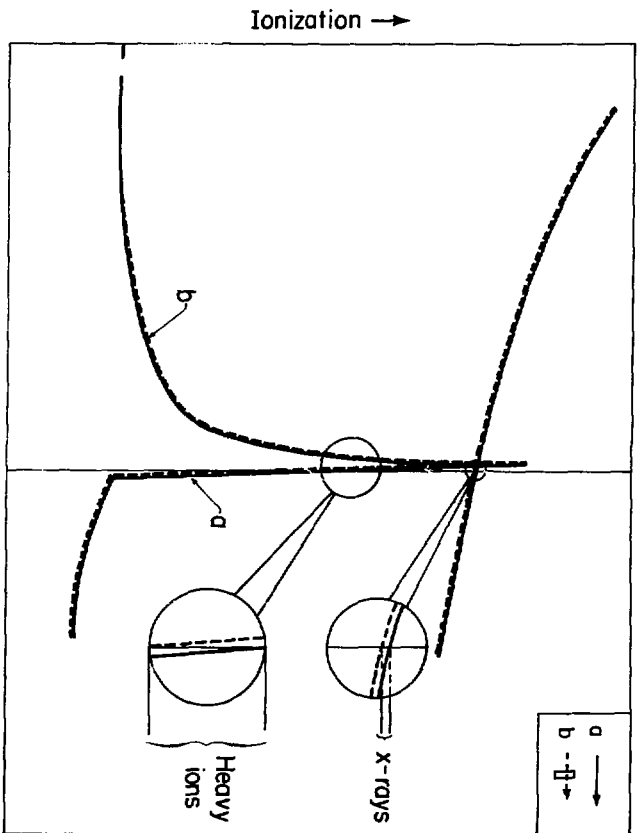
Figure 4

XBL 8012-2458
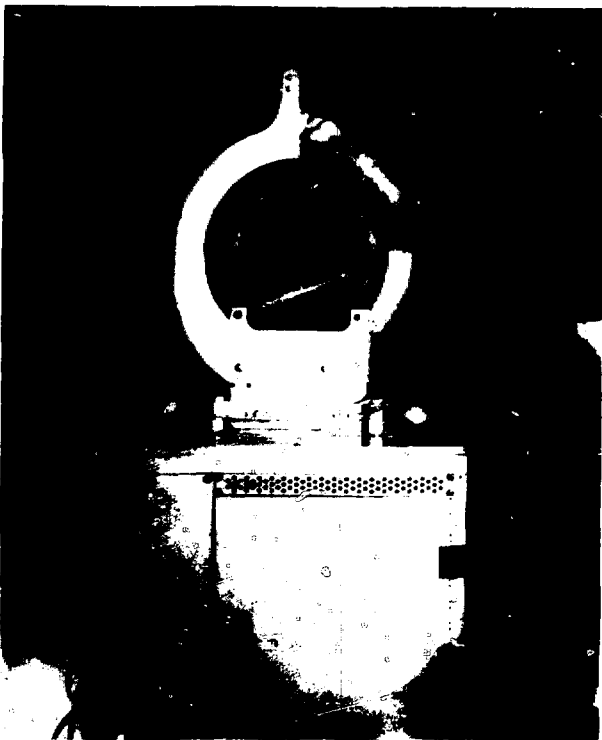
Figure 5                                    CBB 809-10443

Figure 6                                          CBB 793-2920

Figure 7

-25-

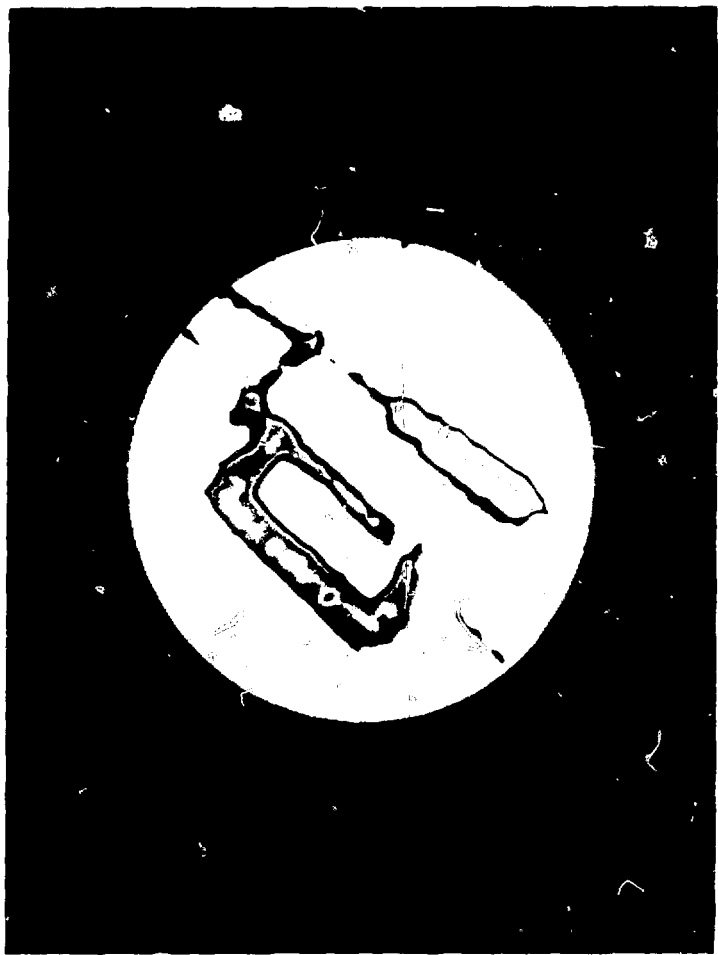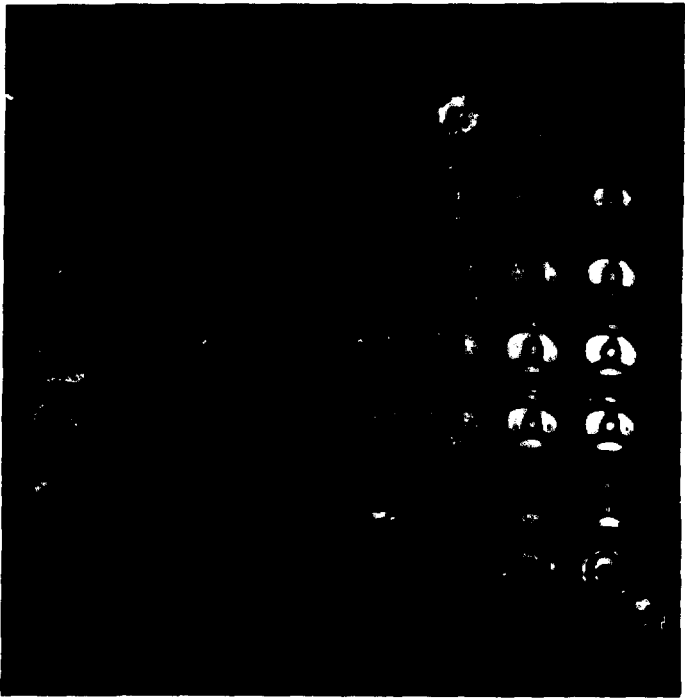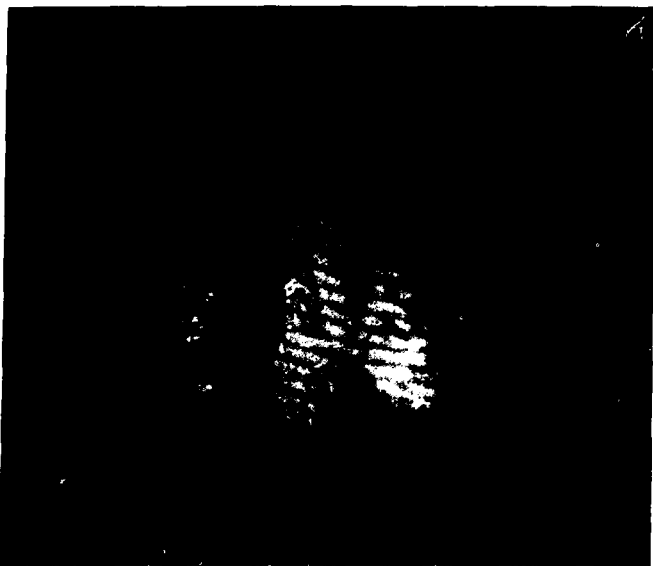Figure 8                                    CBB 800-13561

Figure 9                                        XBC 800-13459

-27-

Figure 10

XBC 800-13458
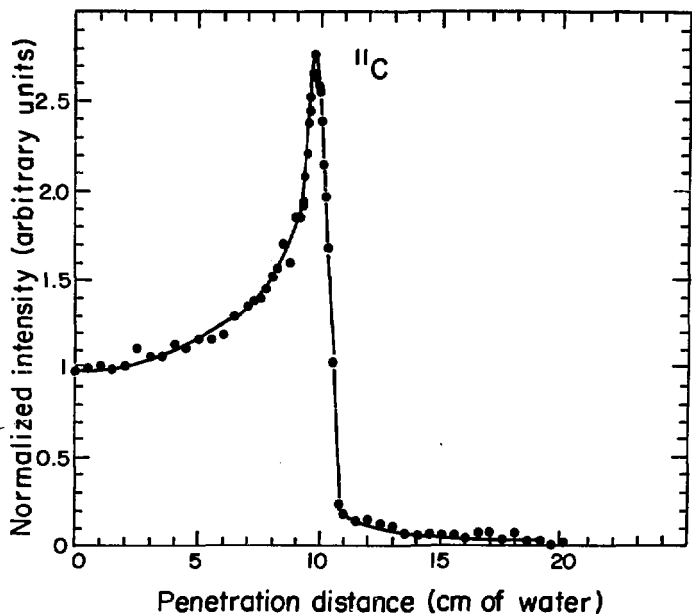
XBB 729-4219

100 μm

Figure 11

Figure 12                                    XBL 793-753
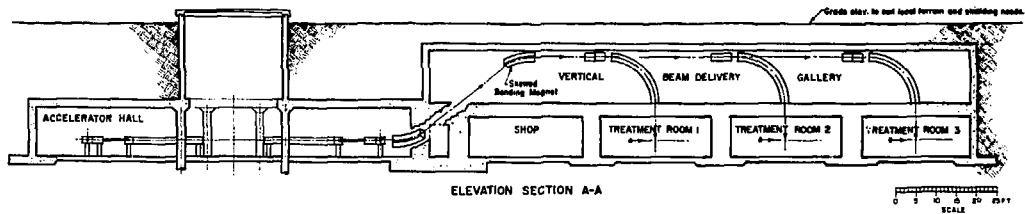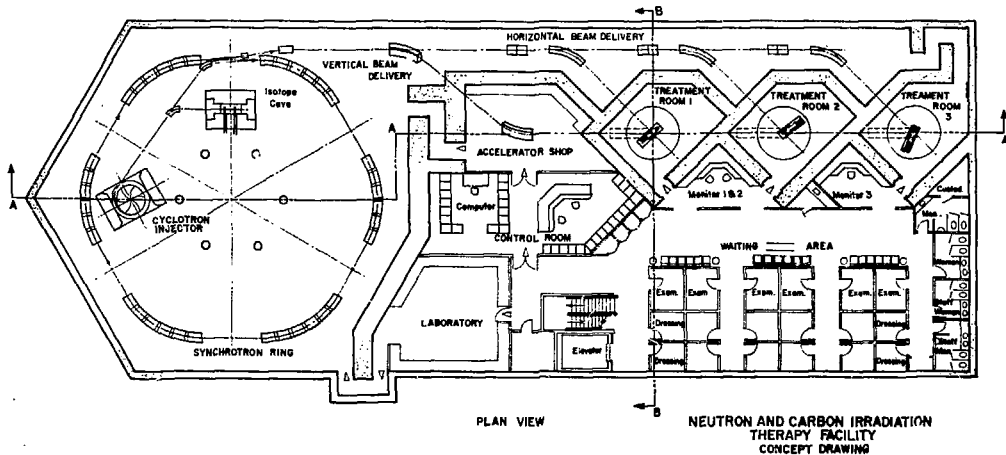
Figure 13　　　　　　　　　　　　　　　　CBB 792-2547

PLAN VIEW

NEUTRON AND CARBON IRRADIATION
THERAPY FACILITY
CONCEPT DRAWING

ELEVATION SECTION A-A

Figure 14