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PRESENT AND FUTURE SOURCES OF
PROTONS AND HEAVY IONS

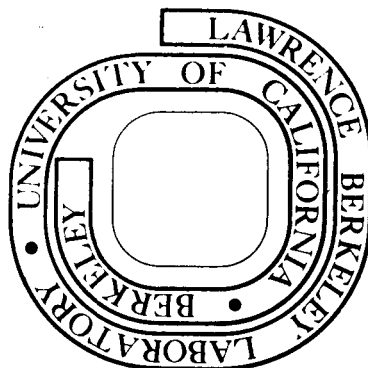
Hermann A. Grunder and Christoph W. Leemann

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PRESENT AND FUTURE SOURCES OF PROTONS AND HEAVY IONS *

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PRESENT AND FUTURE SOURCES OF PROTONS AND HEAVY IONS

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ABSTRACT

A brief outline of existing medical heavy-ion facilities is given. The beam specifications for future dedicated medical ion accelerators are discussed. Machines capable of delivering dose rates of approximately 1 krad/min in volumes of a few liters are shown to represent existing technology. A cost and performance analysis shows the synchrotrons to be the most economical source for the heavier ions while conventional cyclotrons seem optimal for an exclusive proton facility. It is seen that the incorporation of additional capabilities such as neutron generation or radioisotope production can be achieved at modest incremental costs.

In addition to the accelerators, feasible layouts of hypothetical facilities are discussed, and three-dimensional beam scanning is shown to allow the irradiation of large volumes without sacrificing the precise dose localization capabilities of heavy-ion beams. Concepts of quality-controlled engineering and modern computer technology are introduced as a means to obtain the desired high degree of reliability and ease of operation and maintenance.

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INTRODUCTION

The experience of the past few years indicates that ion beams possess tremendous potential as a clinical modality for radiation therapy. However, to fully realize this potential requires the operation of reliable and economic radiation sources.

Today's biomedical studies with protons and heavy ions rely on accelerators designed for physics research. Rarely is the performance of these machines matched to the medical requirements: overall specifications are considerably exceeded while reliability and ease of operation fall short.

In contrast, designing radiation sources strictly to the requirements of a hospital-based dedicated facility can produce dependable, cost-effective installations requiring modest crews and support personnel.

The choice of accelerator type is intimately dependent on the detailed beam requirements. We discuss this relationship, along with aspects of beam delivery, operation and reliability. And we illustrate the layout of a hypothetical facility.

I. A Summary of Currently Used Ion Accelerators for Radiotherapy

Despite the great interest in ion radiotherapy, the number of active programs is relatively small. Outside the San Francisco Bay Area--but

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still in the U.S.--is the Harvard Proton Cyclotron⁽¹⁾. Worldwide, there are the Proton Synchrotron at ITEP in Moscow, the Synchrocyclotron at Dubna, and the pioneering work at the Synchrocyclotron at Uppsala.

It is beyond the scope of this paper to survey the programs at these machines. However, to give an example of current capabilities, we will briefly describe the LBL facilities, with which we are obviously familiar.

The 184-inch cyclotron produces a beam of 200 MeV/amu alpha particles with a 29 cm range in water. This beam can deliver up to 240 rads per minute in an 8 liter volume with a field uniformity of $\pm 2\%$. This outstanding dose distribution at the target site is created by a beam flattening system developed by Ken Crowe, John Lyman et. al.⁽²⁾ The patient facilities at the 184-inch cyclotron are completed with computer-controlled patient positioner--ISAH--and a newly finished patient receiving area.

During the last two decades, some 500 pituitary patients have been treated at this accelerator. Recently, under the direction of Dr. Castro and associates, large field tumor irradiation has been performed on several patients. With NCI grant support, the program is currently gearing up for a randomized clinical therapy trial involving treatments of up to twenty patients per day. It is worth noting that the 184", as well as the Harvard proton-cyclotron, are medically dedicated machines.

A very intense radiobiology program is under way at the Bevalac, an accelerator combination which currently makes available high-energy beams of heavy ions up to mass 40 (argon). The Bevalac employs the Berkeley heavy-ion linear accelerator--the SuperHILAC--as an injector to the

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Bevatron Synchrotron. Beam leaves the SuperHILAC at 8.5 MeV/amu, is guided to the Bevatron via a transferline, and is then boosted to energies between 150 and 1,000 MeV/amu (physics uses even higher energies--up to 2,500 MeV/amu). The resulting heavy-ion beam, unique in possessing both high energy and high intensity, is then extracted and transported to several experimental areas, three of which are reserved for biomedical research (Fig. 1).

One of the three areas is now being prepared for patient treatment, projected to start at the Bevalac next summer. A second area, "the Mini-beam," (not shown in Fig. 1) will provide beams of 2 to 3 millimeters diameter and a potential dose of more than 1 kilorad in a few milliseconds, using neon (mass 20) as an example.

The bulk of the radiobiological work is now in progress in the third biomedical area. Elaborate computerized dosimetry and exposure control systems have been implemented there, yielding excellent monitoring of irradiation conditions. This work has been planned and executed under the direction of John Lyman ⁽³⁾. Jerry Howard is in charge of this part of the operation. Dose rates in the 500 to 1000 rad-per-minute range are typical with a 3 to 5 centimeter field of carbon, neon or argon ions. Corresponding penetration ranges up to 50 cm in water.

II. Beam Specifications

In designing a dedicated radiotherapy facility, the size, complexity and cost are all defined by ion beam specifications such as energy and intensity. The energy is determined by the atomic number Z , mass number A , and the required range in tissue (Fig. 2). Obviously, the proton,

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with its unique charge-to-mass ratio of 1, has an advantage from a pure accelerator point of view.

Beam intensity is derived from dose requirements, treatment volume and shape, and maximum allowable treatment time. The intensity is a function of particle species, because of the dependence of the dose on the atomic number. Since current quantitative radiobiological studies are not yet complete, for the purpose of this paper we are using the physical dose as the basis for calculating beam intensity.

Assuming a superposition of energies yielding a desired depth-dose curve and an arbitrary treatment volume, the current is automatically specified. The required intensities for irradiating 1000 cm^3 with 600 rads in 60 seconds are listed below, using two extreme examples of the same volume--one wide and thin, the other narrow and deep.

<u>Particle</u>	<u>Beam Intensity (particles per second)</u>	
	A = 400 cm^2 , L = 2.5 cm	A = 50 cm^2 , L = 20 cm
P	$1.35 \cdot 10^{10}$	$4.5 \cdot 10^9$
α	$3.4 \cdot 10^9$	$1.1 \cdot 10^9$
C	$6.7 \cdot 10^8$	$2.2 \cdot 10^8$
Ne	$3.0 \cdot 10^8$	$1.0 \cdot 10^8$
Ar	$1.1 \cdot 10^8$	$3.8 \cdot 10^7$

A = Cross-section of volume perpendicular to the beam.

L = Length of volume in beam direction.

Accelerators capable of delivering a few times 10^{10} protons per second, or a few times 10^9 carbon ions per second, are therefore capable of irradiating volumes of a few liters to dose levels of ~ 1 krad in a few minutes. There seems to be agreement that this is a desirable and adequate performance level for a modern facility.

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The technology for reliable medical accelerators meeting these primary beam specifications exists today. In addition, neutron generation from 10 to 50 μ A of deuterons at 20 to 60 MeV, and production of radioisotope substances such as ^{11}C , ^{13}N , ^{15}O and ^{18}F , can be readily incorporated in an economical injector design.

Furthermore, high-energy diagnostic beams of ^{11}C , ^{15}O , etc., can be produced by fragmenting the primary beam into pure, well-defined radioactive, positron-emitting beams with almost the same penetration as the parent particles. Their enormous advantage of determining the dose localization has been discussed by C. A. Tobias ⁽⁴⁾. Finally, high-quality radiography requirements can also be met in a thoughtfully designed radiotherapy facility.

III. Review of Available Types of Accelerators

The established types of accelerators which partially or entirely cover the range of particles and energies considered here are cyclotrons (either isochronous or FM), linear accelerators and synchrotrons. The accelerator's size is determined by the required particle energy and the attainable electric and magnetic field strengths. Using acceleration of ^{12}C to 400 MeV/amu as an example, a linac will, depending on gradient, be relatively long--in excess of 100 meters. A circular accelerator will have a radius from ~1.7 meters to ~10 m, depending on whether a superconducting cyclotron or a moderately fast-cycling synchrotron is envisaged. Equally important considerations of reliability, ease of maintenance, cost efficiency, power consumption, etc., will also dictate choices in parameters. Consequently, the optimum machine may be larger than required by strict technological limits.

We must stress that our comments are based on today's 'state-of-

the-art' technology. The state-of-the-art advances, of course, and ongoing R & D efforts, if successful, may impact on a medical accelerator design in the future. Very large superconducting isochronous cyclotrons and novel developments for the initial (low-velocity) stages of linacs fall into the category of potentially promising tools; we do not consider them here because their technology does not have the required maturity for a dedicated medical facility.

Having made these qualifying remarks, and repeating the assumption that 0.5 to 1.0 krad per minute in $\sim 1000 \text{ cm}^3$ as the design goal, we conclude that circular accelerators (cyclotrons and synchrotrons) are the most cost-effective solutions to ion beam radiotherapy today. For heavy ions of sufficient range, excessive cost seems to rule out linear machines.

The cyclotron is probably the most widely known of the accelerators capable of producing penetrating ion beams. Its magnetic guide-field is constant in time and allows the particles to pass repeatedly through the same RF-accelerating device, gaining energy on each pass.

The relation between guide-field and ion revolution frequency is the following:

$$\omega_{\text{ion}} = \left(\frac{Q}{A} \right) \frac{e \langle B \rangle}{m\gamma} \quad (1)$$

where ω_{ion} = rotational ion frequency

Q/A = ion charge-to-mass ratio

$\langle B \rangle$ = average guide-field

γ = $\gamma(t)$ = relativistic mass increase.

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The RF-frequency can be a multiple of the ion frequency, depending on the choice of design parameters:

$$\omega_{\text{RF}} = h \omega_{\text{ion}}, \quad (2)$$

where h is an integer, e.g. $h = 1, 2, 3, \dots$

To obtain therapeutically useful energies with the heavier ions from a cyclotron, effects of the relativistic mass increase have to be overcome. This can be accomplished in two ways. (1) Form a magnetic guide-field which will satisfy equation 1 and maintain simultaneous axial and radial focusing. Isochronous cyclotrons, as they are called, have been successfully built up to 600 MeV proton energy. (2) If one chooses not to maintain an isochronous field, then frequency will become a function of energy and hence time. This type of machine is called a frequency-modulated cyclotron, or synchrocyclotron, and an example is the 184-inch FM cyclotron at LBL.

The drawback with conventional cyclotron magnets for energies of interest is their excessive size. For that reason, the implementation of compact superconducting coil magnets to produce the time-independent guide-field would be attractive, indeed. We look forward with great interest to the construction and testing of such machines. In fact, thanks to the big bubble chambers, the coil technology is sufficiently advanced that we do not rule out a superconducting cyclotron on technological grounds.

If we abandon the static guide-field in the cyclotron and let both the RF-frequency and the guide-field become a function of time, then we have a machine known as the synchrotron.

Synchrotrons have been built all over the world in all sizes. Their main attraction is the relatively small weight of the guide-field magnet,

because the particle uses the same path during the whole acceleration cycle. Operation is pulsed, but with a duty cycle of up to 50%. Space-charge effects, rf system capabilities, magnetic field errors and (with heavy ions) adequate charge-to-mass ratio of the particles require that particles be injected into the synchrotron at an appropriate energy. Linacs, cyclotrons or Van de Graaff's might serve as injectors.

Figure 3 summarizes how different accelerator options compare in cost and performance. The superiority of the synchrotron is clear, except in the application of accelerating protons only to energies of 200 to 300 MeV. The synchrotron is by nature a multiparticle machine of continuously and quickly adjustable energy. This can be crucial if a three-dimensional scanning device is to be used in the treatment delivery. The isochronous cyclotrons, however, assumed here with fixed rf-frequency, allow operation at a few discrete energies only. The output of FM-cyclotrons for heavier ions is adequate, but the size of any conventional cyclotrons (FM or isochronous) is prohibitive even for α -particles of adequate range. (~ 25 cm).

IV. Cost Optimization

The cost estimates for synchrotrons are all based on or extrapolated from an optimized design to accelerate ^{12}C ions to 400 MeV/amu with the required intensity and a 27.5 cm range. After preliminary configuration studies which yielded values for expected apertures and insured good resonant extraction properties, an optimal combination of repetition rate and magnet aperture has been found.

The beam intensity j is given by

$$j = f_{\text{rep}} \cdot N \quad (3)$$

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where f_{rep} is the repetition rate and N the number of particles accelerated (and extracted) in each machine pulse. For a given particle and injector type there exists a maximum possible N whose value depends on the area of the magnet aperture A . An increase in N implies an increase in A , and therefore in magnet size and stored magnetic energy. The peak power P required is given by

$$P = k \cdot f_{\text{rep}} \cdot U \quad (4)$$

where U is the stored energy and k is a constant whose value depends on the exact details of the field rise.

An optimum is expected to exist where combined magnet and power supply costs are minimal. RF-system costs just simply increase as f_{rep} increases since the energy gain per turn, and therefore the power level, increase with a shortened acceleration cycle. An example of such optimization curves is shown in Fig. 4. Their appearance changes somewhat if injectors with brighter beams are considered, shifting optima towards smaller values of f_{rep} . The cost minima are broad, but show that a repetition rate less than 1 Hz, or much faster than about 5 Hz, will not be economical.

As shown in Fig. 3, the cost for the same heavy-ion capability can vary slightly depending on additional requirements. The most economical heavy-ion facility is a synchrotron with a linac or a cyclotron as injector. Isotope production capability, requiring the cyclotron injector, does not add any extra cost, except for the ancillary isotope production facilities.

The provision for deuteron beams of up to $\sim 50 \mu\text{A}$ and 65 MeV (sufficient for neutron therapy), however, requires a larger injector cyclotron, increasing the total cost somewhat.

Costs as quoted are hardware costs and have to be multiplied by appropriate factors for engineering and contingency.

V. Considerations of Reliability, Computer Control and Operation

A hospital-based facility demands different and more stringent requirements than does a physics research accelerator. Particularly important are reliability--especially fast recovery from breakdowns; ease of operation, and ease of maintenance.

We reiterate that the beam specifications outlined here are met by existing accelerators. However, unscheduled downtime has to be reduced substantially over present research machines. This can be accomplished using modular designs wherever possible to minimize the number of spare parts and allow efficient repair and preventive maintenance. For example, power supplies for beam transport magnets should be standardized and interchangeable. High reliability also dictates use of a modern computer-based control system to set all machine parameters, maintain long-term beam stability, notify the operator of any faulty condition, and record all machine and dosimetry data.

The software package--by far the most expensive part of the control system--consists of the system software and the applications program. The system software has to be available and carefully debugged well before the facility is brought on the air the first time.

A good systems software package enables a person with limited programming skills to be very effective as a machine operator. With interactive operation, the computer will request the next step to be taken and also check against unwanted interactions (software interlock). Also, machine status can be displayed instantly on a CRT screen.

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We are well aware that while any interruption in beam delivery is undesirable, it is also understood that short 5-10 minute delays are far less damaging than long interruptions, even if the average 'on time' is the same. For this reason, a good system software package includes self-diagnosis of the machine, to permit rapid spotting and replacement of any failing component. Finally, the software protects machine operation from abuse because the programming prevents typing random characters to produce a malfunction, or worse--an unexpected start-up, of the machine.

The applications program--the display and data-handling functions used by the machine operator--will likely undergo many changes during the lifetime of a radiation therapy facility in order to meet changing treatment procedures. It is essential, therefore, that the system software be designed so that the applications program can be changed without interfering with the routine functioning of the machine.

IV. Hypothetical Facilities

Conceptual layouts of complete facilities are shown in Figs. (5) and (6). These are to be viewed merely as suggestions; certainly additional effort is required, taking into consideration architectural and other boundary conditions of a particular site. While minimum real estate requirements are obviously determined by the size of the radiation source, a careful analysis of building cost, preferences and convenience is called for in order to arrive at optimal solutions, which might be radically different from those shown here. The accelerator proper could be removed physically and connected through a beam transport system with the treatment rooms.

As shown, each treatment station contains a fixed horizontal and vertical beam to meet what we understand to be a minimum therapeutic requirement. We have also designed isocentric beam delivery systems, but conclude that they are very complex and should only be specified if considered indispensable. Since the application of superconducting magnets is almost a seasoned technology, one should remember that their use might help shrink overall facility size considerably.

The beam transport systems employed pose no special problems and follow well-proven practices developed at physics research facilities. In laying out such a facility, modular units are preferred wherever practical.

V. Beam Delivery and Scanning

It is quite possible that the first dedicated medical heavy-ion installations will use the current well-understood methods of beam delivery and field-shaping with collimators, ridge filters, scattering foils, occluding rings and boluses. These techniques are relatively simple and quite adequate in many situations. However, they do not employ the ultimate capability of a high-quality ion beam.

The excellent dose-localization properties of heavy ions and the very good beam quality of primary beams can only be fully utilized by more advanced schemes. Three-dimensional scanning of a "pencil beam" seems to be the most attractive solution for irradiating large treatment volumes without sacrificing the outstanding physical properties of heavy ions. In this procedure, the beam is swept by two orthogonal magnets over a

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plane perpendicular to its incident direction (coordinates X_0 , Y_0), and its range (Z_0) is adjusted by energy modulation through degraders or by the accelerator itself. To complete the scheme, the total number of particles delivered at (X_0 , Y_0 , Z_0) is precisely ($< 1\%$) controlled. However, for maximum benefit from such a system, a diagnostic capability based on three-dimensional reconstruction techniques is called for.

For the design of a scanning system, its hardware and computer-control system, the central questions, from a designer's point of view, are the required spatial resolution and the frequency response. They are determined by beam spot size, treatment volume, and maximum allowable treatment time.

Based on the lower limits for beam spot size provided by multiple scattering calculations and treatment time/volume ratios of $\sim 30 \text{ sec}/1000 \text{ cm}^3$, the authors and their collaborators have prepared different designs and are engaged in the construction of the most crucial components of such a system. This involves fast magnets, dosimetry equipment, and high-speed digital techniques. Beam current will have to be integrated and controlled to meet prescribed values (depending on instantaneous scanning of magnet position) at time intervals ranging from 250 to 800 μs for spatial resolutions between 2 to 3 mm.

The scanning approach will allow irradiation of highly irregularly shaped volumes, minimizing irradiation of neighboring tissue. Dose flatness of $\lesssim 1\%$ with sharp edges (90% to 10% in 4 to 6 mm) is achievable. Furthermore, tissue inhomogeneities will be compensated for to a degree impossible with a bolus.

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This whole concept of three-dimensional scanning with a high-quality beam obviously presupposes detailed knowledge of the tumor site and extent. The localization of the dose, on the other hand, can be checked to the same accuracy as the treatment beam with positron-emitting ion beams of equal penetration.

CONCLUSIONS

The number of technical, operational and radiobiological considerations in designing an optimized medical accelerator make the process of setting exact specifications complex at this time. Choices of particle, intensity, energy, accelerator type, reliability, operational ease and computer control must be carefully balanced and then matched to similar deliberations regarding ideal treatment conditions.

Finally, the question of capital investment can only be intelligently discussed in a cost-benefit framework with respect to overall objectives and a given set of specifications.

But once these decisions are made, the technological means to execute them are a well understood state of the art. A dedicated hospital-based facility, designed from beginning to end with the goal of consistently optimal operation in all the desired particle modes, can be successfully achieved with thoughtful application of present knowledge.

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SOURCES OF PROTONS AND HEAVY IONS, H. A. GrunderFIGURE CAPTIONS

Fig. 1: Biomedical Research Areas at the Bevalac.

Fig. 2: Range-Energy Relation for H, He, d, Ne and Ar Ions in Water.

Fig. 3: Cost versus Maximum Energy for Circular Accelerators.

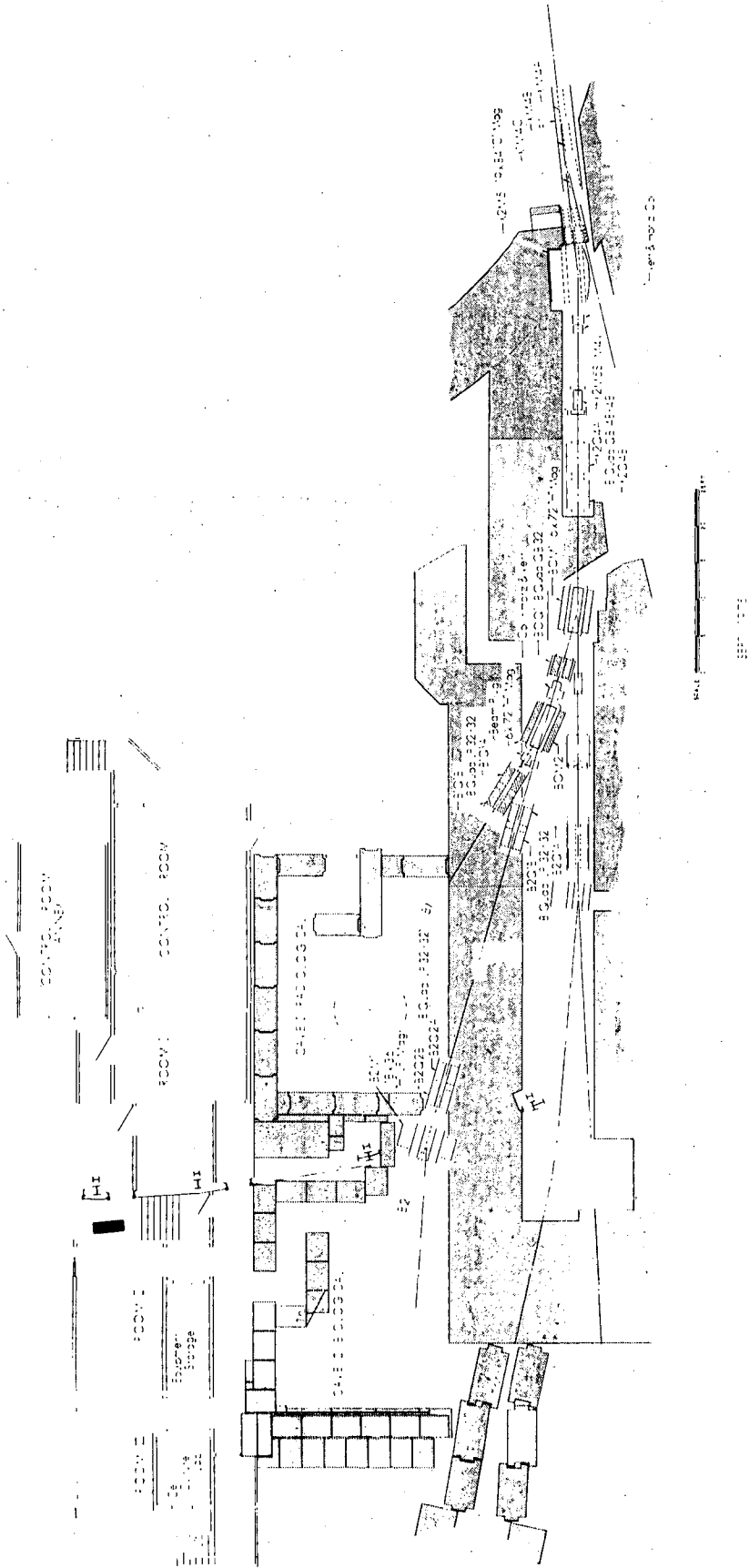
Cyclotrons are identified in the figure. Curves A through D correspond to the synchrotron options with the following capabilities:

	Protons	Heavy Ions	Radioisotopes	Neutrons
A	x	x	x	x
B	x	x	x	
C	x	to mass 4	x	
D	x	to mass 4		

Fig. 4: Repetition Rate-Dependent Synchrotron Costs.

Fig. 5: Hypothetical Facility, Conceptual Design.

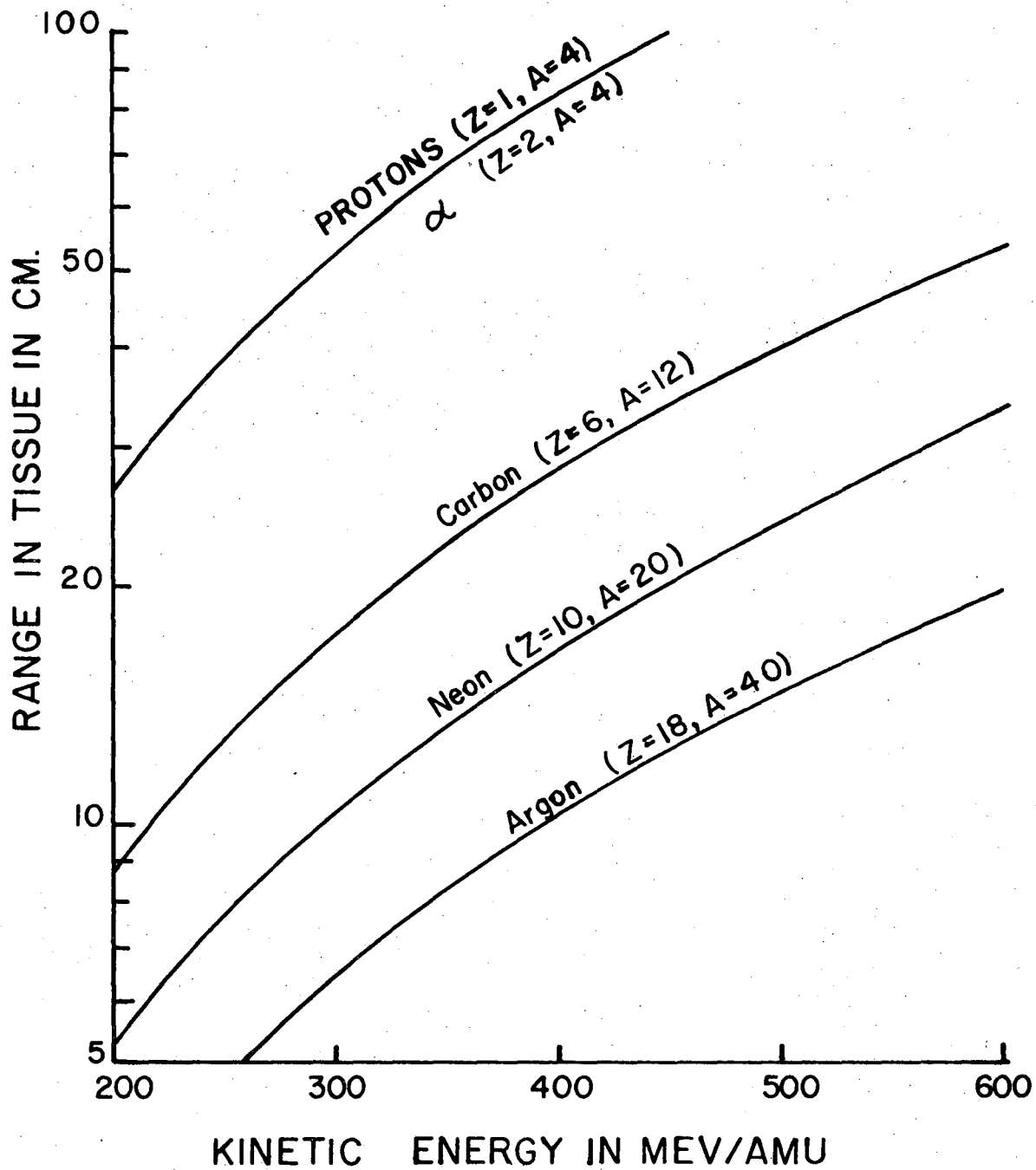
Fig. 6: Compact Hypothetical Facility, Conceptual Design.



BIOMEDICAL BEAM B1 & B2

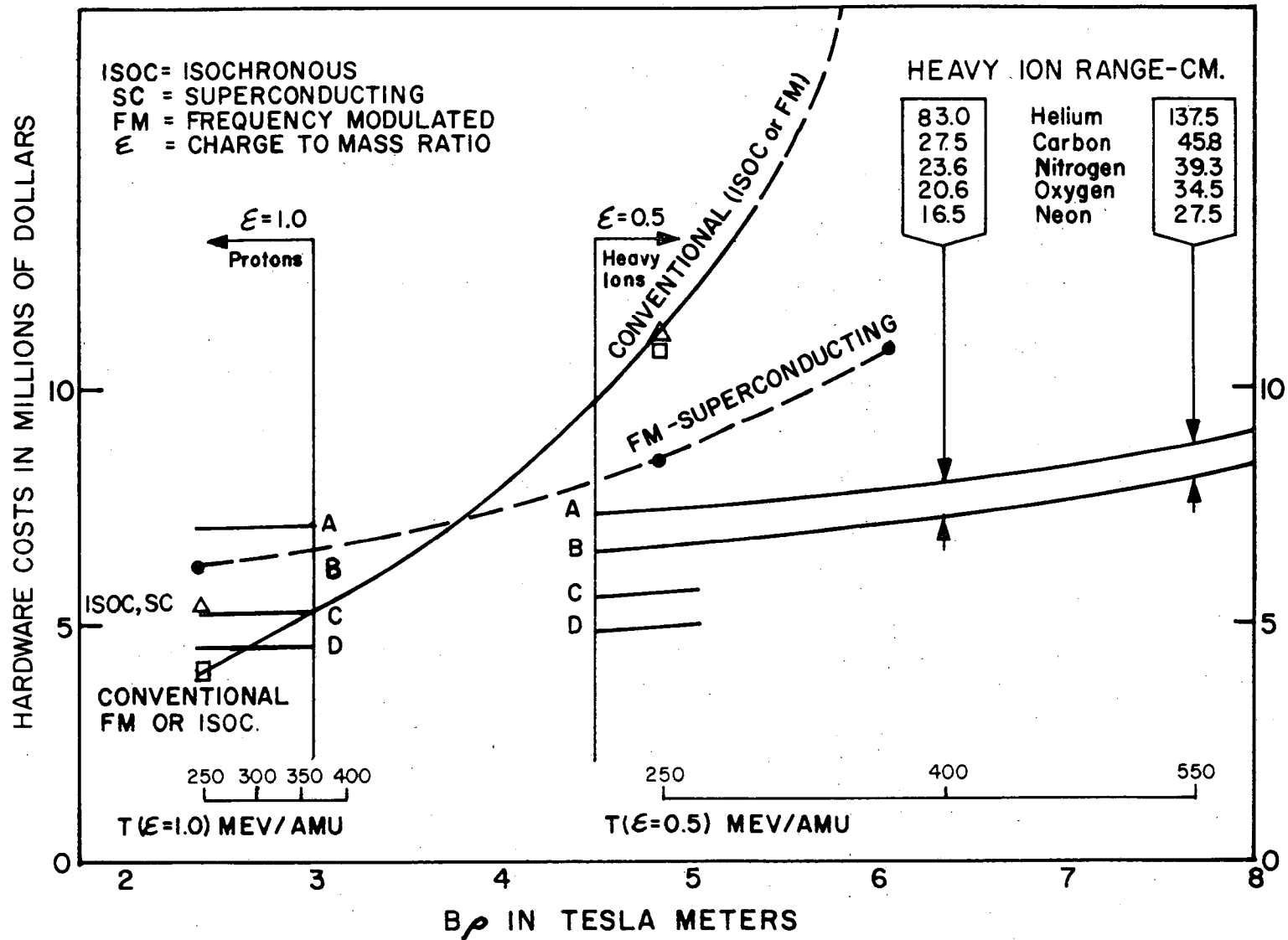
Fig. 1

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FIG. 2

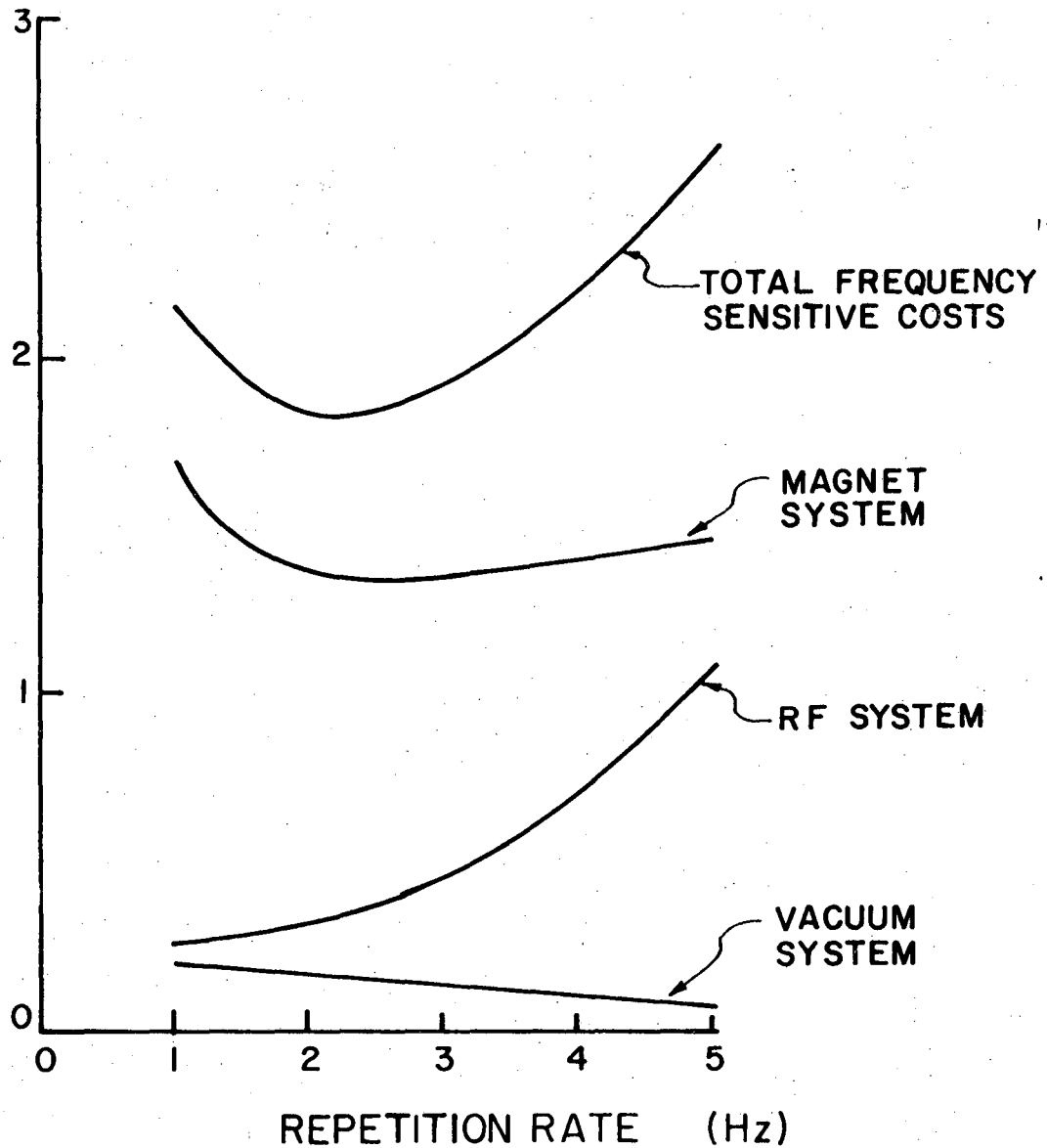


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FIG. 5

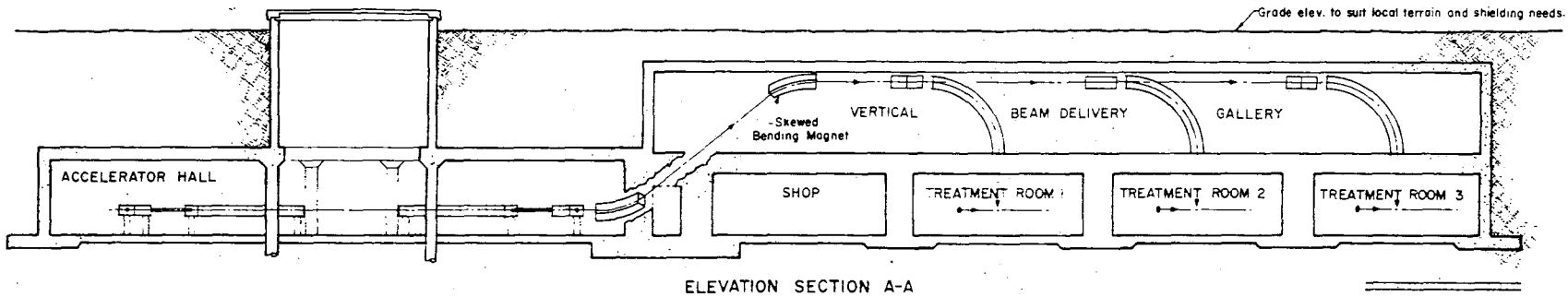
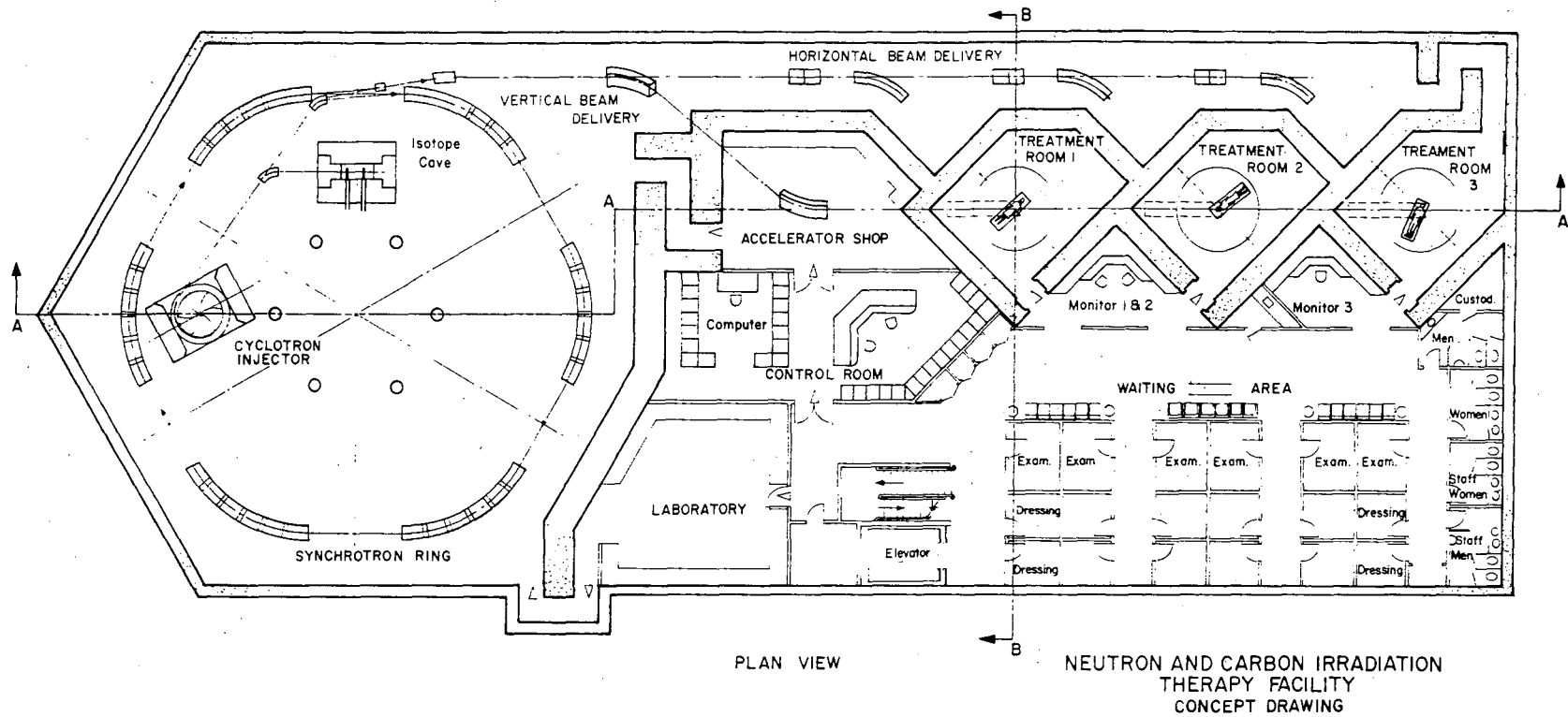
FREQUENCY SENSITIVE SYNCHROTRON COSTS
AS A FUNCTION OF REPETITION RATE FOR A
C⁺⁶ 400 MEV/AMU SYNCHROTRON WITH A
C⁺³ CYCLOTRON INJECTOR. (FY 1977 \$)

DOLLARS x 10⁶ - FREQUENCY SENSITIVE SYNCHROTRON COSTS



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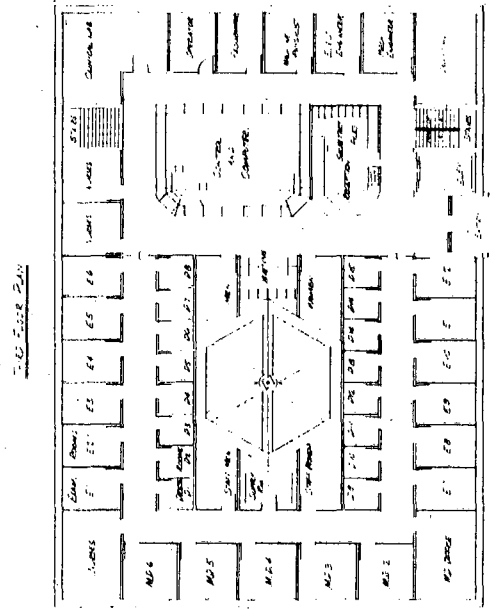
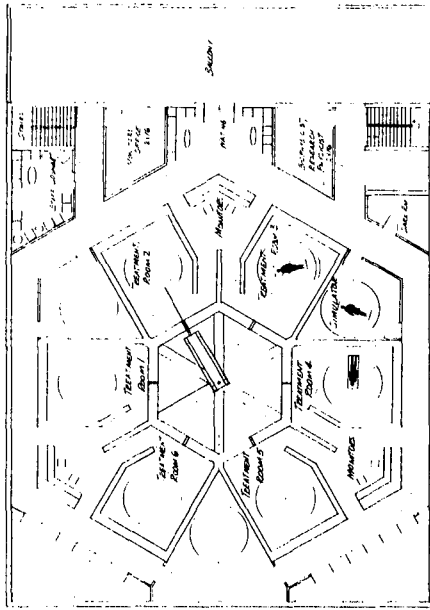
FIG. 4



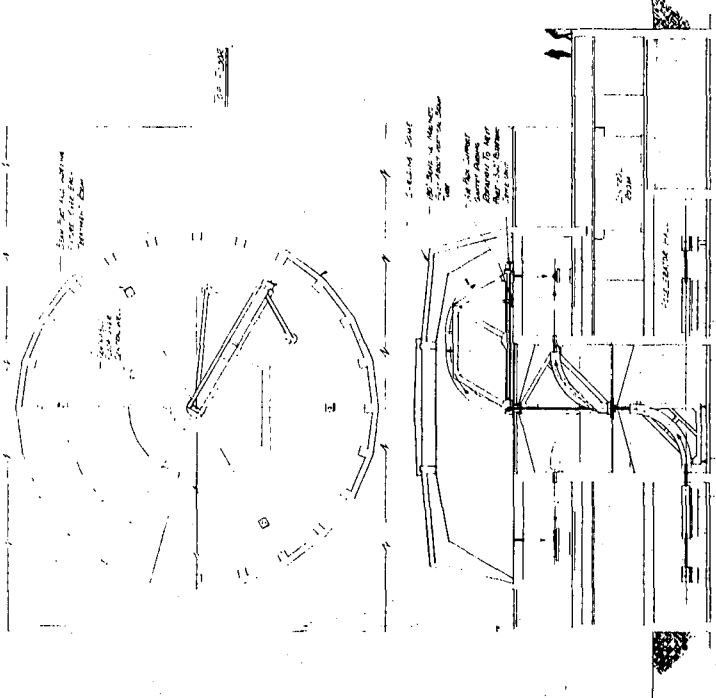
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SCALE
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FIG. 5

LEUKEMIA AND HEALING RADIATION THERAPY FACILITY - CONCEPTUAL DRAWING



SCALE: 1/8" = 1'-0"



ELEVATION SECTION

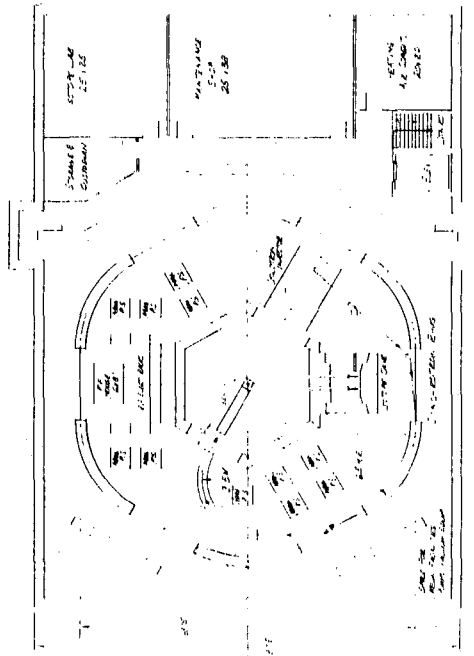


FIG. 6

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