Proceedings of a Medical Workshop on Accelerators for Charged-Particle Beam Therapy

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CONFERENCE SUMMARY

F. T. Cole

The results given here are from notes and may not be complete. Although I have tried to reflect all viewpoints, the conclusions also include a measure of my own opinions and may not be agreed to by every participant.

1. Active therapy work is now being done with primary charged-particle beams (protons and heavier ions) at the Lawrence Berkeley Laboratory, KEK (The National Laboratory for High Energy Physics) and the University of Tsukuba in Japan, the Harvard Cyclotron Laboratory and Massachusetts General Hospital, and at the Institute for Theoretical and Experimental Physics, Moscow, USSR and at Gatchina (Leningrad), USSR. Work was done at the Gustav Werner Institute in Uppsala, Sweden during the years 1957-1968 and at Dubna, USSR. In all these hospitals, good clinical results have been obtained with tumors of the head and neck regions and genital organs. An extensive accelerator and facility improvement program is well along at Uppsala with extracted beam scheduled for late 1985. Planning for tests on eye cancers is underway at Argonne National Laboratory using the existing 50-MeV proton linear accelerator and Fermilab has recently completed the conceptual design of a proton-beam facility using the existing 200 MeV linear accelerator.

2. Therapy was considered at the workshop to be the highest priority for the accelerator design. Diagnostic use is not an issue, because that work has been taken over by CT and Magnetic Resonance Imaging (MRI). (It might be possible someday to improve resolution over MRI with proton radiography, but this is not now an active field.) There is not universal agreement about the impact of MRI, but there is a consensus that diagnostic use is of considerably lower priority than therapy.

Production of radionuclides complicates the design of synchrotrons and makes them much more expensive than synchrotrons without radionuclide capability. Cyclotrons and linear accelerators inherently have high enough intensity that useful radionuclide production comes automatically. In fact, the cyclotron at Uppsala is planned to receive significant revenue by producing enough ^{123}I for all Scandinavian medical needs. Radionuclide production is, even in these cases, considered to be significantly lower in priority than therapy.

3. The two lines of work, low-LET (protons and helium) and high-LET (heavy ions) have been almost entirely separate. The high-LET work has all been done at Lawrence Berkeley Laboratory, where a new medical accelerator is being proposed for this work.

4. For low-LET accelerators, there was somewhat of a consensus on the following specifications:

Energy: Protons 250 MeV
(He ions might also be of interest.)

Intensity: 1 Gy/min over a sizeable area (perhaps 30 by 30 cm^2 or a little larger) (1 Gy = 100 rad). This corresponds to an extracted current of the order of a nanoampere or more, or 10^{10} particles/sec if scanning can be used, or 10 nanoamps (10^{11}/sec with existing techniques.

Repetition Rate: At least 1 Hz, preferably higher. There is some interest in 20 to 50 Hz.

Facilities: Several treatment rooms with expansion capabilities.

Very high reliability (better than 95%) and ease of repair were stressed by all speakers as a critical part of any accelerator for this purpose.

5. Linear accelerators inherently have much higher intensity than needed and are also much more costly than other accelerators. It is believed that a linear accelerator should be considered for this application only if there is an existing free accelerator.

6. Cyclotrons and synchrotrons can be compared as follows:

Cyclotron	Synchrotron
Fixed Energy	Easily Variable Energy
Intensity 1μA	20 n A
Proven Technology	Proven Technology
Detailed Design: considerable experience with CW cyclotron	Detailed Design: not avail.; possibly cheaper

The Michigan State Laboratory has built and operated CW cyclotrons with some applicable design features. If one were ordering an accelerator today, one would choose a cyclotron.

7. R. L. Martin suggests that it is possible to make significant economies in a synchrotron that depends on scanning to cover the entire area, but whether the technology of scanning and monitoring is advanced enough to depend on it exclusively and what its costs are compared with those of a reduced-intensity synchrotron are controversial at this time.

8. The existing cyclotrons at Michigan State have superconducting magnets. Robert Wilson showed an extremely attractive concept for a superconducting synchrotron, small enough to fit on a table top. Superconducting technology is advanced enough to be completely dependable and commercially available. It may be interesting to consider building a superconducting accelerator directly into the gantry to achieve flexibility in beam delivery.

9. The minimum cost of a low-LET accelerator appears to be 1 to 1.5 M$. The minimum cost for a facility, starting from scratch, with at least marginally adequate treatment rooms appears to be 8 M$. Economies may be possible in existing facilities. The cost of the accelerator is not a major fraction, but is large enough to hope for significant savings through careful design. There are widely divergent views on costs of accelerator and complete treatment facilities.

10. This workshop has performed a valuable function in getting medical people and accelerator people to talk and understand each other's viewpoints on instruments for therapy. We may hope that in is this way the workshop was a beginning for new initiatives in charged-particle beam therapy.

11. The costs estimated for a cyclotron are firmer than those for a synchrotron because of the more advanced state of design. It was decided to hold a second workshop when the estimated costs for synchrotron designs have been better established. It is expected that this second workshop will be held in the fall of 1985.

Proton Beam Therapy at Tsukuba

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Abstract - KEK-University of Tsukuba proton-beam-therapy facility, its preliminary treatment results and some requirements for a medical facility are described briefly.

1. PARMS

After completion of the 12-GeV proton synchrotron at KEK, the booster synchrotron utilization facility (BSF) was built. It uses 500 MeV pulsed protons for a pulsed neutron source, a pulsed meson source and medical purposes. There is no medical doctor at KEK, so that a branch of the Particle Radiation Medical Science Center of the University of Tsukuba (PARMS) was built there. It has three projects, proton therapy, proton diagnostics and neutron therapy.

Construction of PARMS facility was directed by Professor S. Suwa, the former director general of KEK. It was started in April of 1980 and was completed in March of 1983. Clinical trial of cancer therapy by proton beams was started in July of 1983 but was discontinued at the end of February of 1984, because of a long shutdown of the 12-GeV PS due to tunneling of TRISTAN, a 30-GeV e^+e^- collider. It will resume next June.

As there was no such facility plan in the original design of the 12-GeV PS, it is impossible to extract a 250-MeV proton beam from the booster synchrotron without disturbing stable injection of the 500-MeV beams into the main ring. Therefore, the 500-MeV protons are degraded to about 250 MeV after deflection into the medical proton beam line. The time-average primary proton intensity is at most 2 μA, and it decreases by a factor of several times 10^{-3} by a carbon degrader and a following spectrometer system. A vertical beam line and a horizontal one were made, the former was used for therapy so far whereas the latter for development of the proton diagnostics.

2. Preliminary Proton Therapy

All cases of proton therapy are shown in the Table. Beam intensities used were about 100 rad/min and irradiation time was 3 ∿ 4 minutes for a patient a day. Only primary tumors without distant metastasis have been treated, otherwise the patients might die before evaluating whether the proton beam is good or not. Although the number of patients was limited so far and times after treatments were short, the effect of proton beam is as expected.

3. Requirements for Medical Proton Facility

Including experiences of the preliminary clinical trials, the following conditions should be fulfilled by a proton therapy facility:

a) Proton energy is 200 ∿ 250 MeV. Tumors in the deep-seated organs are the major targets of the protons.

b) Beam intensity is 100 rad/min or more. Irradiation time of 3 to 4 minutes is maximum permissible duration for patients.

c) The maximum field required is generally as large as 15 x 15 cm, and a field of 8 x 8 cm may be sufficient in most cases.

d) Bragg peak should be expanded to 5 cm. A vertical beam is superior because of easy and reproducible fixture of the patient. However, to obtain high peak/plateau ratios, if possible more than 3, an additional horizontal beam is beneficial, and such a beam is being designed at PARMS.

e) There is a labyrinth which ensures quick access of medical doctors to the patient in a treatment room. A concrete shielding door separates the patient from the doctors at PARMS and it takes too much time to go into the treatment room for an accident.

f) A distance between the patient and a nozzle of the proton beam is more than 50 cm. The space is useful to put additional tools for improvement of dose distribution, and the nozzle should be mechanically strong enough to support the tools.

g) Obviously low neutron contamination is favorable. Although neutron dose is usually less than 1% of proton dose in a target, the whole body of the patient is exposed to the neutrons.

h) Normal operation is 8 hours a day and 5 days a week. A shutdown should not last more than a week but this is not the case for high energy accelerators.

i) It seems difficult in Japan to provide proton facilities in the future unless two medical doctors and two nurses can manipulate a machine without accelerator specialists. The medical doctors are primarily concerned about dose distribution and setting up of the patient, so that the accelerator and beam-handling equipment should be dependable and automated.

4. Ongoing Plans

An analyzer magnet and detectors to measure residual energies have been made for proton CT following the horizontal beam line. The horizontal beam will be used for therapy too.

Emphasis will be put on proton therapy of lesions in the deep-seated organs such as lung, liver and rectum.

Neutron cell biology was started. It will be continued further.

The KEK proton complex will sometimes be operated from the pre-injector to the booster synchrotron for BSF. During this mode of operation, protons are no more accelerated to 12 GeV for high energy physics experiments.

Proton beam therapy started at the National Institute for Radiological Science (NIRS) in Chiba-city prior to PARMS trial in some limited extent, because protons are accelerated up to 90 MeV by the cyclotron. Attractive irradiation techniques of spot scanning have been developed.

Acknowledgments

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Supplementary Note

A thorough survey on medically dedicated particle accelerators was made by Miyakawa Committee of Japan Radiological Society in 1978-1980. It was supported by Science and Technology Agency. The report contains[1]:

1. Study on medical use of particle accelerators.
1.1 Therapy by existing accelerators.
1.2 Diagnostics by existing accelerators.
1.3 Investigations of medical systems with accelerators and their suitable distribution planning.

2. R & D of medically dedicated accelerators and beam-handling equipment.

2.1 Conceptual design of accelerators.

2.2 Development of irradiation and beam-handling equipment.

Following the survey, Inada Committee continued the study and submitted two reports:

Study on developemtn and utilization of medically dedicated particle accelerators for cancer therapy and diagnostics, 1981. Design of Proton Irradiation Facility, 1983 - it was supported by Cancer Study Grants of Ministry of Health and Welfare, and mostly concerned with proton beam facility.

Reference

1. Investigations of medically dedicated particle accelerators (in Japanese), September 1980, Japan Radiological Society.

Table Caption:

List of patients treated by proton beams at PARMS from June 1983 to February 1984. In Improv. + is good, ++ better and +++ best. In Rec. - shows no recurrence.

Organ	Histology	Dose(rad) / (days)	Lesion Improv.	Lesion Rec.	Add. treatment	Late injury	Prog.
Skin	Squam. c. ca.	P 8795 / 50	++	−	−	−	Alive (14 ms)
Skin	Bowen disease	P 8800 / 37	++	−	−	−	Alive (14 ms)
Skin	Bowen disease	P 7300 / 23	++	−	−	−	Alive (8 ms)
Tongue	Squam. c. ca.	P 8250 / 47	++	−	−	±	Alive (10 ms)
Tongue	Squam. c. ca.	P 7750 / 46	++	−	−	±	Alive (10 ms)
Buccal mucosa	Squam. c. ca.	P 6350 / 39	++	−	−	−	Alive (10 ms)
Middle ear	Basal c. ca.	P 3700 / 16 E 1980 / 16	++	−	−	−	Alive (7 ms)
Parotis	Adenoca.	P 4700 / 17	++	−	−	−	Alive (8 ms)
Ut. cervix	Squam. c. ca.	P 3850 / 19 Co 3246 / 29	++	−	−	−	Alive (9 ms)
Liver	Hepatocell. ca.	P 3250 / 24 (+ BUdR)	+	−	−	−	Alive (11 ms)
Liver	Hepatocell. ca.	P 2950 / 22 (+ BUdR)	+	−	−	−	Alive (11 ms)
Retroperitoneal space	Neuroblastoma	P 2550 / 25	+	−	Chemoth.	−	Alive (9 ms)
Brain	Meningioma	P 7250 / 42	++	−	−	−	Alive (8 ms)
Brain	Meningioma	P 6450 / 24	++	−	−	−	Alive (8 ms)
Brain	Astrocytoma	P 5550 / 32 Co 3050 / 28	++	−	−	−	Alive (10 ms)
Brain	Astrocytoma	Co 5060 / 42 P 6400 / 61	+	−	−	−	Alive (8 ms)
Brain	Astrocytoma	P 4700 / 18 Co 2415 / 21	++	+	−	−	Alive (7 ms)
Brain	Glioblastoma mutiforme	Co 3020 / 28 P 5400 / 32	±	+	Operation	−	Alive (10 ms)
Brain	Glioblastoma mutiforme	P 3150 / 24	±	+	Operation	−	Alive (8 ms)
Brain	Glioblastoma mutiforme	Co 1500 / 18 P 5750 / 32	++	+	Radiation	−	Alive (7 ms)
Brain	Glioblastoma mutiforme	Co 4000 / 44 P 4300 / 18	++	+	−	−	Dead (6 ms)
Brain	Glioblastoma mutiforme	P 7650 / 43	++	+	−	−	Dead (7 ms)

P : Proton beam E : Electron beam Co : ^{60}Co γ ray

EXPERIENCE WITH THE UPPSALA 230 cm CYCLOTRON AND PREPARATIONS FOR FUTURE USE IN RADIOTHERAPY

B. Larsson and S. Graffman

(References are found on the attached slide copies and in an additional list at the end of the paper).

ACTIVITIES 1952-1976

In 1952 the construction of the 230 cm synchrocyclotron (slide 1) was completed at The Gustaf Werner Institute in Uppsala. This institute is located in the middle of a conglomerate of scientific departments and is less than a kilometer from the University Hospital serving a population of 1.5 million inhabitants. During the years 1957-1968 69 patients were treated with large field, range-modulated proton beams (slides 2a,b and 3a,b).

The first series of patients included only such advanced tumours that curative treatment was judged impossible. Among these were 10 cases of verified recurrences of cervix carcinoma. A total dose of 30 Gy was given in a single fraction with a perineal portal to the pelvic region (slide 4). Fractionated treatment of advanced genital carcinoma was also performed as a second series. We had confidence in our technique and the equivalence of protons and cobalt radiation seemed fairly well established from the biological point of view. Further work was therefore concentrated on cases in which the geometrical advantages of the proton dose distribution could be better exploited. It should be mentioned that in parallel with this radiotherapy project, the proton beam was also used for narrow beam irradiation of intracranial structures (see "Additional Reading" 1-8, 10, 12 and 30).

The next series consisted of 19 patients with cancer of the nasopharynx.[11] A proton dose of 20-40 Gy was given in 2-4 fractions, supplementary to earlier X-ray treatment. Two opposing lateral proton fields were directed on the primary tumour region. The range of the beams was adjusted by a bolus so that overlapping fields gave a full tumour dose in a region of 5 cm around the midline while the dose at the parotides and skin was less than 50% of the tumour dose as indicated in the next slide. By visual and biopsy control the radiation effect on normal and tumour tissue could be studied. No unexpected pathological or clinical findings were made. Twelve out of 19 responded well.

Reference 16 describes the technique used for treatment of malignant glioma by means of a range modulating ridge-filter, absorbers and a bolus made of thin sliding sticks of lucite. Fixation at the auditory canals and the base of the nose was found

to be very effective. The dose was 51 Gy in 10-11 fractions during about one month. One of our 8 patients treated for malignant glioma is still alive. The survival of the other patients was similar to what is expected from other treatment modalities. The brains secured at autopsy were carefully examined. In all brains the tumour cells were altered but viable tumour cells were seen within the treatment volume.

Slide 5 gives the proton dose distribution to a patient suffering from a very advanced thyroid cancer. It was the last patient treated and it illustrates the state of development and the versatility of the technique. By using an appropriate bolus, the whole tumour volume could be treated homogeneously without exceeding the tolerance level of the spinal cord. The same homogeneity of the dose distribution could rarely have been achieved with conventional high energy radiation even if complex multifield arrangements were used. The patient is still alive after 15 years.

The patient material in Uppsala does not lend itself to a statistical analysis since it is small and diverse and most patients were in very advanced stages. Some of the patients are, however, still alive 15-20 years after the treatment.

The following conclusions were drawn in 1968, and are still valid:

1. High energy protons can safely be used for radical radiotherapy.

2. The therapy can be based on experience from conventional therapy since the effects of protons are similar to those of other types of low-LET radiation.

3. The flexibility of the proton field permits an accurate dose distribution in good conformance to generally accepted clinical criteria.

4. There are tumour patients for which proton therapy would obviously be preferable to other types of therapy due to differences in the macroscopic distribution of dose.

The reason for recalling the old situation is that the clinical work in Uppsala paved the way for the later, technically more advanced, studies at Harvard, Berkeley and Moscow. It also forms a basis now that the programme is being resumed in Uppsala. Here, a Swedish national accelerator center is being established based on three different accelerators: the existing tandem van de Graaff, the synchrocyclotron under reconstruction and the CELSIUS ring for the storing and cooling of ions injected from the cyclotron. From the radiotherapy point of view, the Gustaf Werner

cyclotron continues to be the accelerator of major interest. After reconstruction, this new facility, the SFSC-200, will operate both as a synchrocyclotron and as an isochronous cyclotron with K=200 (slides 6-8).

THE CYCLOTRON SFSC-200

The improvement programme for the 185 MeV Gustaf Werner synchrocyclotron started in 1977 and aimed at the construction of a three-sector, variable-energy cyclotron. The necessary new buildings (slide 9) were approved and funded by the government in May 1981. Early in 1983 the power supply and control rooms were finished, and in 1984 a 650 square meter area for physics and biomedical research was completed. The present time plan predicts external ion beams from the cyclotron in late 1985. Most of the buildings shown are below ground and closely surrounded by a number of other university buildings. The proximity to other laboratories is an advantage but has, in fact, been a major difficulty and explains much of the special features of the general layout.

Slide 9 also shows the various beam lines under construction. A neutron and nuclide production area, the "spallation crypt", is located on the same level as the cyclotron. All other experimental positions will be about 5 meters above the cyclotron floor and the beam will be brought to this level by two 30 degree magnets. The first target room will be used for neutron production. After this comes the physics area, which is divided into one room with two spectrometers, one 135 degree ion spectrometer and one pair spectrometer and finally a room for low-background gamma measurements. The biomedical research will be supplied with four different beam lines for experimental and clinical research.

The layout of the experimental and therapy areas is given in slide 9. The cyclotron is located 10 meters underground and the new areas are about 5 meters above the cyclotron level. The small rectangular area next to the right of the cyclotron was the only laboratory that existed before. The new biomedical area is shown in the upper right corner and two treatment rooms are planned at this level, one for narrow beams less than 3 cm in diameter, and one for broad beams up to 30 cm in diameter. Next to the treatment area is an old building that will hold some patient-related areas.

The reconstructed cyclotron will be able to operate either with frequency modulation (FM) or at fixed frequency (CW). The FM mode must be used for protons in the energy range of 110 to 200 MeV, while protons of lower energy and heavier particles can be accelerated in CW mode. Slide 8 shows the energies obtainable for various particles. The K value of the cyclotron has increased

from 185 MeV to 200 MeV by the modified pole geometry. Protons in the very highest energy range (i.e., above 185 MeV) will be reached only at reduced modulation frequency due to the increased bandwidth requirements.

The design philosophy for the field was given by Holm and Renberg (1978). A three-sector polegap geometry which is now installed was studied in an extensive set of field measurements and orbit calculations on a 1:4 model. The field of the full scale magnet has been mapped over the useful range of the cyclotron, from 2.5 to 17.3 kGauss.

The acceleration will be performed by two identical RF systems of the "master oscillator + power amplifier" type in both CW and FM modes. The amplifier chain of each system consists of a 1 kW, a 10 kW and a 100 kW stage. The systems are tunable from 12 to 24 MHz for operation on the harmonics number 1, 2, 3 and 4. The dee electrodes have an azimuthal width of 72 degrees at the center and 42 degrees at extraction. Built around a strong but light, supporting structure of stainless steel and clad by sheet copper, they are cantilevered from the vacuum feedthrough and tuned by moving shorts in air. The equivalent dee capacity is about 315 pF at 24 MHz. The natural quality factor is reduced in FM mode from about 200 to 100 by connecting a 40 kW resistor in parallel to the dee stem. The maximum dee voltage is approximately 50 kV in CW mode and 12 kV in FM mode. The final amplifiers (capable to withstand an anode dissipation of 100 kW in the FM mode) are inductively coupled to the dee resonators and move together with the dee tuning shorts on a rail.

The cyclotron will initially be equipped with an internal PIG ion source with a double arc chimney for operation in both first and second harmonic with the same geometry. Due to the difference in dee voltage between FM and CW operation, different sized geometries have to be used. There are also plans for external injection. A special ion source room has been built for this purpose outside the cyclotron hall.

Beams will be extracted from the cyclotron with either regenerative or precessional techniques. The two main deflecting elements are an electrostatic deflector and an electronagnetic channel (EMC). A passive focussing channel will be placed in the fringe field about 20 degrees downstream from the exit of the EMC.

Regenerative extraction will be used when operating in FM mode and in some cases of first harmonic CW operation when the energy gain per turn is low. A peeler and a regenerator will then be inserted.

The vacuum chanber is designed with a prevacuum part housing the epoxy-moulded trim coils. The construction material in the

chamber is an aluminum alloy. In the high vacuum region most of the seals consist of soft aluminum wire. Conventional pumping by diffusion pumps backed by roots pumps is foreseen for the initial operation. The calculated ultimate vacuum lies in the 10^{-7} Torr range.

The cyclotron will be computer-controlled with distributed microprocessors, organized at three levels. At the lowest level the processors will be integrated in the equipment serving both local control and communication with the higher level. The processors in the middle level will supervise the different systems such as magnet, RF and so on. The main computer (TMS 990-12) is connected to the control console and helps the operators to set and read the data bases in the lower systems.

In slide 8 the expected performance of the reconstructed cyclotron is summarized, assuming an internal ion source. Estimated current for heavy ions are based on results from other cyclotrons. When operating with frequency modulation the phenomenon most likely to limit the current will be space charge close to the centre of the cyclotron. Based on a simplified calculation of that limit the maximum external proton current in the high energy range will be around 10 μA. For CW acceleration of P and D beams, assuming conservatively 80% extraction efficiency, a maximum septum power of 1 kW will permit a 40 μA external beam. For heavier ions the ion source will be the limiting factor.

The ΔE values given for the FM case have been calculated assuming radial amplitudes less than 4 mm and a dee voltage for 185 MeV protons of 12 kV. Both the radial amplitudes and the accelerating voltage influence the energy spread of the external beam in the method gives smaller values.

In FM operation the beam will be pulsed with a maximum frequency of 1000 Hz. For injection into the CELSIUS ring, and for radiobiological studies, it may be desirable to have short pulse lengths. The number of protons in a beam pulse will be up to $6 \cdot 10^{10}$. With normal setting of the cyclotron in "short burst operation", the bucket half width will be 25 μs, the shortest pulse length possible from the cyclotron with a filled bucket. Due to the conditions for particle capture at the center of the cyclotron, however, the bucket will in practice be empty at the center. Cyclotron orbit studies have shown that the unfilled bucket will cause the beam pulse to be shortened, typically from 25 to 8 μs. A further reduction of the pulse length is possible by adiabatically increasing the accelerating voltage in the cyclotron and at the same time the rate of frequency change. For example, with a doubling of the dee voltage during a short time prior to extraction (which may be done without excessive power loss) df/dt can be increased by a factor 2.9 without loss of particles. This will cause a further reduction of the pulse length to about 3 μs.

In this example, the time for capture at the cyclotron center was 12-17 μs. Thus the cyclotron is expected to bunch by a factor 5.

COLLABORATION WITH ITEP 1976-1985

Since 1976 there has been a collaborative programme between the Institute of Theoretical and Experimental Physica (ITEP) in Moscos and the Gustaf Werner Institute on physical, radiobiological and technical aspects on the use of proton beams in medicine. Considerable experience in the development of proton therapy methods has accumulated at ITEP and at the Gustaf Werner Institute during this time. Methods of treatment planning, radiobiological research and labelled compound productions have improved. Among joint research projects may be mentioned:

1. Proton beam transport and control.

2. Production of short-lived radionuclides and labelled compounds such as ^{11}C-methionine and ^{11}C-glucose which are used for tumour studies in patients and animals with the positron emission tomograph in Uppsala.

3. Intercomparison of methods for dosimetry. In this context special attention has been paid to semi-conductors. In collaboration with Therados Company, Uppsala, a silicon detector was developed that showed dose rate independence up to a dose of 0.2 Gy per pulse suitable for the high pulse dose rate of the ITEP accelerator.

We have had the opportunity to exchange clinical experiences also with the groups in Moscow and Leningrad and at Dubna (slide 21). At Dubna about 30 patients with cancer of the oesophagus, lung or larynx have been treated with protons. A major reconstruction of the accelerator and the radiotherapy sites is performed allowing treatment with protons, neutrons and pi-mesons in separate rooms. The treatments have not yet been reinstituted.

At Gatchina[17] only therapy with narrow beams using cross-fire techniques has been given. Thus, more than 12 cases of functional disorders of the brain and more than 60 pituitary irradiations for ablative purposes of patients with cancer of the breast and of prostate have been performed. About 100 patients with pituitary adenomas have also been treated.

At ITEP patient irradiations have been carried out since 1969. Radiotherapy can be given independently of simultaneous physical investigations. Up to the end of 1981, 575 patients had been treated at this facility with one single treatment room with two irradiation sites, one for broad beams and one for stereotactic radiosurgery. Recently two new treatment rooms have been added and the patient load is expected to increase considerably.

The clinical results appear to be similar to those achieved at Harvard and Berkeley. It is a common understanding, however, that the possible merits of proton radiotherapy over conventional radiation can only be demonstrated through randomized trials. It is also generally agreed that a randomized comparison is only allowed when the investigator cannot predict the outcome of the trial. The only known difference between high energy protons and other types of conventionally used radiations is the macroscopic dose distribution. Very large groups of patients must be included to have a chance to detect a significant difference in result. We therefore undertook a design study of a large scale proton treatment facility in Uppsala in order to evaluate the clinical, technical and economical prospects. The potential patient load was estimated from tumour indicence tables and the number of patients treated curatively with radiotherapy. About 1/4 of the patients were found to gain from being treated with protons. Assuming an eight million population, about 200 proton treatments per day should be needed provided conventional fractionation schemes were followed and all radiotherapy was given with protons. Fixed proton beams were supposed and the patients should be treated in a supine position. It was estimated that four fixed beam directions should be needed. The beam directions and the relative treatment loads are shown in slide 10a. With five treatment rooms, the requirements of 200 treatments per day should be satisfied. Separate facilities for radiosurgery and radionuclide production should also be provided. A model of the facility is shown in slide 10b. The total cost of the building, cyclotron beam transport and computer equipment was estimated and it was found to be comparable to that for a clinic with five electron accelerators. The facility for radiosurgery and radionuclide production may even make the balance in favour of the cyclotron facility. There are no plans for building such a large scale facility in Sweden. It would probably be more favourably located in a densely populated large metropolitan area, as is now discussed in the U.S.S.R. In Uppsala only a restricted number of patients will be treated at the new facility. The primary aim is research and technical development.

PLAN FOR THE WORK AT SFSC-200

So far, most attention has been paid to the clinical aspects on the use of proton beams in oncology and surgery. In parallel with the above investigations, however, a scientific program evolved with weight put upon basic radiation research in which the various beams and radionuclides from the cyclotron were exploited. Its main elements are various aspects on the radiation response of mammalian cells and tissues, quantification of effects in biochemical and pathophysiological terms, and the search for efficient effect-modifying principles.

One major task of technical development prior to the clinical use of SFSC-200 seems to be particularly relevant, in the present context. Several steps towards optimization of the depth dose distribution with protons have been conceived following the ideas of Drs. A. Koehler and M. Goitein, et al., at Harvard. We are also interested in "spot scanning" with variable modulation and compensation as described by Kawachi, Kanai and others. We are contemplating the use of the latter technique incorporated in a gantry system, as illustrated in slides 11 and 12. It would give a fully isocentric proton delivery system with a flexible collimator by means of a 60^{o} bending magnet, a quadrupole lens and a cross plane steering magnet, a 143^{o} bending magnet. Inside this magnet there will be a scattering foil to assure uniform proton coverage of the elementary beam and mask any internal inhomogeneity which may be present in the beam from the accelerator. The location of the foil and the exit angle of the magnet are chosen such that the beam is essentially parallel when leaving the magnet. This pitch will allow a 180^{o} rotation of the gantry which is already constructed.

Slide 12 shows a close up of the scanning magnets, the dual wedge range shifter and the flexible collimator. In order to make the size of gantry reasonable there is one stationary scanning magnet and one pivoting around the virtual scanning center of the first scanning magnet. This solution will allow 30 x 30 cm large fields with an effective SSD of 100 cm using conventional magnet technology. All three scanning motions and the flexible collimator should be accurately coordinated and controlled by the same computer. The second scanning magnet pivots mechanically so that its median plane coincides with the direction of the proton beam as it leaves the first scanning magnet. At present we have no funds for the construction of this gantry system and so, when treatments are started again at the end of next year, the work will first focus on the narrow beam for treating eye tumours, pituitary adenomas and other small intracranial targets.

The mentioned development does, indeed, put rigourous demands on the beam handling system. At first glance the uniformity of the beam cross sections seems to represent a problem, since the cross section of the "raw" beam may be very inhomogenous. It was easily solved, however, already in the previous installation, by letting the beam describe a rectilinear Lissajou pattern (slide 13). (A thin scatter foil was used to soften the beam structure.) This technique for beam homogenization by pencil sweeping has the obvious advantage that it minimizes beam intensity losses and production of contaminating secondary radiation. In fact, the system has turned out to be reliable and permits excellent homogeneity without sophisticated electronic control. A modified version is now being conceived based on computer control of a more flexible beam-sweep system (slides 14-20). Reference is made to a study done for the ITEP, Moscow, where 200 MeV proton pulses are

tapped at a frequency of 0.5 Hz from the 10 GeV synchrotron. Under such conditions, a relatively small number of pulses are delivered in a typically therapeutic sitting, such as 300 in 10 minutes, and the beam sweep pattern has to be optimized for maximum homogeneity of flux density.

OBSERVATIONS AND CONCLUSIONS

We observe that medium energy protons have largely been accepted as a potentially useful treatment modality in oncology and neurosurgery, also in a large-scale clinical context. Their social impact is still to be seen, however, there is still no hospital-based proton-beam facility installed or projected. The main reason for this inappropriate situation seems to be that proposed installations are considered fancy, clumsy and too expensive.

Now, when computerized tomography (CT, NMR, PET) create new rationales and possibilities for precision in radiotherapy and radiosurgery, the challenge is increasing: new, convenient technical concepts have to be sought!

The renovated Uppsala cyclotron, the SFSC-200, may serve as a convenient test facility in the present phase of development.

ACKNOWLEDGMENT

Described developments at the Uppsala cyclotron have been supported by the Knut and Alice Wallenberg Foundation, the Swedish Cancer Society, the Swedish Medical Research Council, the Swedish Natural Science Research Council, the National Swedish Board for Technical Development, and the Swedish Academy of Engineering Sciences.

ADDITIONAL READING

In addition to references given on the attached slide originals, the following papers contain information of relevance in the context of proton radiotherapy and other medical applications of medium energy particle accelerators:

1. C. A. Tobias, H. O. Anger, and J. H. Lawrence: Radiological Use of High Energy Deuterons and Alpha Particles; Am. J. Roentgenol. 67: 1 (1952).

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4. B. Rexed, W. Mair, P. Sourander, B. Larsson and L. Leksell: Effect of High Energy Protons on the Brain of the Rabbit; Acta Radiol. 53, 289 (1960).

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15. Bragg Peak Proton Radiosurgical Hypophysectomi for Pituitary Adenomas. in Proc. of the First International Seminar on the Use of Proton Beams in Radiation Therapy. Moskva 1977, s. 22-35.

16. S. Graffman, W. Haymaker, R. Hugosson, and B. Jung: High Energy Protons in the Postoperative Treatment of Malignant Glioma; Acta Radiol. Ther. Phys. Biol. 14: 445 (1975).

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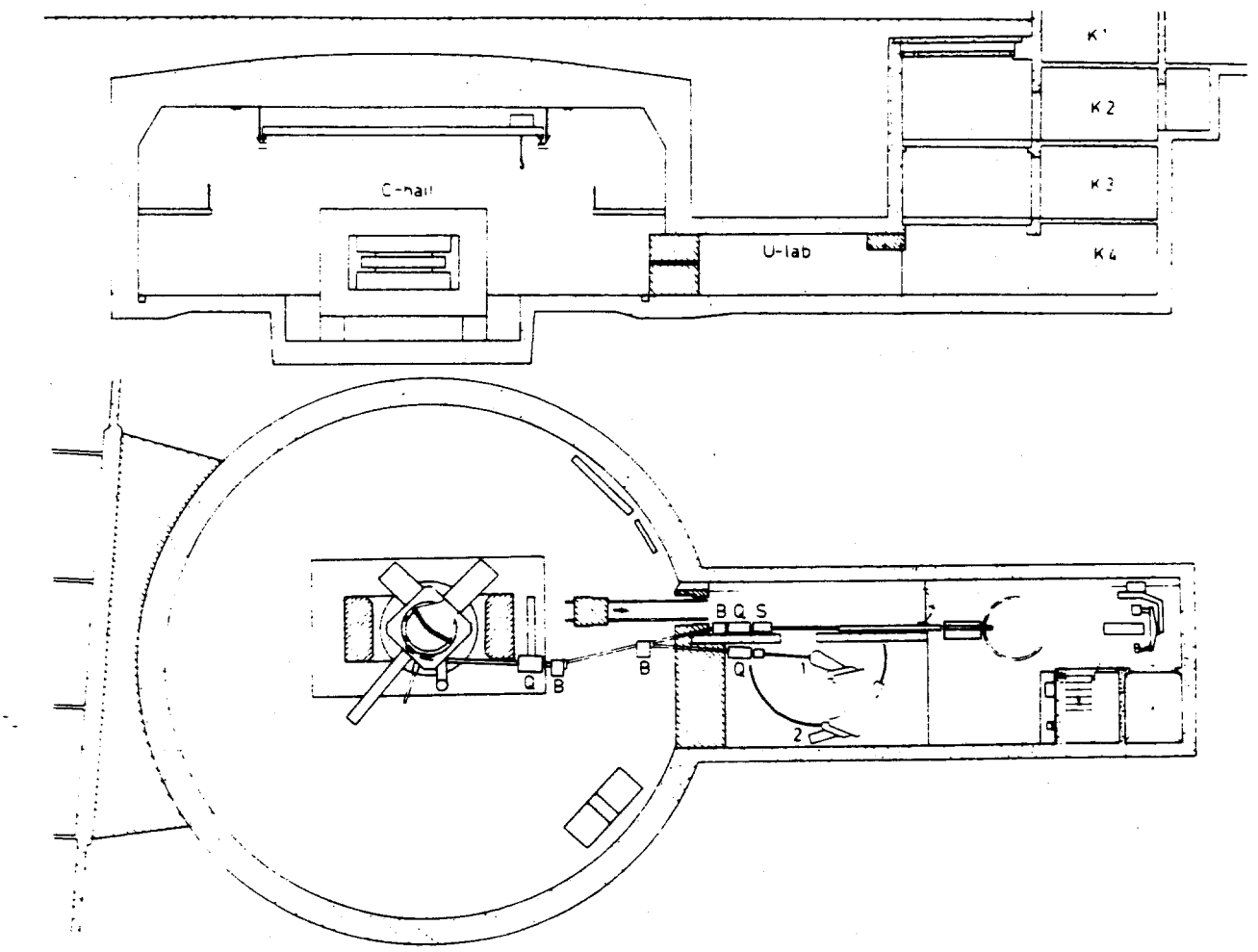
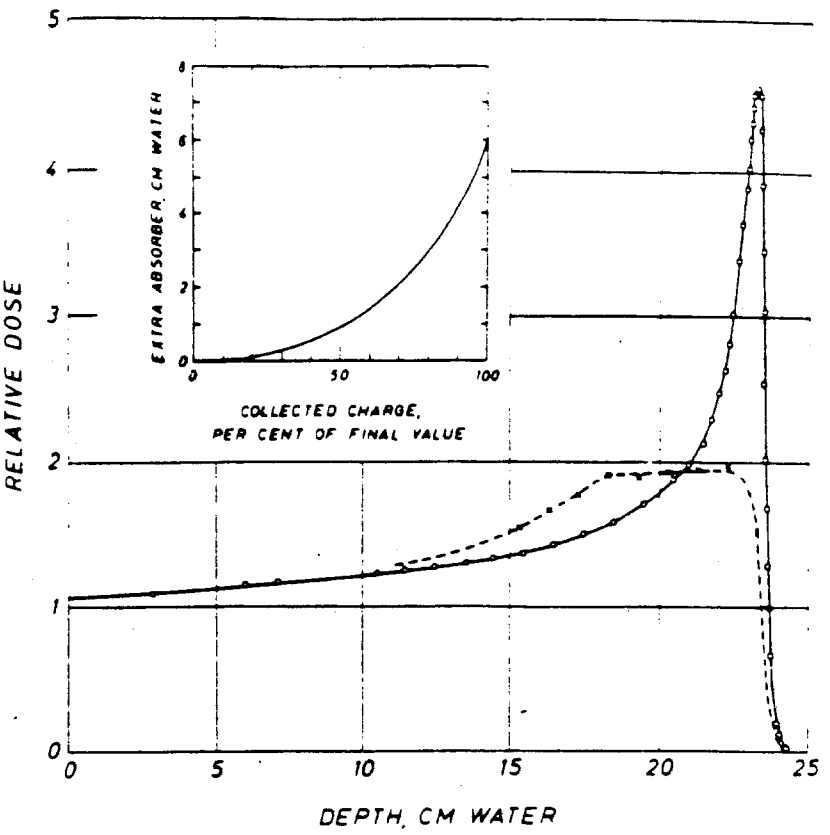
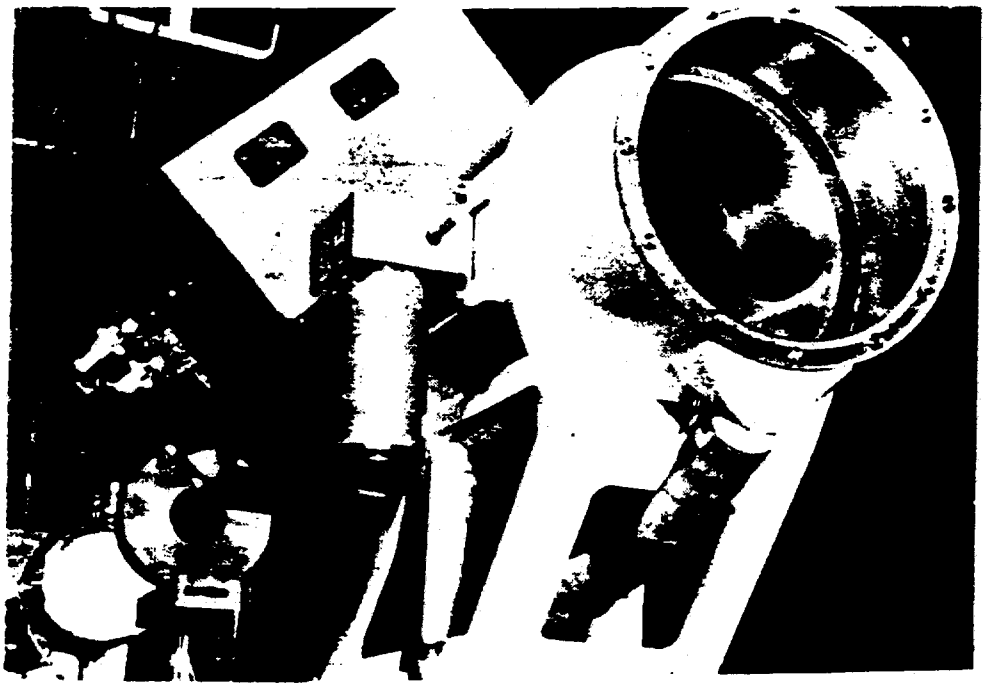


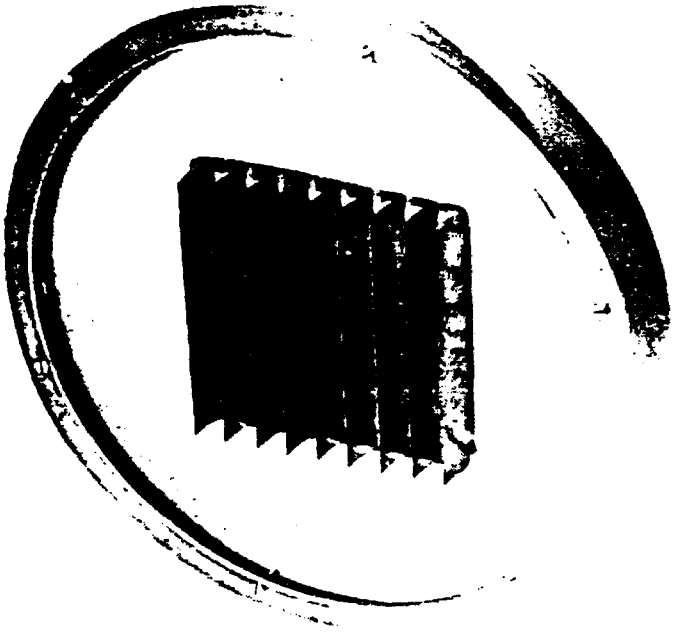
Slide 1: Plan of the cyclotron hall and adjacent experimental rooms in operation 1956-1977. The external beam laboratory ("U-lab") was used for physical and biomedical experiments as well as for clinical applications.

Slides 2a and 2b:
Transformation on the Bragg peak. Variation of the water absorber in front of the target was performed, during irradiation, according to the curve in the inset diagram. The original (————) and the transformed (------) depth-dose curves are shown. Points of measurements (x) on a depth-dose curve obtained by the use of a ridge filter (Slide 3) are indicated. The profile of the ridges was determined by the shape of the curve in the inset diagram, 1 cm water being equivalent to 0.18 cm brass. (Courtesy Brit. J. Radiol.)

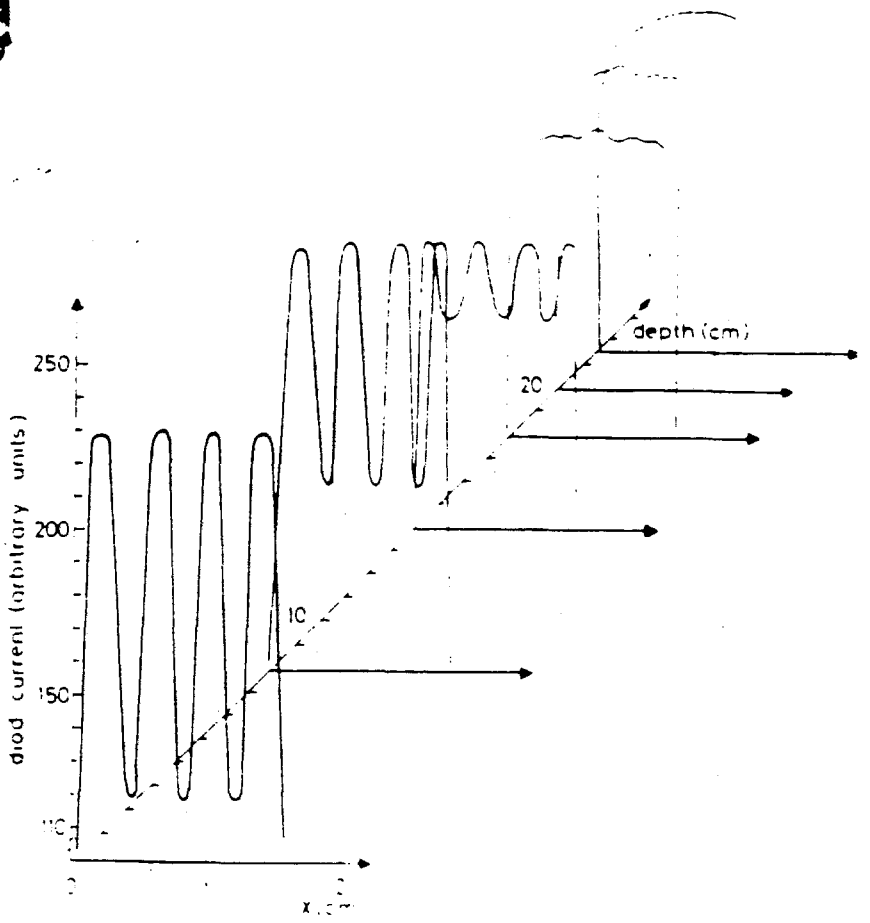




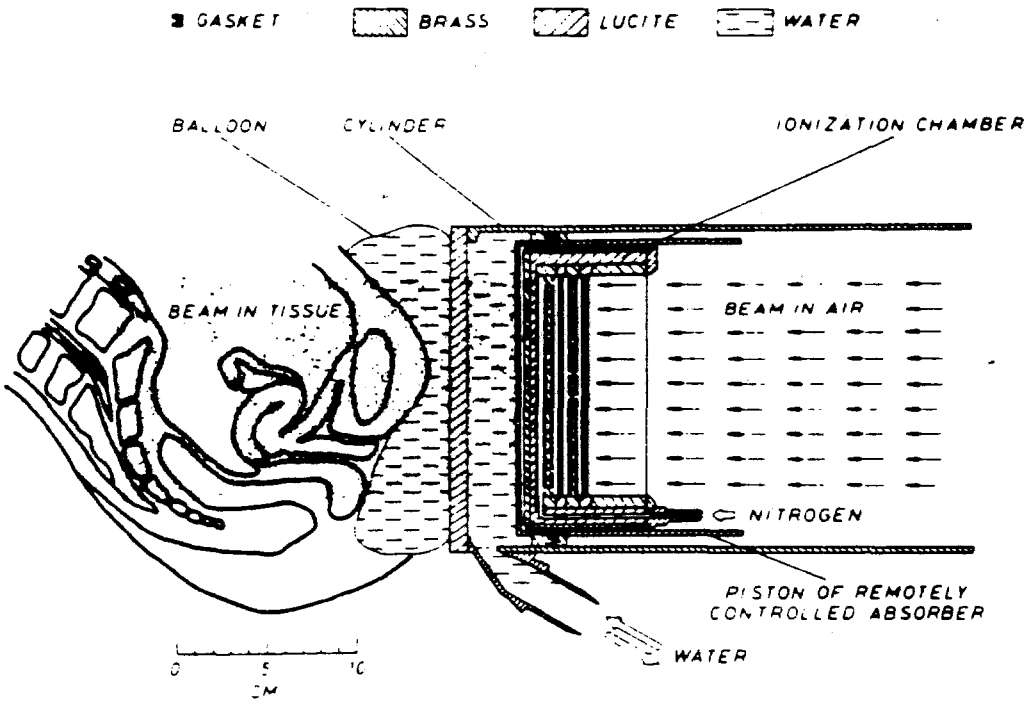
B. Larsson: Pre-therapeutic Physical Experiments with High Energy Protons; An extended version of the contribution to the Symposium on Therapy with Beams of High Energy Particles, at the Annual Congress of the British Institute of Radiology on Dec. 10, 1959; Brit. J. Radiol. 34: 143 (1961).



Slide 3a: A ridge filter designed for 185 MeV protons. Its characteristic profile and effects on the depth-dose, distribution are designed on Slide 2a.



Slide 3b: The ridge filter affects the depth-dose distribution by introducing pre-calculated differences in the particles' range of penetration. The ridge structure, reflected in the lateral distribution of dose at shallow depths, becomes of little importance in the region of the "Bragg plateau". This distribution of dose was measured with a small signal diode at linear response by Dr. H. G. Rikner, Uppsala.



Slide 4: Section through the apparatus in Figure 4 arranged for irradiation of tumours in the pelvis by a spread-out Bragg peak. The piston controlling the varying thickness of the water absorber is shown at a moment when its position gives maximum penetration of the beam.

S. Falkmer, B. Fors, B. Larrson, A. Lindell, J. Naeslund and S. Stenson: Pilot Study on Proton Irradiation of Human Carcinoma; Acta Radiol. 53: 33 (1962).

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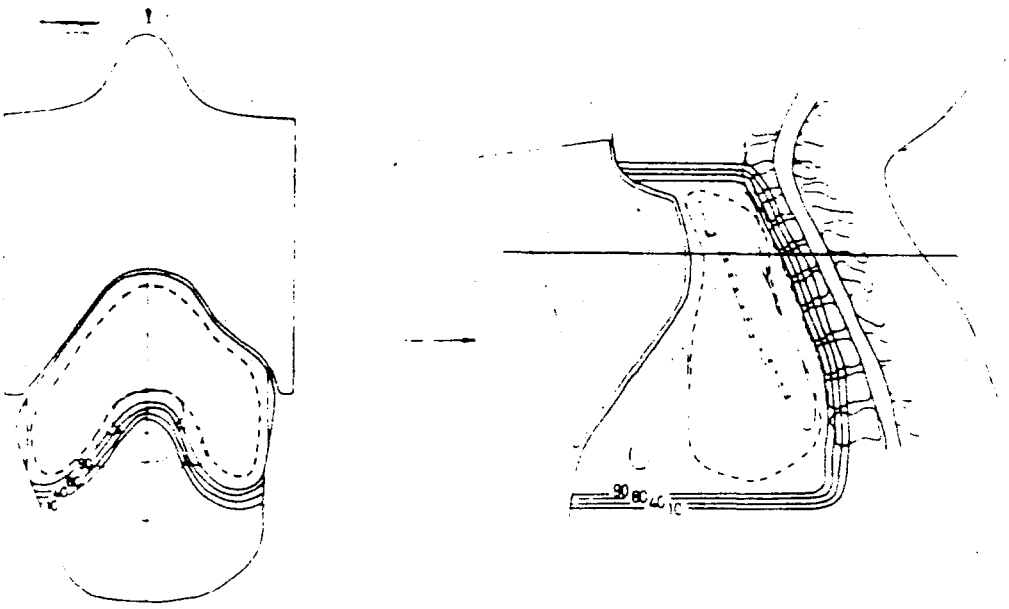
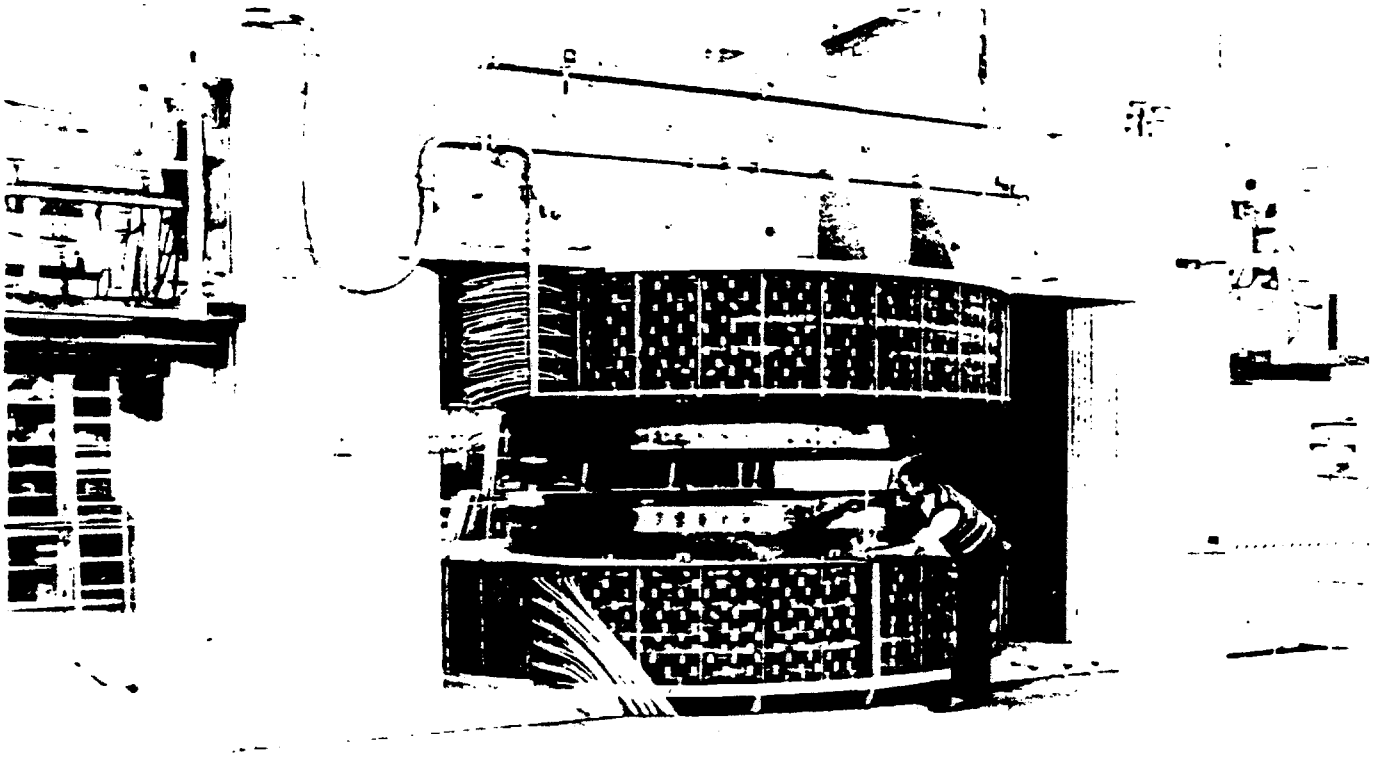


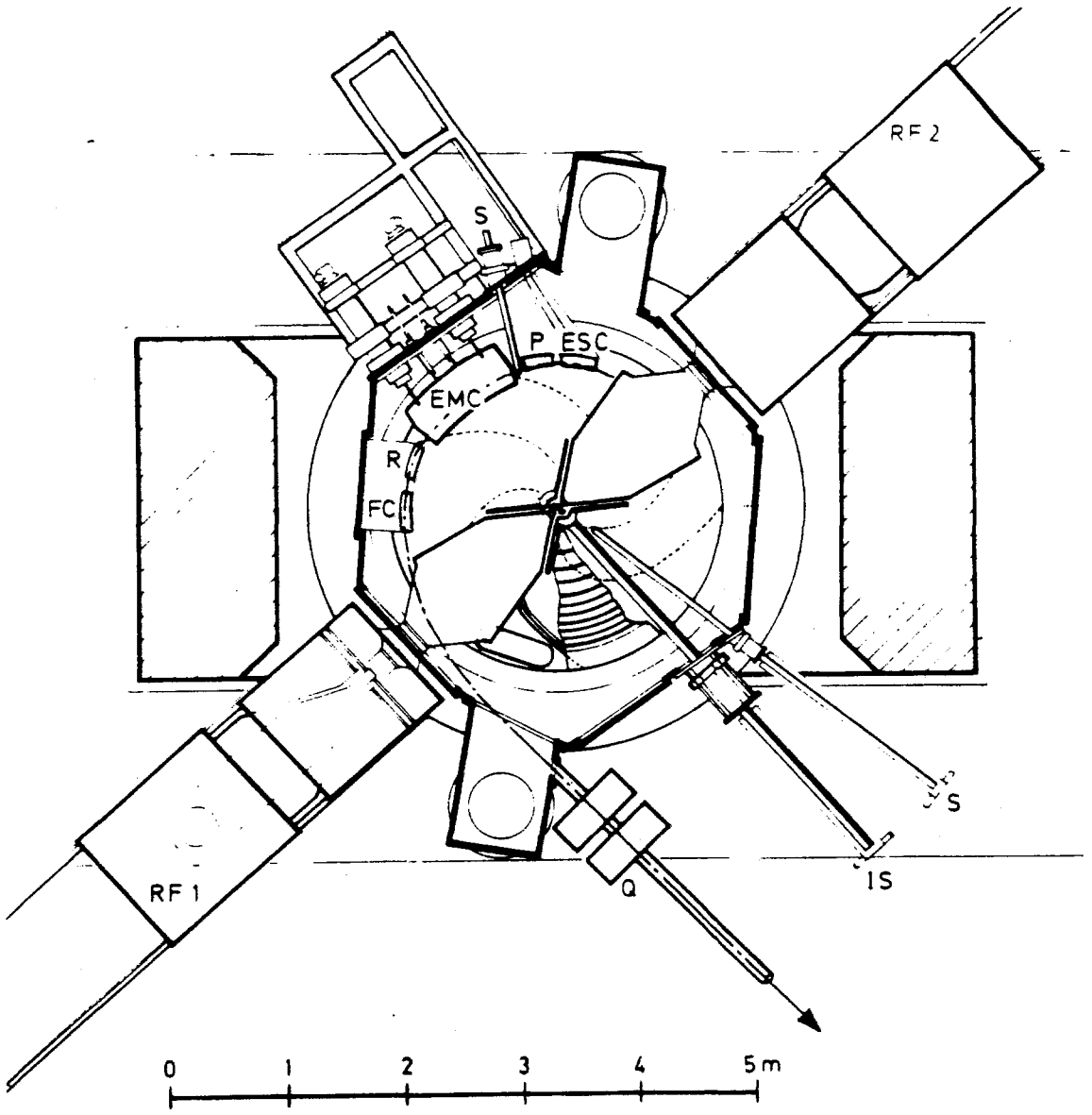
Slide 5: Distribution of dose in a single field of 185 MeV protons tailored to a target volume (------) containing an infiltrating thyroid carcinoma. (Courtesy Atomkernenergie)

S. Graffman: Thesis, Umea University (1975). Referred to in: S. Graffman and B. Larsson, High-Energy Protons for Radiotherapy - A Review of Activities at the 185 MeV Synchro-Cyclotron in Uppsala, Atomkernenergie 27: 148 (1976).



Slide 6: A sector-focusing synchrocyclotron, the SFSC-200, is being constructed at the Gustaf-Werner Institute on the basis of the magnet of the 230-cm synchrocyclotron.

S. Dahlgran, A. Ingemarsson, S. Kullander, B. Lundstrom, P. U. Renberg, K. Stahl, H. Tyren, and A. Asberg: Conversion Studies for the Uppsala Synchrocyclotron, in "Seventh International Conference on Cyclotrons and Their Applications, Zurich 1975", W. Joho, ed., Birkhauser Verlag, Basel (1975).



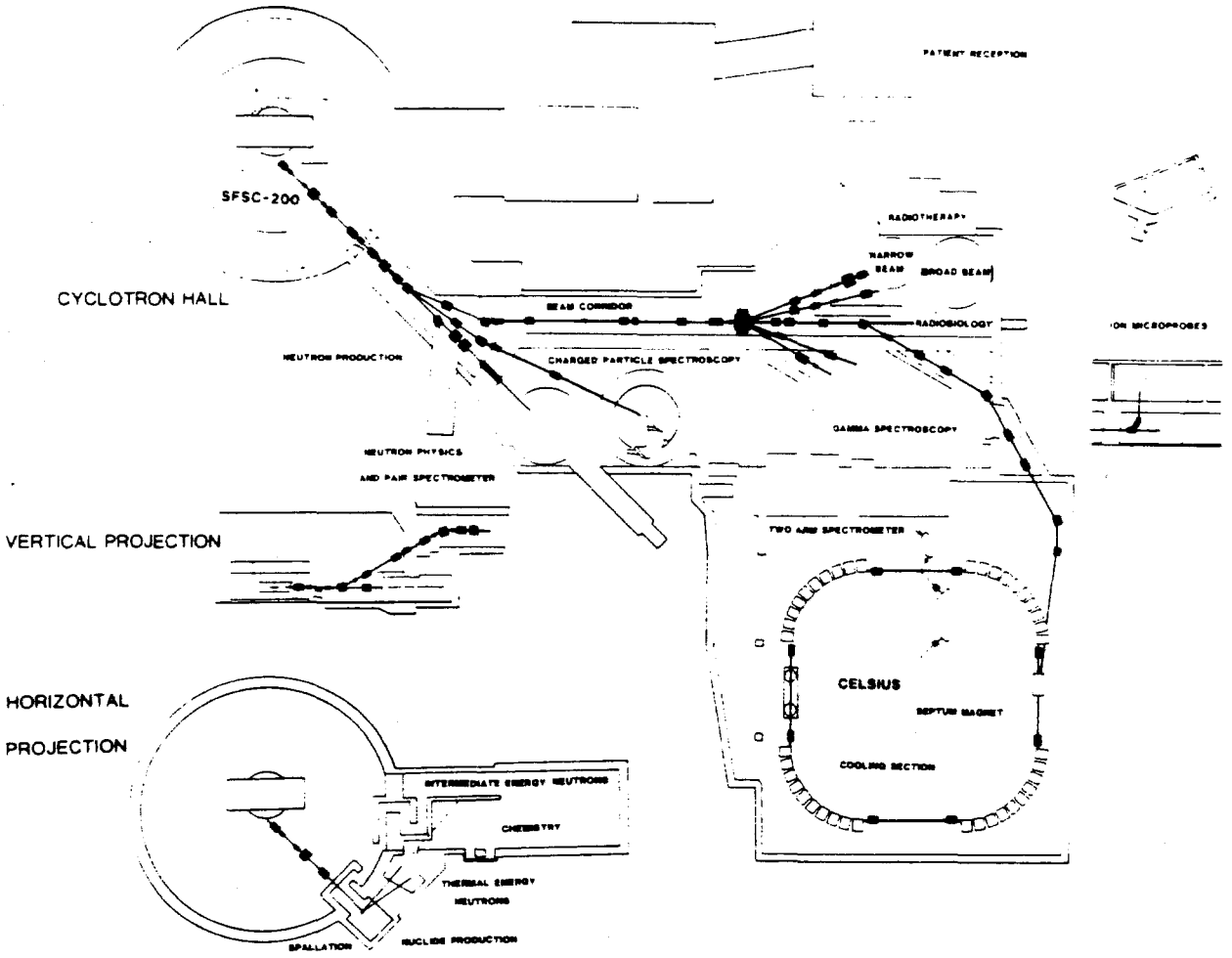
Slide 7: The Cyclotron SFSC-200. The reconstructed cyclotron will be able to operate either with frequency modulation or at fixed frequency. The FM mode must be used for protons in the energy range of 110 to 200 MeV, while protons of lower energy and heavier particles can be accelerated in CW mode.

A three-sector polegap geometry is now installed. The field of the full scale magnet has been mapped over the useful range of the cyclotron, from 2.5 to 17.3 kGauss. The acceleration will be performed by two identical RF systems of the "master oscillator + power amplifier" type in both CW and FM modes.

Ion	Energy (MeV)	Acc mode	Extr meth	Energy res %	Hor emitt mm-mrad	Estim intens (eμA)
P	110-200	1-FM	Reg	0.22	6-8	10-1
P	45-110	1-CW	Reg	0.5	4-5	40
P	45-110	1-CW	Prec	0.17	20	40
$^{3}He^{2+}$	250-267	1-FM	Reg	0.22	6-8	2
$^{3}He^{2+}$	137-250	1-CW	Reg	0.5	4-5	20
$^{3}He^{2+}$	35-137	2-CW	Prec	0.17	20	20
D	25-100	2-CW	Prec	0.17	20	40
$^{12}C^{4+}$	133-267	2-CW	Prec	0.17	20	5
$^{16}O^{5+}$	167-312	2-CW	Prec	0.17	20	10
$^{20}Ne^{7+}$	223-490	2-CW	Prec	0.17	20	0.1

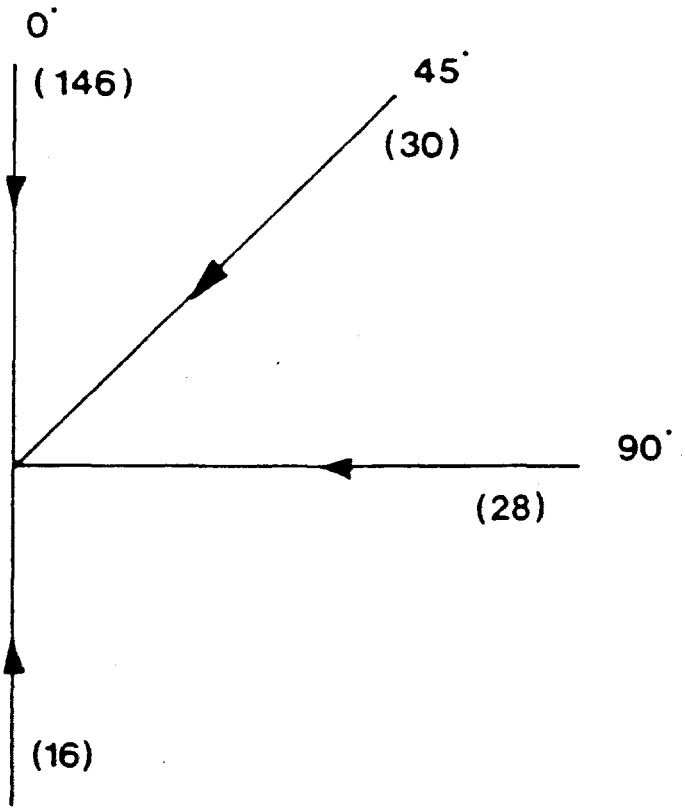
Slide 8: The expected performance of the reconstructed cyclotron SFSC-200 assuming an internal ion source. Estimated currents for heavy ions are based on results from other cyclotrons.

Slides 7 and 8, as well as the technical data on SFSC-200, in the text are from S. Holm, A. Johansson and the GWI cyclotron and CELSIUS groups.



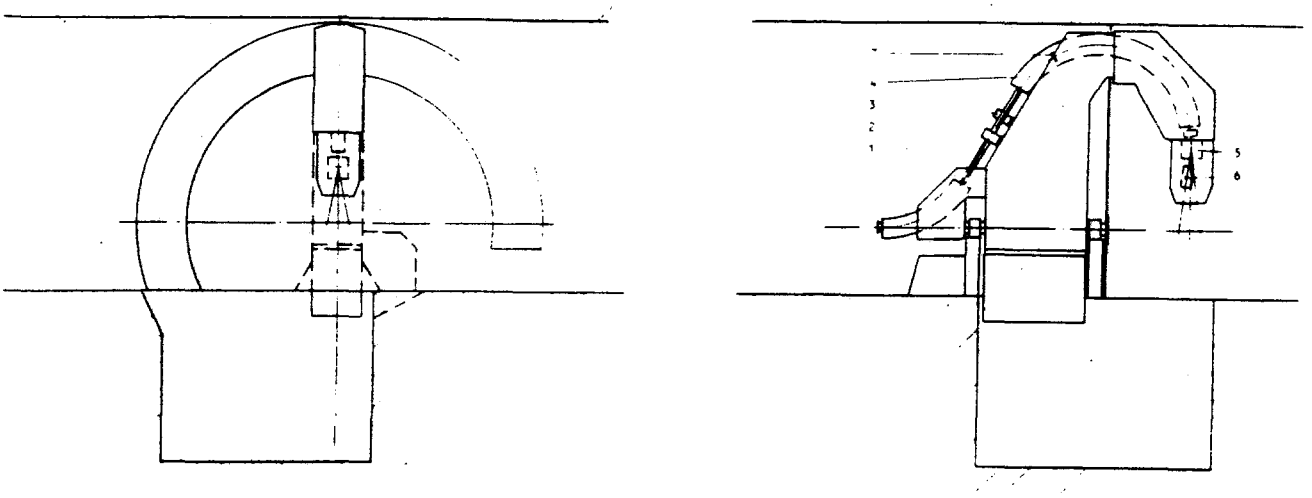
Slide 9: Outline of the various beam lines planned. A neutron and nuclide production area, the "spallation crypt", is located on the same level as the cyclotron. All other experimental positions will be about 5 meters above the cyclotron floor and the beam will be brought to this level by two 30 degree magnets. The first target room will be used for neutron production. After this comes the physics area which is divided into one room with two spectrometers, one 135 degree ion spectrometer and one pair spectrometer, and finally a room for low-background gamma measurements. The biomedical research will be supplied with four different beam lines: broad and narrow beams as well as a micro-beam.

There is also a beam transport line from the cyclotron to CELSIUS, over 100 meters long. Two switching magnets will allow short injection intervals into CELSIUS to minimize interference with other beam users, independent of what target position they may use.



TREATMENT ANGLES

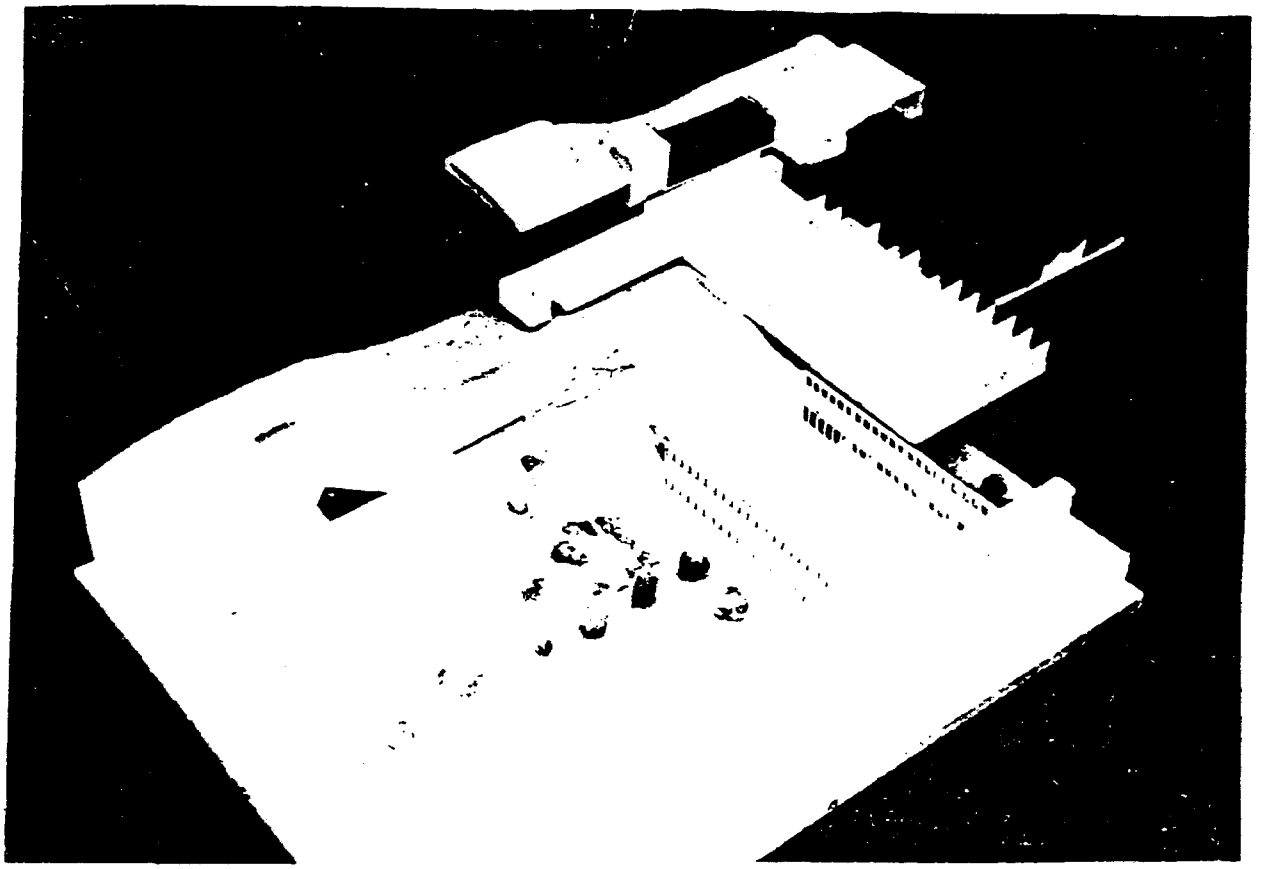
Slide 10a: A study was made of different patient categories that may preferably be treated at a hypothetical Swedish proton therapy center. The diagram indicates the preferred beam directions and the corresponding numbers of patients per day.



Slide 11: Several steps towards optimization of the depth dose distribution with protons have been conceived. Such a technique may be incorporated in a gantry system which is illustrated here and in the following slide.

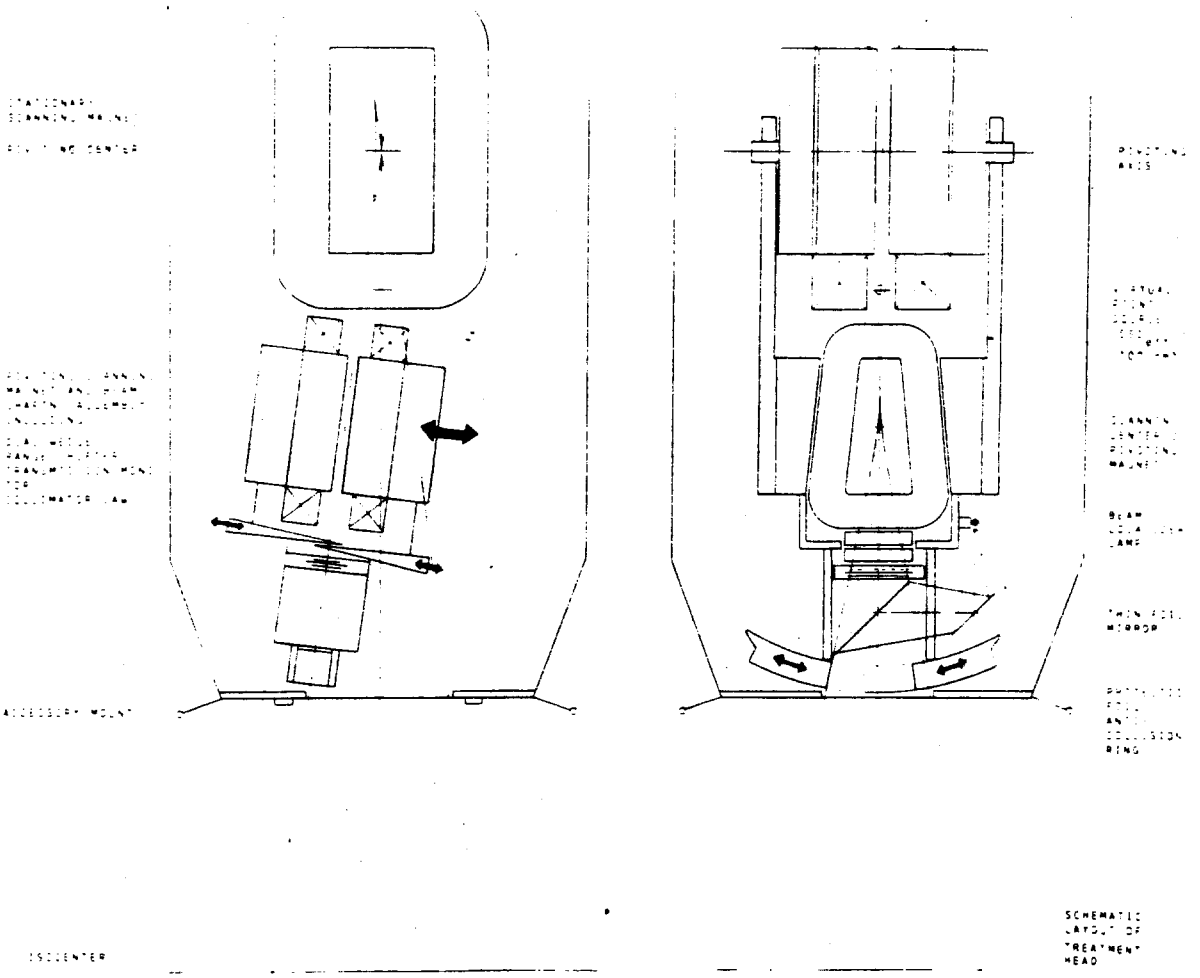
It would give a fully isocentric proton delivery system with a flexible collimator by means of a 60 degree bending magnet, a quadrupole lens and a cross plane stearing magnet, a 143 degree bending magnet. Inside this magnet there will be a scattering foil to assure uniform proton coverage of the elementary beam and mask any internal inhomogeneity which may be present in the beam from the accelerator. The location of the foil and the exit angle of the magnet are chosen such that the beam is essentially parallel when leaving the magnet.

From S. Graffman, B. Larsson and A. Brahme, to be published.

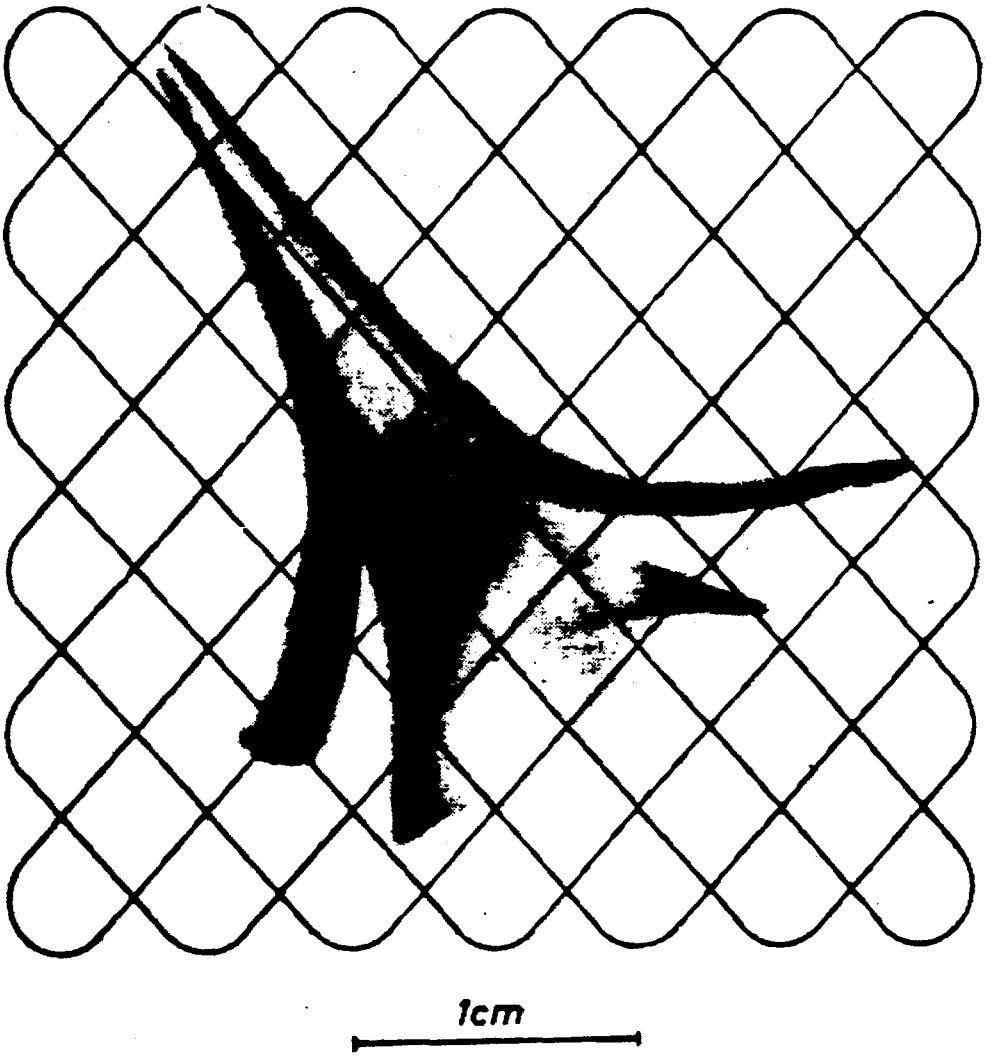


Slide 10b: The architect's model of the proton therapy center constructed from principles outlined in slide 10a. The beam transport tunnel is indicated, leading from the cyclotron cave to five treatment rooms and additional facilities.

From S. Graffman, B. Jung and B. Larsson: Design Studies for a 200 MeV Proton Clinic for Radiotherapy, in "Proc. Sixth International Cyclotron Conference, Vancouver 1972", American Institute of Physics (1973).

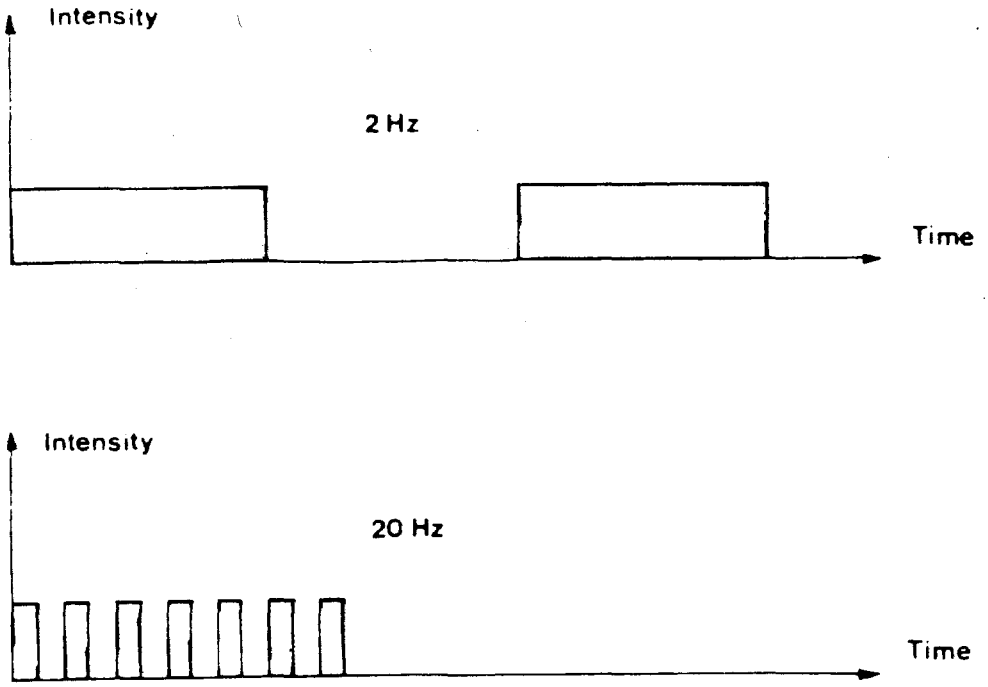


Slide 12: Close up of the scanning magnets in Slide 11, the dual range shifter and the flexible collimator. In order to make the size of gantry reasonable there is one stationary scanning magnet and one pivoting around the virtual scanning center of the first scanning magnet. This solution will allow 30x30 cm large fields with an effective SSD of 100 cm using conventional magnet technology. All three scanning motions and the flexible collimator are accurately coordinated and controlled by the same computer. The second scanning magnet pivots mechanically so its median plane coincides with the direction of the proton beam as it leaves the first scanning magnet.



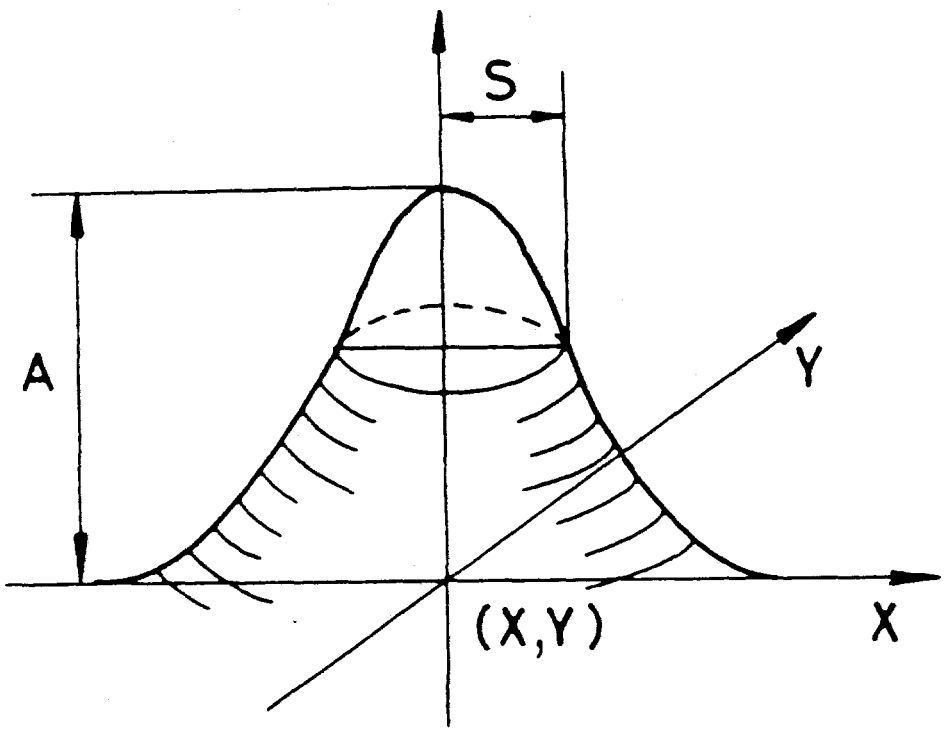
Slide 13: From early experiments with 185 MeV protons: photographic record of the cross section of an extremely inhomogeneous beam pencil, as it appeared in the biomedical target area. By scanning the beam pencil over a 2 cm wide, field-defining collimator as indicated by the line pattern, excellent homogeneity of flux density was achieved in the collimated beam.

From B. Larsson, L. Leksell, B. Rexed and P. Sourander: Effects of High Energy Protons on the Spinal Cord; Acta Radiol. 51: 52 (1959).

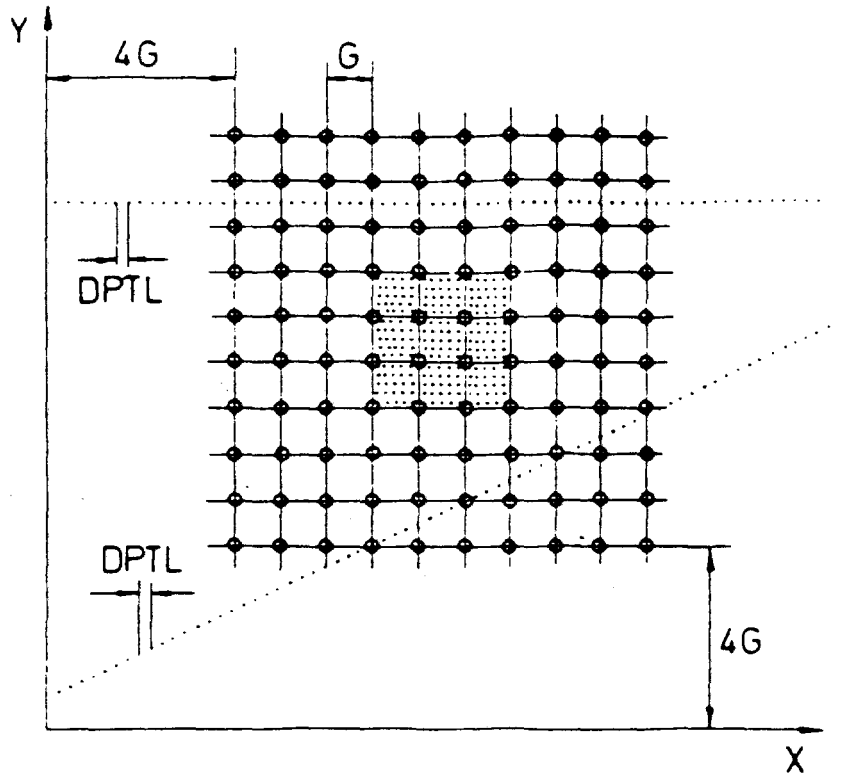


Slide 14: Illustration of prerequisites for beam homogenization by beam pencil sweeping. This is an idealized representation of two trains of "macroscopic" beam pulses as they would appear in a single treatment room at, respectively, a synchrotron operating at a repetition frequency of 2 Hz (above) and a cyclotron operating at several hundred Hz (below); in the latter case the beam is thought to be modulated at 20 Hz by a beam switching magnet (see text).

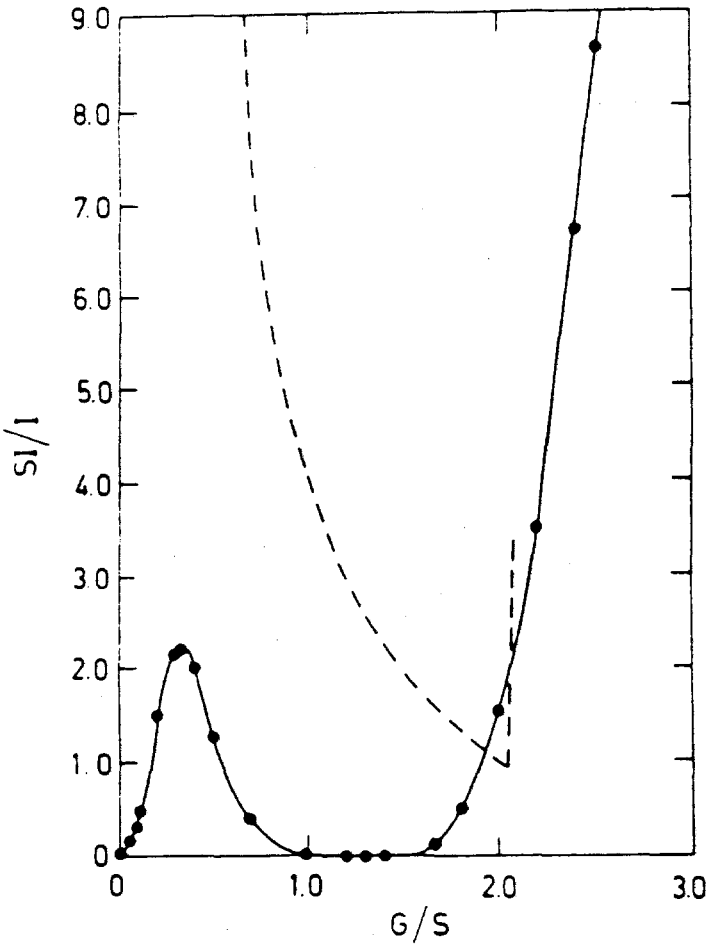
Slides 14 and 15-18 from S. I. Blokhin, V. M. Breev, J. Carlsson and B. Larsson: Homogeneous Transverse Distributions of the Accelerated Ions at Dose Fields for Radiotherapy, in "Proceedings of the First International Seminar on the Uses of Proton Beams in Radiation Therapy, Moscow, Dec. 6-11, 1977", Vol. 1, p. 106, M. I. Lomakin, ed., Atomizdat, Moscow (1979).



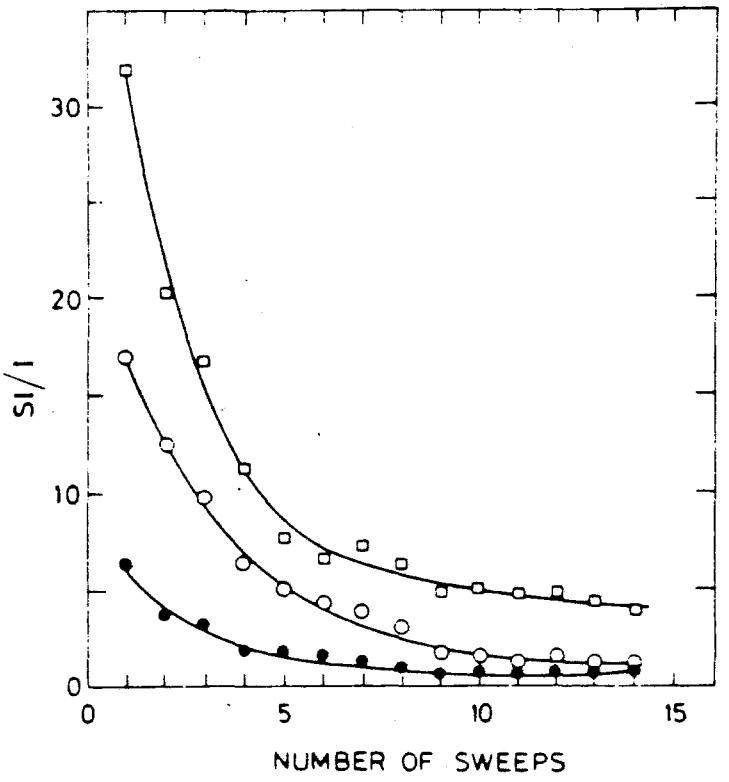
Slide 15: This and the following three slides consider the conditions for homogenization by step-wise scanning of a narrow beam pencil, as simulated in a computerized model. The cross-section of the beam, in the x,y-plane, is represented by a Gaussian distribution of fluence, typical for a well-collimated beam scattered by a thin foil.



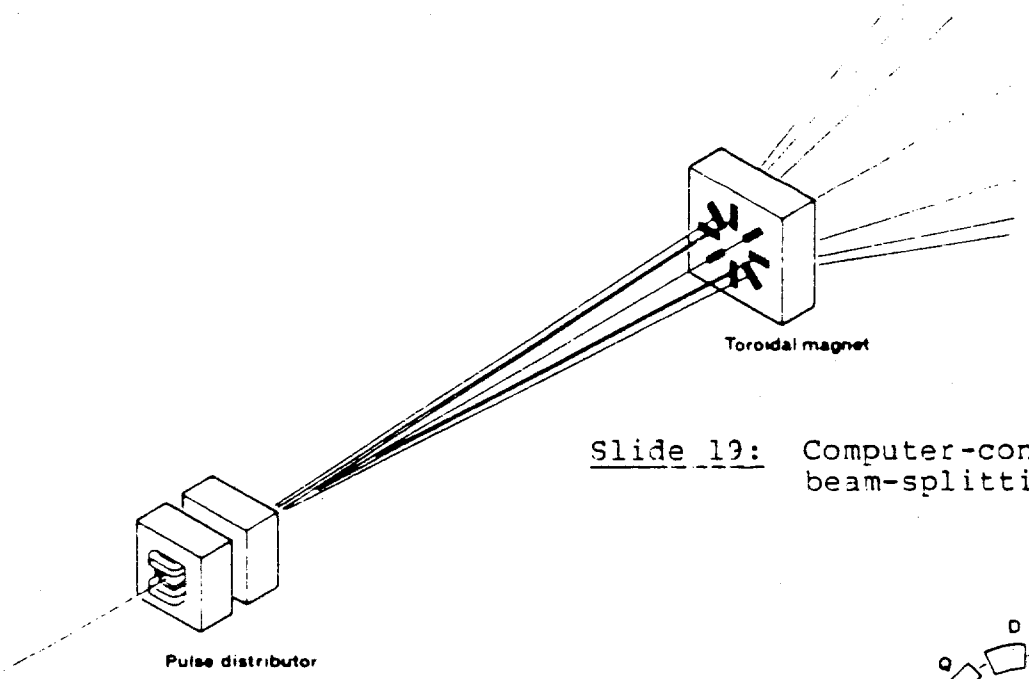
Slide 16: Distribution of beam pulses in the x,y-plane.



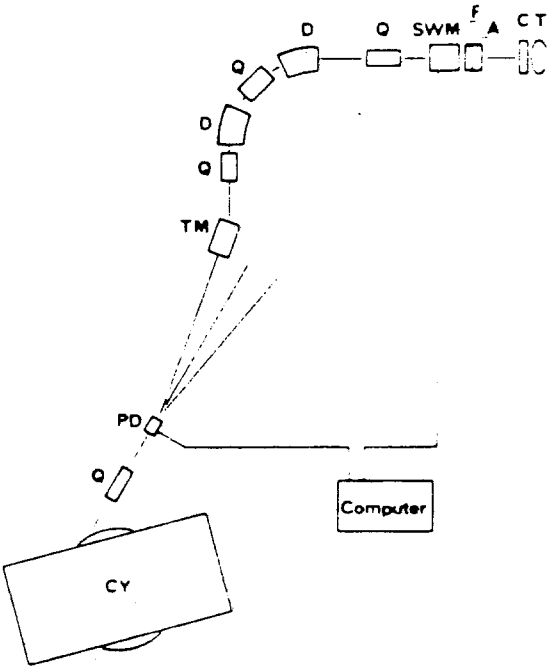
Slide 17: Result of computerized simulation of step-wise beam pencil scanning in accordance with Slides 15 and 16. The relative spread of the flux density (SI/I), within the field demarcated and analyzed, is given as a function of the ratio G/S, assuming that all parameters, X, V, S and A are unafflicted by stochastic spread. Excellent homogeneity is achieved for G/S = 1 to 1.5 after one or several complete sweeps.



Slide 18: When the parameters X, Y, S and A (Slides 15 and 16) are allficted by statistical spread (sX, sY, sS and sA) the homogeneity will depend on the number of complete sweeps. The three curves shown were obtained for different sets of parameters;
Upper curve: G/S = 1.4; sA = 0.5; sS = 0.1; sX = sY = 0.3.
Middle curve: G/S = 1.0; sA = 0.5; sS = 0.1; sX = SY = 0.3.
Lower curve: G/S = 1.0; sA = 0.198; sS = 0.055; SX = sY = 0.04.



Slide 19: Computer-controlled beam-splitting device.



CY cyclotron
PD pulse distributor
TM toroidal magnet
Q quadrupole, triplet or doublet
D bending magnet
SWM sweeping magnet
F filter
T target (patient)
C collimator
A pulse current meter

Slide 20: Suggested beam transport system for an accelerator facility that would meet the demand specified in Slide 10b.

Slides 19 and 20 are from S. Graffman, B. Jung and B. Larsson: Design Studies for a 200 MeV Proton Clinic for Radiotherapy, in "Proc. Sixth International Cyclotron Conference, Vancouver 1972", American Institute of Physics (1973).

Functional disorders of the brain, "radio-surgery"	25 (GWI) ; 2 (LBL) ; 12 (Gatchina)
Cancer of breast or prostate, irradiation of pituitary	250 (LBL) ; 50 (HCL) ; 60 (Gatchina) ; 174 (ITEP)
Diabetic retinopathy irradiation of pituitary	450 (HCL)
Pituitary adenomas	1,000 (LBL) ; 1.300 (HCL) ; 86 (Gatchina) ; 59 (ITEP)
Arterio-venous malformations in the brain	362 (HCL) ; 35 (Gatchina)
Small eye tumours (usually ocular melanomas)	300 (HCL) ; 45 (ITEP) 85 (LBL)
Malignant brain tumours	8 (GWI ; 7 (HCL)
Cancer in the head and neck region	20 (GWI) ; 35 (HCL) ; 85 (LBL)
Cancer of oesophagus, lung or larynx	30 (Dubna)
Osseus sarcoma	27 (HCL) ; 17 (ITEP)
Cancer of anus or rectum	16 (HCL)
Cancer of the prostate	90 (HCL) ; 1 (ITEP)
Cancer of the uterus	110 (ITEP) ; 10 (GWI)
Cancer of the external genitals	89 (ITEP)

Slide 21: Clinical experiences with medium-energy proton beams. Data from Uppsala (GWI) and Dubna are not going to change before current rebuilding programmes have been completed. Data from Harvard (HCL) are from 1983. Data from Berkeley (LBL), Moscow (ITEP) and Gatchina are mostly from late 1981. Singular, exploratory studies have not been included.

From B. Larsson, J. Eur. Radiol. 5: 223 (1984).

Clinical Specifications for a Charged Particle Medical Facility

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INTRODUCTION

The specification of a charged particle accelerator for use in a hospital setting must emanate from clinical considerations. These in turn must be translated into technical specifications more familiar to accelerator designers. The purpose of this memo is to spell out some of the clinical requirements and, secondarily, suggest (in indented text) some machine parameters which these may affect.

The use to which the accelerator is to be put will of course determine the specifications. Two primary applications are considered here: (1) the radiation therapy of cancer, usually using a fractionated technique in which the treatments are delivered in several (from 5 to 40) sessions over from 1 to as many as 8 weeks; and (2) the treatment in one or a few fractions of non-mailignant diseases. There are several other potential medical applications of a particle accelerator, including radioisotope production, secondary particle production (such as of neutrons for neutron therapy), elemental determination by activation analysis, and charged particle radiography. It may well be desirable to assess whether it would be economically feasible to provide capabilities which would support some or all of these features in addition to radiation therapy. However, the additional requirements for these options are not considered below.

A medical facility must be conceived and designed as an integrated whole. It is not sufficient to consider only the accelerating structure and to consider the remaining features as trivial details. This is both because the ancillary devices may carry implications for the design of the particle generator, and because the medical need is for a complete facility and not

a component of it.

The specifications elaborated below have grown out of an active program in which protons from the Harvard Cyclotron Laboratory (HCL) have been used for medical applications. In particular, fractionated radiation therapy of cancer patients has been carried out in a collaboration between the staff of the HCL and that of the Department of Radiation Medicine of the Massachusetts General Hospital (MGH)[1] (in collaboration also with members of the Retina Service of the Massachusetts Eye and Ear Infirmary for treatments of ocular melanomas[2]). Single fraction treatments of pituitary targets and of AVMs have been carried out in a collaboration between the staffs of the HCL and of the Department of Neurosurgery of the MGH[3]. The specifications which follow would in every case be consistent with the clinical activities pursued to date, and would rectify deficiencies in the current facility which have placed limitations on the present medical program.

SITE

Hospital setting

Experience with satellite operations at distant facilities has universally convinced those involved that a particle accelerator to be used for clinical purposes should be located within a large tertiary care hospital. The reasons for this are:

(1) That patients need access to medical facilities available only in a major medical centre. These include: anaesthesia services, complementary radiation facilities (such as photon treatment units), laboratory testing facilities, radiologic services (CT etc.)

(2) Treatment at a remote site interferes with the optimal choice of

therapy since choice of the proper mix of conventional and particle treatments and the best timing of them tends to be influenced by logistic factors. Treatment of malignant tumors of the oral cavity and oral pharynx, where x-ray treatment is indicated for part of the target volume and particle treatment is desirable in the remainder, is a case in point.

(3) Staffing a remote charged particle unit fully (with MD and PhD professionals as well as a full range of support personnel) is inefficient - and leads to an undesirable disassociation between the staff of the charged particle unit and the staff at the parent facility.

> One of the scarcest resources in most medical centres is space. Thus, it is widely recognized that a hospital-based accelerator must be compact. However, it is important to recognize that the size of the facility is not only that of the accelerating structure itself - whose size may therefore not dominate the final space requirement. Additional space is required for: ancillary power and control electronics; shielding (up to 4 metres of concrete at HCL outside the treatment room alone); the beam transport system; the beam delivery system (including, perhaps, an iso-centric gantry); treatment rooms (? up to 4); and, depending on other facilities at the hospital, examining rooms, a patient waiting room, offices, a treatment planning area, an engineer's workshop, a machine shop, and storage for spare parts. In a study commissioned by the HCL the space needed to reproduce the HCL facility in a hospital setting was estimated to be aproximately 870 m^2.

Shielding

The appropriate safety regulations (4) must be satisfied. Neutron background will likely be the dominant problem. Experience at HCL is with

160 MeV protons. Higher neutron yields can be anticipated from higher energy protons, and they are more penetrating, and still higher neutron production is likely if helium ions are accelerated.

> Shielding is a problem in part because it can use up appreciable space, especially if an isocentric gantry is provided. It might be advantageous to consider: high density shielding very close to the main sources of radiation; use of iron in the forward direction; and compact designs for an isocentric gantry which minimize the volume it sweeps out. Good extraction efficiency can save one or even more tenth-value layers of shielding.

Number of Treatment Rooms

The variety of types of treatment and the potential number of patients for whom particle therapy might be appropriate make provision of several treatment rooms desirable. Our experience at the HCL has been that the equipment needed for different types of therapy is sufficiently different and alignment sufficiently critical (so that it takes too long to swich beam tailoring apparatus) that it has been efficient to provide separate rooms for small field (ocular & small brain targets) and large field treatments. We envision at least three treatment rooms: one with small field capability; one for an omnidirectional beam delivery system; and one for a fixed horizontal beam providing large fields. One could imagine providing a fourth room for possible expansion and for experimental work. Since charged particle treatments often require very precise patient positioning they tend to take longer than conventional treatments, so that such a 3 room facility would have a patient capacity closer to that of 1 or 2 conventional treatment rooms.

While beam time-sharing is entirely practical, and makes efficient use of an expensive device, it is possible to overestimate the number of treatments, and hence treatment rooms, likely to be called for in a practical facility. Very few centers in the U.S. are large enough to have more than 4 treatment rooms in the entire radiation therapy department and, while the proportion of patients who might be eligible to be treated by charged particles is unclear at this time, the poor skin sparing characteristics of charged particles implies that many treatments could not be delivered primarily with charged particles. On the other hand, it may be that particle facilities will be established as national resources with quite atypical patterns of patient referral - in which case a larger number of treatment rooms might be appropriate.

Beam switching is needed between treatment rooms. There is probably no need to provide this on a pulse-to-pulse basis. Treatments will be short enough that it will be acceptable to wait for a treatment in one room to be completed before that in another room begins. Switching times should be shorter than treatment times - of the order of 30 seconds at most. However, if very many treatment rooms were contemplated, so that the ratio of patient set-up time divided by treatment + switching time were comparable to the number of treatment rooms simulataneously in use, pulse-to-pulse time sharing might be desirable.

Shielding between treatment rooms should be adequate to allow patient set-up in one room while beam was being delivered in an adjacent room. Safety interlocks would be essential.

RELIABILITY & MAINTAINABILITY

While charged particle accelerators in this general class are by no

means novel, no synchrotrons (which I presume will prove to be the accelerating structure of choice) have ever been built with the level of reliability and maintainability which is required in medical therapeutic applications. These areas, above all others, pose the greatest challenge to machine designers.

A patient's therapy is generally delivered daily over the course of several weeks. An interruption of more than a day or so from the scheduled treatment is medically undesirable. An interruption of more than an hour or so on any given day badly disrupts that day's schedule. Thus great pains are taken to make therapeutic equipment highly reliable. Linear accelerators used routinely in conventional therapy have of the order of 98% availability - defined as the percentage of the normally scheduled workdays during which the unit is actually available to treat. (Routine maintenance is performed evenings and weekends and is not counted against this time.) A medical charged particle accelerator needs to have that same level of reliability.

When an equipment failure does take place which prevents the accelerator from being used for therapy, the mean time to repair must be as short as possible. As the above considerations imply, this means that "short" repairs should be possible within an hour or at most two, and longer repairs should be capable of being done within a 24 hour period. These requirements are the more absolute because one is dealing with a unique facility for which no reasonable alternative may exist - with conventional equipment there is often an identical or similar unit within the same facility, or nearby, to which the patient can be transferred if medically necessary.

Since operating costs must be minimized, the design of the

facility should promote the possibility of repair by the least number of trained engineers - ideally a single on-site engineer should be able to handle most problems. The design should also address the issue of how such a solitary individual would obtain assistance should this be necessary.

Reliability obviously is the product of innumerable design decisions about which little can usefully be said here. Redundancy is certainly one parent of reliability, mentioned here to point out that cost and reliability may sometimes be in conflict and we must be very careful that, in our enthusiasm to design as inexpensive an accelerator as possible, we do not compromise other perhaps more important goals.

Modularity of components will certainly promote repairability, and will make possible the provision of an adequate pool of spare parts. Looking towards the years and perhaps decades after the machine's designers have moved on to other challenges, the use of standard commercially available components where possible may promote the long term maintainability of the machine.

Ease of repair, as well as ease of operation mentioned below, are promoted by providing extensive diagnostic capabilities. There is a danger that these, too, may be omitted or skimped in the interests of keeping down the initial cost.

Good documentation of the accelerator and its ancillary facilities is necessary.

The vacuum system needs to be carefully designed to allow rapid pump-down after the machine has been brought up to atmospheric pressure.

Above all, keeping the machine design within the range of easily obtained performance, and not "pushing" the design too close to any technical limit is likely to be the hallmark of reliable operation.

EASE OF OPERATION

A single operator should be able to run the entire facility under normal conditions. Since, for economic reasons, the machine is likely to be turned off on nights and weekends, it should be possible to turn the machine on and have it running from a cold start in about half an hour. The level of training needed to operate the machine should be reasonably modest, and adequate documentation must be provided to make this possible.

> These requirements would seem at the least to require: (1) very robust sub-systems which as much as possible "run themselves"; (2) extensive "sampling" of machine performance; (3) automatic setting of machine parameters; and (4) a centralized control system. It may well be an issue of substantial controversy, but it seems to me that overall computer control will be necessary to assure the desired "push button" operation.

PARTICLE SPECIES - PROTONS?

We are concerned here with so-called low-LET radiation therapy - using particles whose ionization density is sufficiently low that their biological properties are little different from those of, say, cobalt-60 radiation. The potential advantage of such particles lies entirely in the superior dose distribution they make possible. Protons are the natural candidate for this purpose[5]. Their dose distribution is excellent, and they are likely to be the most cost-effective source of radiation.

Nevertheless, superior low-LET dose distributions are possible with light ions such as helium ions. Their greater mass and charge results in less range straggling and hence more rapid distal fall-off of dose in a

range-modulated beam, and in a lesser degree of multiple scattering which leads to better lateral edge definition. On the other hand, the radiobiological properties of helium may be something of a disadvantage. They are sufficiently different from x-rays in radiobiological effectiveness (RBE) that dosimetry may be a problem while not being sufficiently different in oxygen enhancement (OER) and other high-LET characteristics for these to be advantageous.

The lateral fall-off of the proton beam seen in practice at the HCL and of the helium ion beam at LBL are:[6]

Depth (cm)	90% to 20% Lateral fall-off (mm.)		
	PROTONS	HELIUM IONS	
2 cm	3.5 mm	1.5 mm	(small field eye beam)
~5	6	2	
~8	7.5	3	
12	8*	4	(* 7mm in some beams)
16	9	5	
20	-	6	

For these differences to be of practical importance one must demonstrate that organ localization and patient immobilization are possible at the millimeter level, and that there are clinical situations in which the better edge definition of helium ions would be an advantage. In so far as the former is concerned, techniques have in fact been developed which permit localization at the millimeter level.[7] As far as the clinical need for very sharp beam edges is concerned, it turns out that one very exciting treatment with protons is that of chordomas and chondrosarcomas which abut sensitive central nervous system tissues such as the cord and brain stem.[8] In these situations the tumor is often within millimeters of the CNS tissue, if not directly pressing against it,

and better beam edge definition than protons provide would be desirable. A second clinical situation in which better edge definition is of interest is in the treatments of choroidal melanomas[2]. There the tumor is often close to sensitive structures of the eye such as the optic disc and macula. The HCL proton beam treats a millimeter or so more tissue than would be necessary if ideally sharp edge definition were available, and this is sometimes undesirable.

> It would therefore be desirable to investigate the cost of providing (say) helium ion beams, either for the full range of depths to be provided, or for ranges up to 3.0 cm which would be suitable for the treatment of choroidal melanomas.
>
> It is also likely that careful design of the beam transport system could minimize the divergence introduced into a proton beam by the various necessary monitors and modulators and thereby improve the proton beam edge definition. Variable energy beam extraction will in any event be necessary to assure adequate distal fall-off of the low energy protons used in treatment of eye tumors.

DOSE RATE

Large field (> 4 cm. diameter) fractionated treatments are generally given in 2 Gy (1 Gy = 100 rad) treatments. Such treatments should be given in times which are sufficiently short that the patient can hold still - and which are short compared to the set-up time. A treatment time of from 1 to 2 minutes meets these requirements. Thus a dose rate of at least 1 Gy/minute is needed for large field treatments.

Small field (< 4 cm. diameter) treatments of ocular and pituitary targets generally deliver close to an order of magnitude greater dose per

session. A dose of 14 Gy is standard for ocular melanoma, and should be delivered in from 1 to 2 minutes. Thus a dose rate of 10 Gy/minute is desirable for small field applications.

The dose rates outlined here could be compromised for unusually large irradiated volumes. Treatment times of 5 minutes are acceptable, and times of up to 10 minutes could be tolerated in extreme and infrequent cases.

> The implications of these dose rates for the beam intensity obviously depend on the volume to be irradiated. This depends on the range of depth to be covered, on the area of the field, and on the techniques used to spread out the beam across the field. These issues are taken up below.

PENETRATION & MODULATION

The maximum beam energy is dictated by the maximum penetration required within the patient plus some additional energy to allow for energy losses in the sundry scatterers, monitors and other beam-modifying devices needed to tailor the beam. The maximum penetration in tissue would in the extreme case be that of the largest body dimension, but this is quite excessive in practice. A penetration sufficient to completely traverse the patient in a lateral field through the pelvis could be argued for; this would entail a range of at least 45 cm. of water (penetrations are stated in the distance in water which would cover the same range in tissue). Such a penetration would permit verification measurements in the exit beam. However, we consider that a penetration sufficient to allow a lateral beam to reach the contralateral pelvic wall, a distance typically of some 27 cm., would be clinically acceptable. When

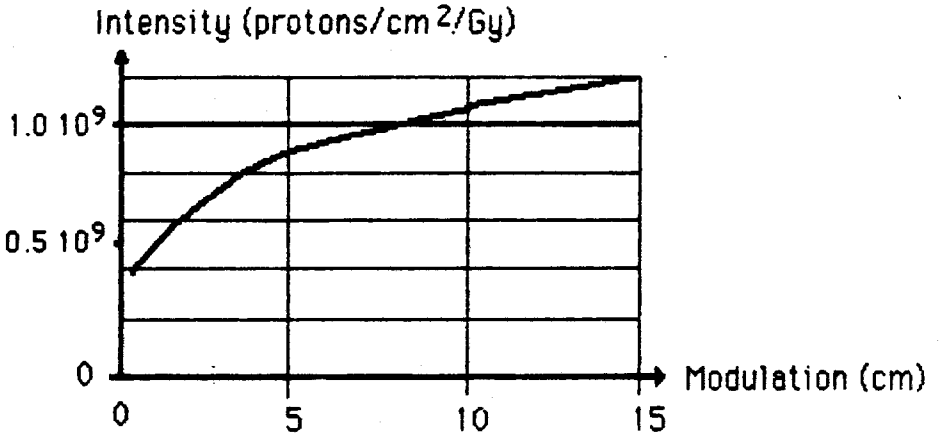
the additional range needed to penetrate bone is accounted for, this translates into a penetration of some 29 cm. of water. Allowing for beam attenuating devices (including scatters - see below), this means that an overall range of from 30 to 32 cm. in water is required. For the treatment of ocular melanomas we have analyzed the ranges we have needed in our treatments[10], and concluded that a range of 3.0 cm. in water would be adequate (excluding the additional range necessary to overcome beam monitoring and modifying devices).

The beam penetration needs to be varied over the field so as to match the target shape and compensate for non-uniformities in the tissue densities and for curvature of the entrance surface. These variations could in principle be achieved by beam scanning (see below) and the provision of synchronous variation of the energy of the extracted beam or of the thickness of a variable degrader. However, the distance over which such adjustments need to be made is of the order of millimetres[11] which would put enormous demands on a scanning system. A computer designed compensating bolus[12] has been used at the HCL with good effect. This solution is sufficiently effective, easy and cheap that it is hard to argue for any more complicated approach.

The depth-dose distribution of a single Bragg peak is a seductive one, but totally impractical for most tumors whose size mandates some spreading out of the ionization in depth. This is usually done by introducing a time-varying range modulation of the beam.[9] It can also be achieved by time-varying variable energy extraction - which, however, would be likely to complicate beam extraction, transport and delivery. In either case, modulation over a range from 1.5 to ~15 cm. is required.

The greater the depth over which a uniform dose is required the

greater the beam intensity necessary to provide a given dose rate. However, the dependence of beam intensity on depth of modulation is far from linear (which is why the irradiated volume is a poor parameter to specify). The following graph gives this functional relationship. It represents the conditions of the 160 MeV HCL proton beam, but should be generally applicable to any proton beam in the energy range considered here, with the exception that slightly greater losses from inelastic collisions will raise the intensity requirements for higher energy protons (by about 1.5% per additional cm of range).



A proton energy of 240 MeV would satisfy these requirements. If helium ions were used, an energy of 945 MeV would be necessary and, if they were provided only for ocular melanomas, an energy of 280 MeV would be required (which implies a rigidity equal to that of 140 MeV protons).

The range modulation scheme needs to be carefully addressed in any machine design. In particular, the issue of energy rather than range modulation should be considered. In any event, variable energy extraction, or at least extraction at a series of discreet energies, is needed.

DISTAL BEAM FALL-OFF (beam energy spread)

The sharpness of the fall-off of dose at the distal (far) end of range is, of course, the key attribute of charged particles which makes them of clinical interest. How sharp need this be? The requirement is based on the accuracy with which anatomic structures can be identified and the accuracy with which the areal density (integral of density along the particle path) between entrance surface and desired end-of-range can be ascertained. Both depend on the situation.

In ocular tumors localization of structures can be made with sub-millimeter accuracy - at depths of the order of 2 cm. In tumors of the brain and base of skull where the end-of-range is established relative to stable bony landmarks, 1 millimeter accuracy (typically at depths of 5 to 10 cm. from the skin) can be required. In the body 2 mm. or more may be quite adequate. These reqirements all translate into the need to control the particle penetration at the level of from 1% to 2% of its range.

Knowledge of the areal density to be traversed is made by measurement of distance for ocular tumors and for some sites in the brain. It is measured by CT scan for most other situations. In either case, the uncertainties are of the order of from 1 to 2% of range - and can be as much as 5% of range for some CT scanners in some situations. These parameters suggest that a beam energy spread which would lead to a range spread of 1% would be clinically quite acceptable. This, of course, is quite well matched to the range straggling of protons.

VARIABLE MODULATION - BEAM SCANNING

A rotating range modulator or a variable energy extraction scheme result in uniform range modulation over the entire radiation field. Since tumors are irregular in shape the ideal radiation field would be contoured to match the tumor's shape - and this requires that the depth modulation be varied over the beam cross section. The most general solution involves a beam scanning approach in which a pencil beam is scanned across the beam cross section, and the range modulation is allowed to differ as the beam is scanned. Chen and I have explored some aspects of the dose advantage to be gained from this approach[13]. A simpler alternative would be to provide a mechanism for variation of the beam cross-section in synchrony with depth modulation.

It would seem desirable to design the accelerator so that beam scanning is at least possible in order to permit the full dose distribution advantage of charged particles to be realized. In contrast to compensation for inhomogeneities which should be done on a rather fine grid, a relatively broad pencil beam (perhaps a centimeter or two in full width at half maximum) is generally all that is needed, or indeed useful, for variable modulation.

> The ability to support beam scanning is a complicated issue. The problem arises because there is a complicated interplay of time constants. Three scanning dimensions (the two transverse beam directions and beam penetration) must be controlled, and these must be phased to the pulse repetition rate and duration of the accelerator. One must either be able to control the beam intensity so carefully that, say, 2% dose accuracy can be achieved for each complete scan cycle - which can then be allowed to take the full minute or two of the

treatment time, or one must be able to deliver very many scan cycles during the course of a treatment in order to average out beam intensity fluctuations.

As a general guideline, it would appear that to permit beam scanning one must: (1) be able to control beam intensity during the extraction process, including the ability to throw away the remaining beam after some point; and (2) the duty factor of the extracted beam should be large, of the order of 50% or so. However, beam scanning has not been analyzed sufficiently carefully to allow one to have much confidence in these generalizations.

FIELD SIZE

Conventional photon therapy machines provide fields up to 40cm. on a side - and these sometimes are too small. While it is true that protons have become associated with very accurate small field treatments, there is reason to argue that they may be of substantial value in large volume irradiation also[14]. Therefore, it is probably wise to allow for 40cm X 40cm. fields, at least in one treatment area. At the HCL a maximum field size of approximately 30 cm. diameter has been adequate to date (although range limitations have precluded consideration of many of the sites for which larger fields would normally be used). Most HCL treatments have used a beam transport configuration which limits the field to a maximum diameter of 20cm.

One could readily accept a rectangularly shaped maximum field, particularly in an isocentric gantry where limiting the field dimension in the direction normal to the bending plane could reduce the magnet aperture and lead to significant cost savings. A field size of 25 cm. X 40 cm. would be acceptable in this context.

The dose rate requirements given above (1Gy/minute) should probably be considered for volumes of up to 400 cm^2 in area and up to 15 cm. in depth.

The specification of the maximum field size, depth of penetration and dose rates leads to a beam intensity specification. Unfortunately, this also depends on the techniques used for spreading the beam. If passive scattering is used there are two possibilities: a single scatterer; or a double scattering technique[15]. The latter is probably the superior method. It reduces the energy loss in the scatterer, thereby reducing the maximum beam energy required to get a given penetration in the patient, and makes more efficient use of the beam. At HCL we use approximately 20% of the beam after collimation/double-scattering. If beam scanning is used, a much greater efficiency is possible the magnitude of which depends on the relative sizes of the beam and the field of interest - reaching at least 80% for the maximum field sizes discussed here. It is probably wise to assume that a passive technique would be used, since even if scanning were developed it likely would not be used in all treatment bays.

These considerations (400 cm^2 square field; 15cm depth; 1 Gy/min; 20% efficiency) lead to a required extracted beam intensity of 0.011 microamperes. (The HCL extracted beam is 0.006 microamperes on a good day.) Internal beam clearly must exceed this by a factor which is the inverse of the extraction efficiency. Good design practice would probably require that the design be for an intensity at least double that of this specification.

BEAM DELIVERY - OMNIDIRECTIONAL GANTRY

Heavy charged particle treatment facilities, with the exception of the piotron multi-channel pi meson treatment device, have always featured single fixed beams. Some have been vertical, most horizontal.

For a fixed beam we strongly favour a horizontal over a vertical beam. However, there are good reasons to wish for a beam delivery system which could permit treatment of a patient lying on a couch from any direction from straight overhead to directly underneath (only 180^0, rather than 360^0 are needed since a couch rotation can take care of treatments from the opposing hemicircle). These reasons include:

* Better immobilization of the recumbent as compared to the seated or standing patient

* More rapid and easier set-up of the patient leading to more efficient use of the facility and reduced demands on personnel

* Better ability to match fields with conventional radiation (which would be delivered to a recumbent patient)

* No need for special computed tomographic scanner capable of scanning a seated or standing patient - as is required if the patient is treated either seated or standing

The argument against an omnidirectional beam delivery system is purely an economic one. The cost of such a system needs to be established and set in context with the cost of a completed proton facility and of the operating expenses of such a facility - none of which costs are at present known.

The design of an omnidirectional beam delivery system has many challenging aspects which have received inadequate attention to date. The most immediately attractive option is an isocentric gantry which rotates about an immobile patient. The size of this system depends on the scheme adopted for spreading the beam. If a scattering technique is used and the scatterers placed after all magnets the radius of the gantry gets very

large since a large throw is needed after the scatterer if not too much energy is to be lost in it. In addition, a fairly large distance (~ 3 metres) is required between the effective source and the patient if inverse square fall-off of dose is not to degrade the depth-dose characteristics of the protons. A beam scanning system is entirely feasible, but the same caveat with regard to source-patient distance applies. A patient scanning system may have some advantages in this regard. Putting the scatterer upstream of the last magnet(s) should be looked into.

A set of fixed beams at a few angles has been suggested. It is my view that an effectively continuous range of treatment directions is needed. This can be obtained by tilting the patient. However tilts of more than +/- 15^0 are difficult for the patient. This would require 7 fixed beams (from $+90^0$ to -90^0 in 30^0 intervals) which would likely obviate the intended economy of this approach.

Another approach which has been considered is one in which the patient is moved in a wide arc and the beam follows. This geometry allows for a simpler beam transport system, at the expense of a considerably more complex patient support assembly. It nevertheless could be a satisfactory solution.

> The design of a rotating beam system will be the easier the smaller the magnet apertures and hence the lighter the magnets. This means that a small beam emittance could be very desirable.

PATIENT SUPPORT SYSTEM

An accurate adjustable patient support system is required. Experience at existing charged particle facilities suggests that this is a more complicated and expensive proposition than is usually initially

appreciated. The patient must be positioned relative to the beam defining devices at the millimeter level or better (in the case of ocular and perhaps some other sites). This must be done quickly, reliably and reproducibly.

COST (INITIAL CONSTRUCTION & OPERATION)

Implicit in much that is discussed in connection with a medical charged particle facility is the desire to take advantage of certain unique aspects of the problem, in particular of the very modest beam intensity requirement, to make the costs small. Certainly, the widespread application of heavy charged particles will be enormously advanced if it proves to be possible to make a cheap accelerator. If protons were as inexpensive as electrons, which are presently widely used in conventional therapy, there would be no reason to use the latter.

On the other hand, as the above discussion has already emphasized, there are other unique requirements, particularly that the machine be reliable, repairable and easy to operate, which can tend to increase the expense of designing and building a machine. These requirements are no less important.

The cost of the accelerator is but one aspect of the cost of the overall facility. It is the latter quantity which is of concern to potential users.

Nor should attention be focussed exclusively on the capital cost of making the machine and building the facility. In practice the operating expenses of the facility are likely to dominate the overall cost. These expenses are affected by power consumption and by the cost of equipment maintenance and replacement, but they are likely to be dominated by personnel expenses. Design decisions which minimize the number of

people needed to operate the facility will bear valuable fruit.

It is essential that a close interaction take place between those who propose clinical specifications and the machine designers in order that the cost-benefit ratio of the various options is examined. Some secifications are near absolute, others can be relaxed or given up if their price proves too great. The specifications developed above must be interpreted in this light.

Finally, it has not escaped the notice of potential purchasers that very low figures for the cost of a proton machine have been mentioned. It is very important that a framework be established for such cost estimates which ensures that they relate to a total facility and take into account all relevant features on a comparable basis. Only if this is done will it be possible to compare cost estimates for alternative designs.

ACKNOWLEDGEMENTS

These specifications have been reviewed and amplified in discussion with a large number of MGH and HCL investigators.

SUMMARY

I summarize here some of the more concrete specifications mentioned above. However, I hope this paper will not be read as a list of isolated parameters but as a discussion of design considerations - which cannot be reduced to a list of discreet numbers.

Site	Compact; total facility dominates size; shielding design required; $\geq$ 3 treatment rooms.
Reliability	98% availability
Maintainability	Short mean time to repair; most repairs in 1 hr. or 24 hrs; Vacuum pump-down rapid; 1 on-site engineer; Documentation of equipment
Operation	"Push-button" operation by a single operator;
Particle	Protons, probably. Helium ions should be explored.
Dose rate	1 Gy/min in beams > 4 cm; Lower dose rate acceptable in largest fields (>20 cm); 10 Gy/min in beams < 4 cm.
Penetration	30 - 32 gm/cm^2 for large fields 3+ gm/cm^2 for eye treatments
Energy spread	1% of range
Modulation	from 1.5 to 15 gm/cm^2; variable modulation over the field should be possible.
Field size	Up to 40 cm x 40 cm. 25 cm x 40 cm acceptable in omnidirectional mode.
Beam transport	Horizontal beam if and when fixed beam direction; Omnidirectional beam delivery in at least one treatment area; Patient support system.

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Requirements for Charged Particle Medical Accelerators -- LBL Experience*

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I. Introduction

At the Lawrence Berkeley Laboratory of the University of California, Berkeley, the 184-Inch Cyclotron and the Bevalac have provided accelerated heavy ions for biomedical applications ranging from basic research to radiation treatment of human cancer. These experiences coupled with the LBL expertise in accelerator technology have prompted us to plan for a hospital-based heavy-ion medical accelerator (Alpen (1984).

At this proposed facility, accelerated heavy ion beams can be produced suitable for treatment of human cancer. These same beams can be effectively utilized to pursue other clinical and basic research activities. The accelerator system is contemplated to reliably accelerate a wide range of ion species, from helium to argon, to energies as low as 70 MeV/amu for 4-cm range ^{4}He beams to as high as 800 MeV/amu for 30-cm range ^{28}Si beams, with intensities sufficient to limit treatment times to about one minute. Secondary radioactive heavy ion beams, such as ^{11}C and ^{19}Ne, will also be available to aid the accurate treatment planning as well as broaden the base of scientific research that can be conducted at this facility. In addition, the species of ions could be extended to include protons and moderate intensities of ^{56}Fe beams, adequate to support research programs in biophysics and related fields of scientific inquiry.

The beams can be delivered sequentially to multiple treatment rooms to accommodate as many as 100 patients per day in addition to provide for the needs of an intensive program in basic research. Estimates of the projects operating costs for this facility suggest that the incremental cost per patient treatment is modest in the context of alternative radiation treatment. The main accelerator component required to produce 800 MeV/amu beams is a synchrotron ring approximately 30 meters in diameter. Such an accelerator could be located in a major medical complex to provide cost-effective medical care and to support a forefront research program in high technology medicine.

II. Advantages of High-LET Charged Particle Beams

There is a strong rationale to perform a randomized radiotherapy trial with heavy charged particles at a hospital-based facility. The hypothesis to be tested may be briefly formulated as follows: Given the fact that particle beams of both low and high atomic numbers can achieve superior dose localization, will the heavier ions produce better local control of human cancer than light ions? We expect better results because of the advantageous radiobiological characteristics of the heavier ions.

Hypoxic parts of tumer tissues, for example cells located near necrotic foci, are much more resistant to conventional radiation. Experiments have shown, however, that while this resistance exists for low-LET charged particle irradiation, it does not exist for heavy-ion irradiation: Hypoxic cells are nearly as sensitive to heavy-ion irradiation as oxic cells.

Cells in rapidly growing tumers are asynchronous. Cells in the S phase of the DNA synthesis cycle are much more resistant to low-LET radiation than cells in other phases of the cycle; therefore, in protracted radiotherapy there are usually surviving cells that are protected against low-LET radiation. Heavier charged particles such as Si ar Ar ions greatly diminish the differences in radiosensitivity for cells at any phase of cell division; fewer protected cells are expected to survive after a dose of heavy ions.

There are several types of molecular repair mechanisms known in cells exposed to low atomic-number particles at low LET. Such repair becomes largely ineffective when heavy ions are used. As a result the Bragg peaks of heavy ions are much effective than low-LET radiations.

The combination of these factors is expected to make heavy ions particularly effective for the treatment of well-localizable tumors that have radioresistant cell populations.

In addition, maximizing the dose to the local cancer while minimizing dose to the surrounding normal tissues offers the highest potential for tumor control. The physical properties of charged particles, including heavy particles and protons, permit dose localization superior to that achievable with neutrons. The particle range, or degree of dose localization in the patient, can be determined with great precision by technique which utilize radioactive beams, such as ^{11}C and ^{19}Ne, and positron emission tomography. Superior treatment planning and verification can be achieved with these particle compared with any other radiation modality including protons and helium nuclei.

Fig. 1 demonstrates how the consideration of both physical dose localization advantage and the corresponding enhancement of biological cell killing effectiveness influences the various radiation modalities. the abscissa in these plots is the ratio of biologically effective doses defined as:

$$\text{Effective dose ratio} = \frac{(\text{Dose} \times \text{RBE}_{50}) \text{ at mid target volume}}{(\text{Dose} \times \text{RBE}_{50}) \text{ at entrance}}$$

It is regarded as more advantageous to use the charged particles that are further out to the right on this axis of the effective dose ratio. When the effective dose ratios are comparable, the modalities that exhibit lower OER (Oxygen Enhancement Ratio) will be the better choice.

The data are based on measurements made with the cultured cells <u>in vitro</u>. The top panel is constructed for a 10-cm x 10-cm x 4-cm deep field with the distal edge of the target volume at 14-cm deep. The bottom panel is for a 10 x 10 x 10 cm^3 target volume with the 24-cm deep distal edge.

For smaller, more shallow target volume (top panel), it appears that C, Ne, and negative pion beams are superior in their ratio of bilogically effective doses. Ar and Si ion beams and p and He ion beams are intermediate in this ratio, but quite different from each other with respect to their OER values.

For a larger, deeper tumer volume (bottom panel), the C and He ion beams are quite similar, as are the Ne ion and negative pion beams; however, there are quite distinct division on OER values between low-LET and high-LET particle beams.

III. Dose Localization

The localization of the radiation dose in the target volume is limited by many causes. The range straggling of the charged particles in the slowing medium makes the distal edge of the radiation field not sharp. The energy spread in the accelerated beams, as well as the energy fluctuation from pulse

to pulse result in the same effect. The emittance of the beam and the multiple scattering of the charged particles in the beam path and inside the patient body both contribute in the lateral spreading of the beam and broader penumbra. Also these effects lower the peak-to-plateau ratios of the charged particle beams that are collimated to small sizes.

(A) Energy Loss Rate for Heavy Charged Particles:

A heavy projectile, much more massive than an electron, of charge Ze, incident at speed βc (β>>1/137) through a slowing medium, dissipates energy mainly bia interactions with the electrons of the medium. The mean rate of such energy loss per unit length x, dE/dx, called the stopping power, is given by the Bethe-Bloch equation. The stopping power is closely related to LET (Linear Energy Transfer). The LET is proportional to the square of the charge of the incident particle, to the reciprocal of kinetic energy (1/E), and to the electron density of the slowing medium.

We may approximately treat media which are chemical mixtures or compounds by computing (Bethe and Ashkin (1959))

$$\frac{dE}{dx} = \Sigma \left(\frac{dE}{dx} \right)_i$$

with (dE/dx) appropriate to the i-th chemical constituent, using the partial density in the formula for dE/dx. For many chemical compounds, small corrections to this additivity rule may be found in Berger and Seltzer (1982).

In the stopping region, the stopping power formula becomes inapplicable. At the very slowest speeds, total energy loss rates are proportional to β. The energy loss rate passes through a small peak at intermediate speeds due to elastic Coulomb collisions with the nuclei of the slowing medium (Sidenius (1974)) and rise through a larger peak at projectile speeds comparable to atomic speeds (β on the order of αc).

The mean range, R, of the charged particles in the slowing medium is obtained by integrating the stopping power equation given above:

$$R = \int_E^0 \frac{dE'}{dE'/dx}$$

The range-energy relationship for several heavy ions in water were calculated by Stewart (1967). Measurements and calculations of range-energy relationship for heavy ions were also made by Northcliffe (1963), by Barkas and Berger (1964), and by Eby and Morgan (1972). For a given medium, the range R' of any other beam particle with mass M' and charge Z' is given in terms of the range R of other particle with mass M and charge Z and having the equal velocity is given by

$$R' = \frac{M'/M}{Z'/Z} R$$

(B) Straggling:

Straggling is a dispersion in path length distribution as a result of statistical fluctuations in the energy loss processes. it was shown by Lewis (1952) and by Berger and Seltzer (1964) that the distribution is Gaussian. However, we know that there are small deviation from this distribution.

For a particle of initial energy E and mean range R, proceeding in the direction x, the range distribution may be written in the form:

$$s(x) = \frac{1}{\sqrt{2\pi}\,\sigma_x} \exp\left(-\frac{(x-R)^2}{2\sigma_x^2}\right)$$

where σ_x is the variance in the path length distribution for particles of range R. There are special corrections to this formula at high and low kinetic energies.

since the atomic composition of soft tissues is similar to that of water, we may use an approximate practical expression for water:

$$\sigma_x \text{ (water)} = 0.0120 \frac{R^{0.951}}{\sqrt{A}}$$

In the range of validity of this formula ($2 < R < 40$ cm), σ_x is almost proportional to range, R, and is inversely proportional to the square root of the particle mass number, A. The relationship between the range and the straggling for various ion beams are shown in Fig. 2(b).

For the range of 20-cm in water, σ_x for various ions are:

Ions	σ_x
Neon	0.046 cm
Carbon	0.06
Helium	0.1
Proton	0.2

The straggling for 20-cm range protons is 4.5 times greater than that for the same range neon nuclei.

(C) Multiple Scattering:

The particles of the beam are deflected in collisions with nuclei of the slowing material. Many of these collisions result in small angle deflections, and multiple scattering leads to a divergence of the beam and to a radial spreading of the particle away from ideal straight line tranjectories. The bulk of deflections is due to elastic Coulomb scattering.

There is a small correction due to the contribution of strong interactions to the total multiple scattering for the hadronic projectiles. The angular distribution from the multiple scattering is roughly Gaussian only for small deflection angles, while it shows much greater probability for large-angle scattering than the Gaussian would suggest.

At range R the projected radial distribution of deflection y of the particle is given by:

$$P(y) = \frac{1}{\sqrt{2\pi}\,\sigma_y} \exp\left(-\frac{Y}{2\sigma_y^2}\right)$$

where σ_y is approximately given by:

$$\sigma_y = \frac{0.0294\ R^{0.896}}{Z^{0.207}\ A^{0.396}}$$

The relationship between the ranges and the multiple scattering for various ion beams are shown in Fib. 2(c). For the range of 20-cm in water, σ_y for various ions are:

Ions	σ_y
Neon	0.082 cm
Carbon	0.11
Helium	0.22
Proton	0.43

The multiple scattering for protons is about 5 times greater than that for the same range neons.

(D) Emittance of the Beam

The emittance of the extracted beam determines the phase space of the charged particles tranported into the target volume. For example, if we consider the Ne ion beam of 20-cm range R with a diameter D of 5-cm (e.g., beam spot size for scanned beam), the multiple scattering gives $\sigma_y \approx 0.05$ cm. A comparable divergence is attained if the emittance is $\epsilon \approx D\,\sigma_y/R \approx 1 \times 10^{-4}$ meter-radian. For focal lesion application, we take 10-cm range of C ion beam with a diameter of 0.5 cm, then the multiple scattering gives $\sigma_y \approx$ 0.1 cm. The comparable divergence is obtained for the emittance $\epsilon \approx 4 \times 10^{-5}$ m-rad.

The design value of the emittance for the proposed accelerator is 2×10^{-5} m-rad, which is about a half of the above estimates. Since the effects of the multiple scattering and emittance add statistically, 1/2 as big divergence due to the finite size of emittance contributes only 1/4 in the spreading of penumbra.

(E) Peak-to-Plateau Ratios and Penumbra

The diverging beams and multiple scattering in the slowing medium generally broaden the beams, and lower the peak-to-plateau ratios. The effect is more pronounced for smaller beams as more particles scatter out of the original trajectories than those scattering in. Fig. 3 shows the 20-cm range proton and He ion beams: the central-ray doses for large beams and collimated beams are normalized at the entrance. Experimentally measured Bragg curves for 225 MeV/amu He ion beam and for 308 MeV/amu C ion beam are shown in Fig. 4 as a function of residual ranges.

The dose profiles of proton and C ion beams through a 1-cm slit are depicted in Fig. 5. The proton beam profiles are shown either normalized at the peak or at the entrance. The former shows that the penumbra for proton beam is about square-root of 12 times bigger than that of C ion beam, and the latter shows that the peak-to-plateau ratio is decreased by about 40% for proton beam compared with that of C ion beam.

Our experiences in clinical situations using He ion beams at the 184-Inch Cyclotron and the heavy ion beams at the Bevalac generally support the above analyses. The double scattering system that laterally spreads the beam by scattering materials in the beam path also contributes in broadening the penumbras. The wobbler system, that uses no scattering material in the beam path, produces narrower penumbra compared with those obtained through the double scattering method.

(F) Radioactive Beam Ranging Technique

Although the charged particle beams exhibit sharply defined ranges as discussed above, the accuracy of delivering the radiation dose into a well-defined target volume is only as accurate as the knowledge of the integral water-equivalent thickness of the intervening tissues. The x-CT supplies information on the distribution of x-ray absorption coefficients, and accurate conversions of the x-CT data into the stopping powers of the medium for charged particles are not possible. The He and Ne ion measurements using a frozen beagle and comparing them with x-CT data indicates that the x-CT measurements are off as much as 0.4 cm out of 5 cm range in brain and thorax (Table 2). The MRI data may augment the x-CT data by measuring the chemical composition of the tissues, yet they are not sufficient to supply the information of the stopping power of the tissues. Whereas the stopping radioactive beams directly measure the integral stopping power of the medium in water equivalent thickness.

Positron emitters, C^{11}, N^{13}, O^{15}, F^{17}, and Ne^{19}, result when their respective stable parent particles, C^{12}, N^{14}, O^{15}, F^{18}, Ne^{20}, pass through an absorbing material. For example, 530 MeV/amu Ne^{20}, beam is put through a 2.5-cm thick Be slab, and momentum analyzing the resulting beam separates the radioactive Ne^{19} beam from the Ne^{20} beam. The added energy spread of the radioactive beam mainly comes from the Fermi momentum of the nucleons in the target nuclei which collide with the incident parent nuclei. A negligible contribution is from the slight difference in dE/dx for Ne^{19} and Ne^{20}

particles, and the fact that the Ne^{19} productions take place distributed across the entire target thickness. The experimentally measured Bragg curves for Ne^{20} and Ne^{19} beams are shown in Fig. 6(a & b). As schematically shown in Fig. 6(c), the range of the radioactive beam is modulated and it is brought to a stop in a precisely defined position in the patient (e.g., the distal egdge of the target volume) by determining the stopping region using a positron emission tomographic camera. The integral water-equivalent thickness of the intervening tissues is simply given by the range of the incident radioactive beam. In this process, the water-equivalent thickness measured using one kind of radioactive beam, e.g., Ne^{19}, is the property of the slowing medium and indepedent of the species of ions used. And therefore it may be applied for therapy planning using any kind of charged particle beams. We have already used the Ne^{19} ranging techniques in several human patients treated with heavy ion beams.

Another application of radioactive beams that appears to have promise is that of injecting a bolus of a particular positron metabolic or flow rates by measuring positron emitter activity as a function of position and time after the beam injection. The absence of radioactivity at location other than those being studied would make for a very clean technique, provided that the hot atom chemistry of the injected ions is well understood.

IV. Requirements for Heavy Ion Medical Accelerator

The requirements for heavy ion medical accelerator are different for different applications of the machine. The applications may be broadly divided into five different uses: namely, radiation treatment of cancer, focal lesion, radioactive beam ranging, radiation biology, and physics. In Table 3, the requirements for these users are listed; the requirements for radiation biology are not listed separately, since its needs are quite similar to those of therapy, focal lesion, and radioactive beams. In Table 3, when applicable, the optimal requirement is listed above the minimal requirement for each category.

The ion species requested ranges from He to Si or Ar. There are interests in obtaining higher Z particles, such as Fe, La, Au, and even U. The ranges of these particles requested for clinical uses span from the 4-cm range He ions to the 30-cm range Si ions. To obtain 37-cm Ne^{19} beam, the radioactive beam users like to have 40-cm Ne^{20} beams. Range-energy relations for various ions are shown in Fig. 7. From these curves, it is seen that an energy of approximately 800 MeV/amu is required to provide a 30-cm range in tissue for Si ions. For particles lighter than Si, such as C and Ne ions, the 800 MeV/amu capability provides a range in tissue considerably greater than 30 cm.

For tumor sizes and treatment plans typically encountered in the ongoing heavy-ion radiotherapy program at the Bevalac, the minimum on-target intensity requirement of 3×10^7 Si ions per second corresponds to approximately 100 rad per minute. The radioactive beam users places the highest particle flux requirement, 10^{11} particles per second for C and Ne ions, as they depend on

the secondary particles whose intensities are only a fraction of the primary particles (e.g., 10^{-3} for Ne^{19} obtained from 530 MeV/amu Ne^{20} through 2.5-cm Be target).

The upper limits for the energy spread (dE/E) of the accelerated beams and the pulse-to-pulse energy fluctuations are placed at 0.1% FWHM. The most strigent requirement of particle beam emittance is placed by the focal lesion applications which use very tightly collimated small beams. Their request is that the emittance be smaller than 2×10^{-5} meter-radian. The duty factor of 75% is generally requested, since most of the clinical applications avoid unnecessarily high instantaneous dose rates. This requirement becomes more important for dynamic beam delivery systems, in which the complexities of the beam handling increase inversely to the length of available time in which to accomplish the task.

It is also desirable for the dynamic modes of beam delivery to extract the accelerated particles with the following characteristics. The intensities of the extracted beam should be uniform over the time, since the wobbling or scanning systems translate the time-structure of the beam into spatial fluctuations. The extraction level and duration of the spill should be reliably controllable. The beam optics for extracted beams must remain stable for a wide range of extraction levels (up to 3 orders of magnitude) and spill lengths.

In general, most of the clinical applications call for long spills; there are occasions that use very short beam pulses. In imaging moving organs in the patients, one would like to have a spill of 1 millisecond duration. Also in studying the high dose-rate biology and physics, very high instantaneous dose rate of short durations is required.

From the practical point of view of using the accelerated heavy ion beams for human patients, all users request short planned delays and down times and few unplanned interruptions. When two different ions are used, the time to switch the ion species is to be 20 seconds, or not more than 2 minutes at most. Similar requests are put on the energy change of a given ion beam. Such a capability will eliminate the need of mechanical beam energy degrader which produces unwanted fragments and lower the beam quality. For dynamic mode of beam delivery, the change of energy in small steps from a pulse to the next pulse will be useful.

In multi-room operation using a single accelerator, several patients will be readied for irradiation at the same time, and some waiting for the patients will be unavoidable. Allowable wait is 5 minutes. Fast beam switching and short treatment time are important; but clearly logistics and planning of patient flow are the deciding factors.

The accelerator specifications that satisfies these requirements are summarized in Table 4. These machine characteristics have been determined from the experience of ongoing LBL programs and from studies over the past ten years, including the LBL/Arizona Design Study (LBL-7230) completed in 1977.

V. Conclusion

Our general goals are to produce precisely located and sharply defined heavy-ion induced radiolesions in target volume. Heavy ion beams aided with the radioactive beam ranging technique attain these goals much better than the proton beams. In addition we wish to deliver to accurately defined tumor regions high doses of heavy charged particle beams at the highest atainable LET while minimizing radiation effects to surrounding normal tissues. The high LET field will minimize the radiobiological oxygen effect, it will reduce radiobiological repair and differences in radiosensitivity during the cell cycle. It will delay cell progression and reduce sensitivity differences between normal and tumor cell populations.

We believe that the proposed heavy-ion medical accelerator could be built in a major medical complex to provide cost-effective medical care and to support a forefront research program in high technology medicine and basic sciences.

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Figure Captions:

Fig. 1 Ratio of biologically effective doses vs. OER for various radiation treatment modalities. The upper panel represents a 10 cm x 10 cm field at 10-14 cm tissue depth. The lower panel represents a 10 cm x 10 cm field at 14-24 cm tissue depth. Available cell data *in vitro* were used for the construction of this plot.

Fig. 2 Multiple scattering and straggling characteristics for various charged particles as a function of the range.

Fig. 3 Calculated Bragg curves on the central rays of large and small fields of proton and He ion beams.

Fig. 4 Measured Bragg curves of He and C ion beam with same residual ranges.

Fig. 5 Beam profiles of proton and C ion beams through 1-cm slit.

Fig. 6 (a) Bragg curve for 530 MeV/amu Ne-20 beam in water.
(b) Bragg curve of Ne-19 beam obtained from the Ne-20 beam of (a) by letting the parent particles traverse a 2.5-cm Be slab and momentum analyzing the resulting beam.
(c) Schematic diagram of setup for end-of-range localization of a radioactive beam.

Fig. 7 Range-energy curves showing the depth to which various ions will penetrate in tissue.

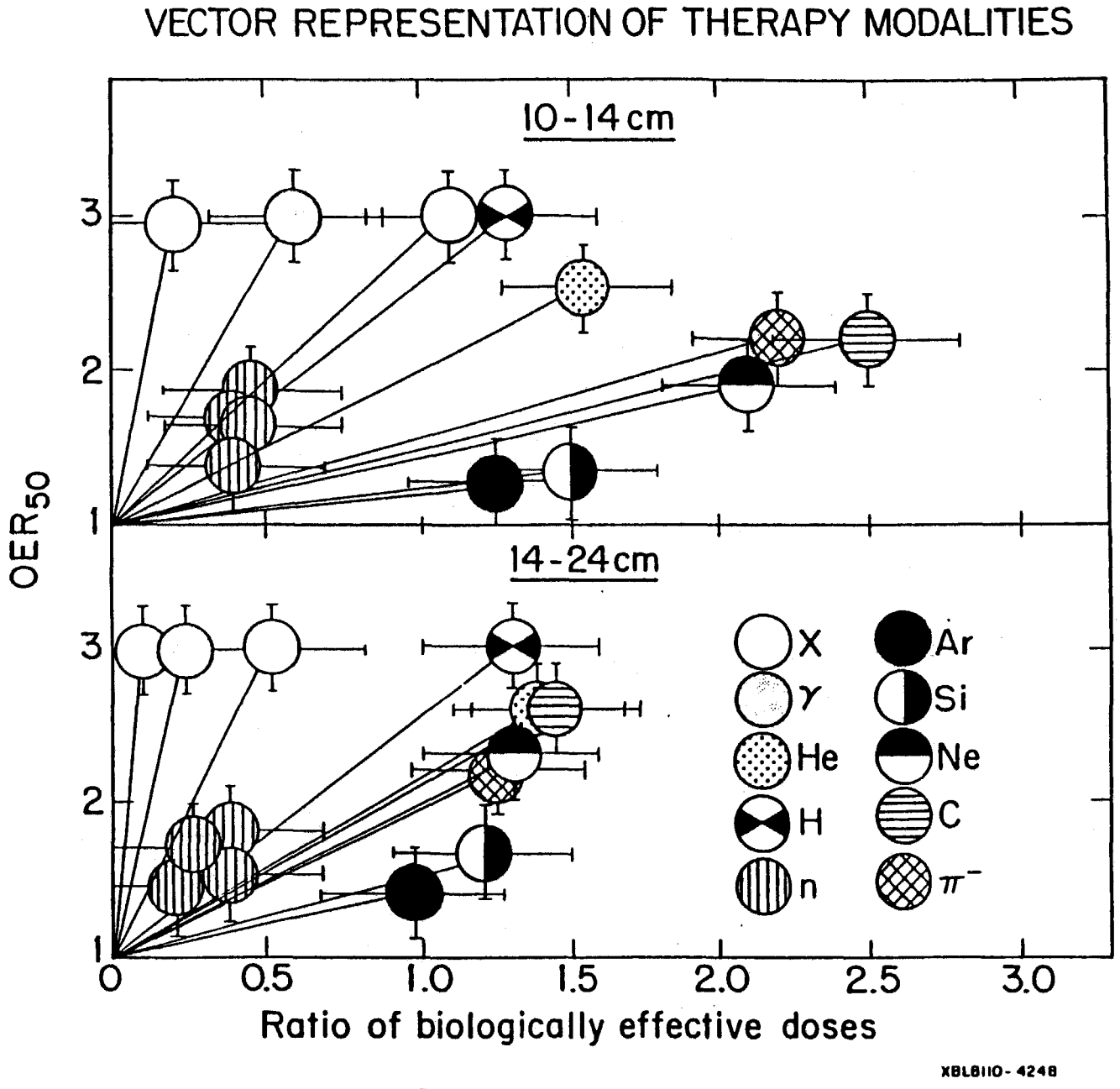
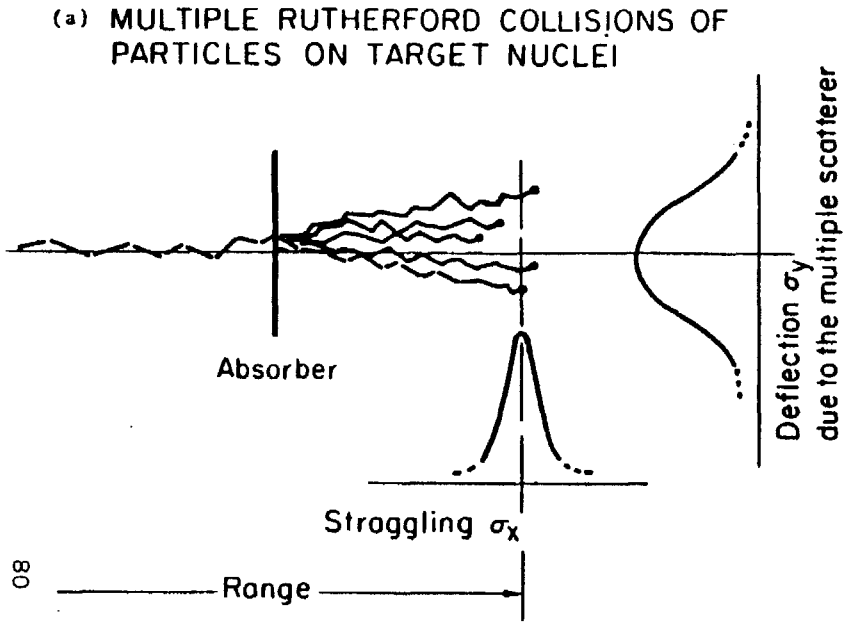

VECTOR REPRESENTATION OF THERAPY MODALITIES
10-14 cm
14-24 cm
OER50
3
2
1
0
0.5
1.0
1.5
2.0
2.5
3.0
Ratio of biologically effective doses
X
γ
He
H
n
Ar
Si
Ne
C
π⁻
XBL8110-4248

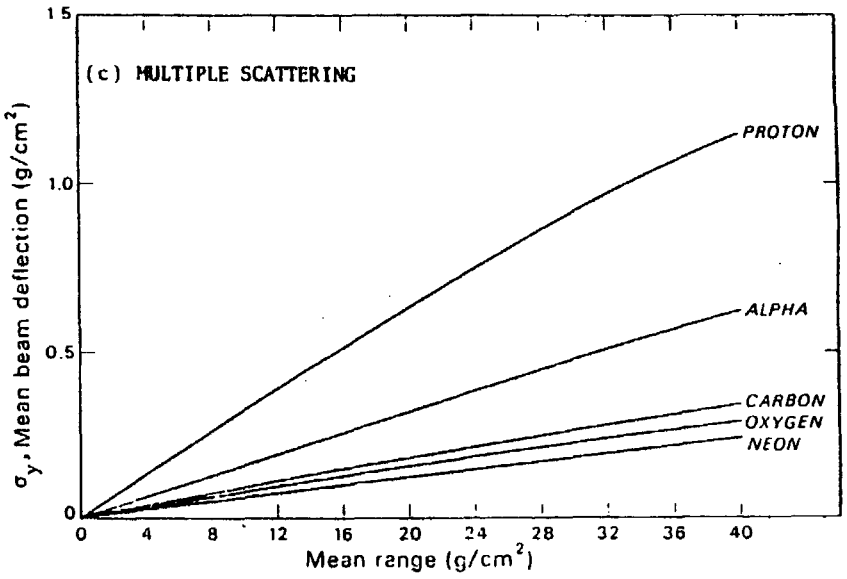
FIG. 1

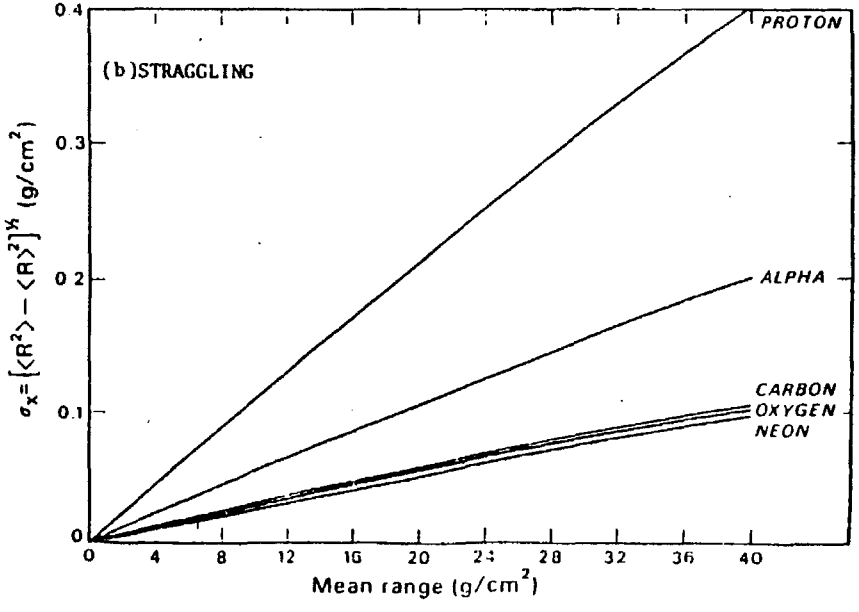


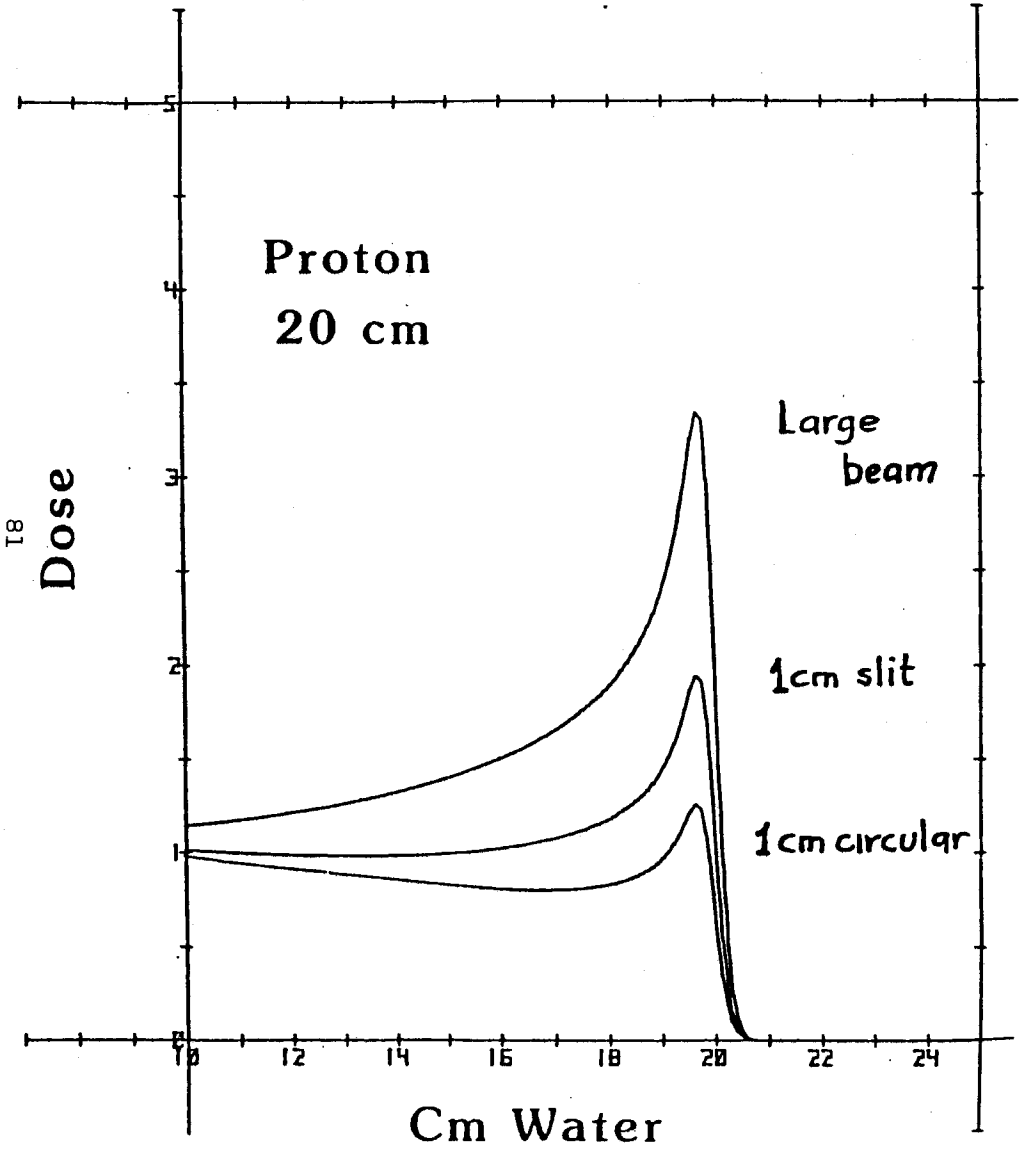
$$\sigma_x \, , \sigma_y \propto \frac{1}{\sqrt{M_{particle}}}$$

XBL811-3516

FIG. 2






Proton
20 cm
Large beam
1cm slit
1cm circular
Dose
Cm Water
10
12
14
16
18
20
22
24

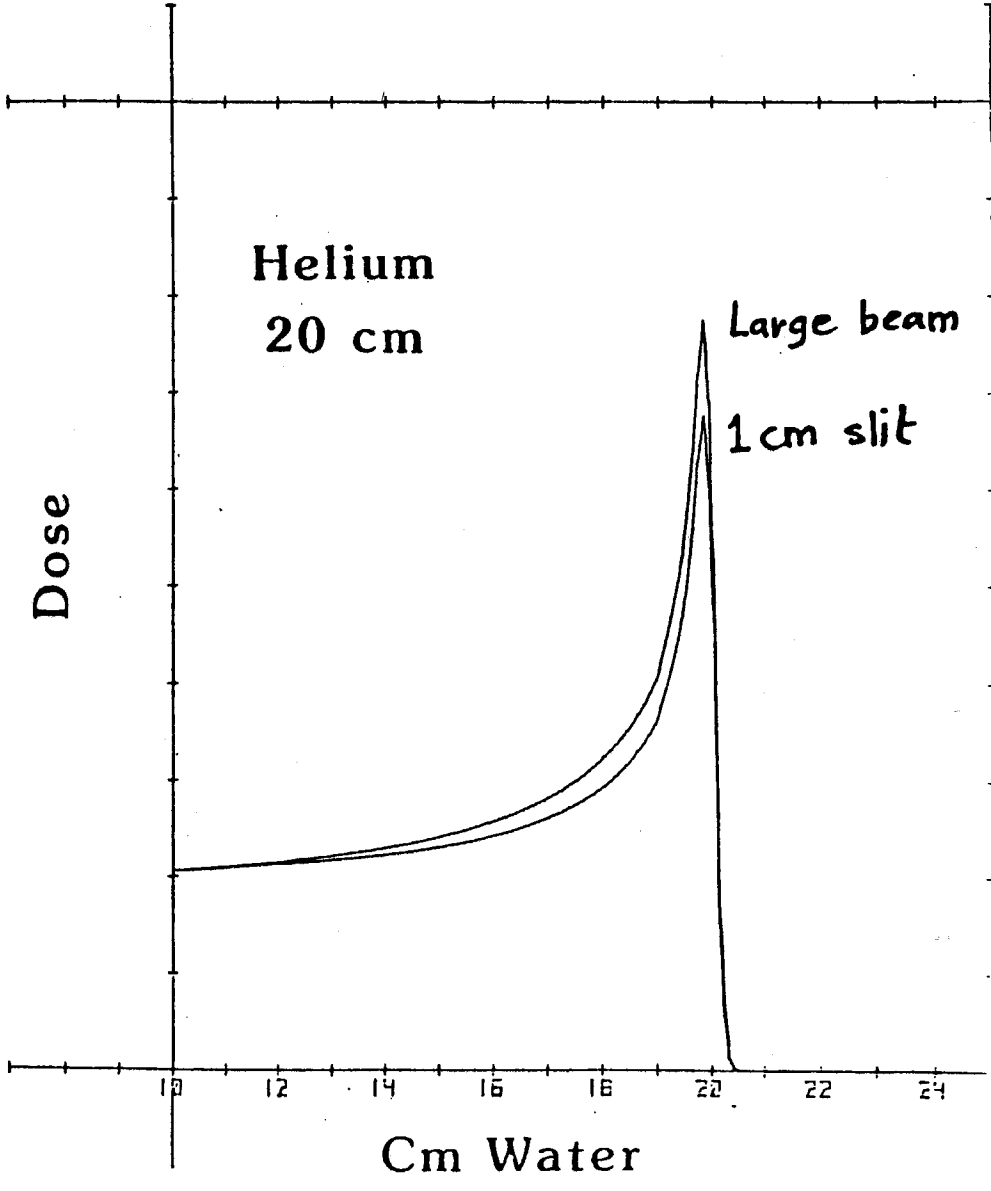
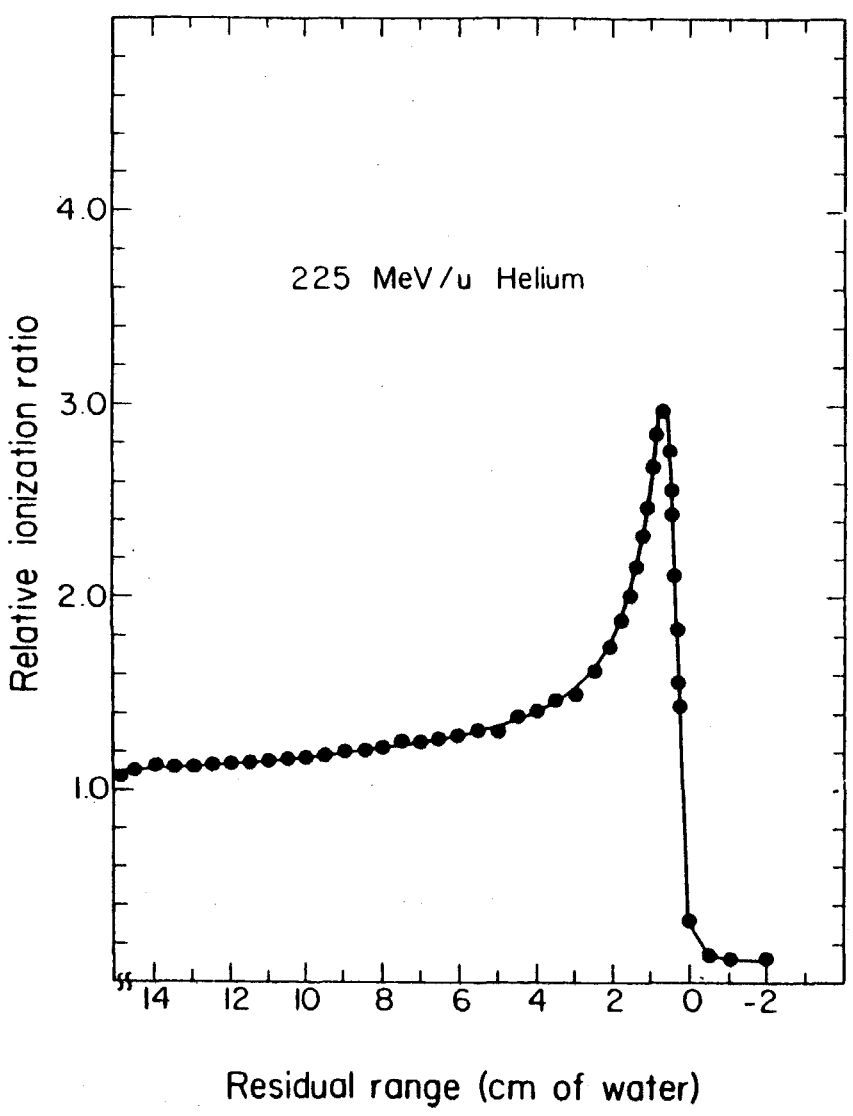

Helium
20 cm
Large beam
1cm slit
Dose
Cm Water
10
12
14
16
18
20
22
24

FIG. 3


225 MeV/u Helium
Relative ionization ratio
4.0
3.0
2.0
1.0
14
12
10
8
6
4
2
0
-2
Residual range (cm of water)
XBL 833-8919-A

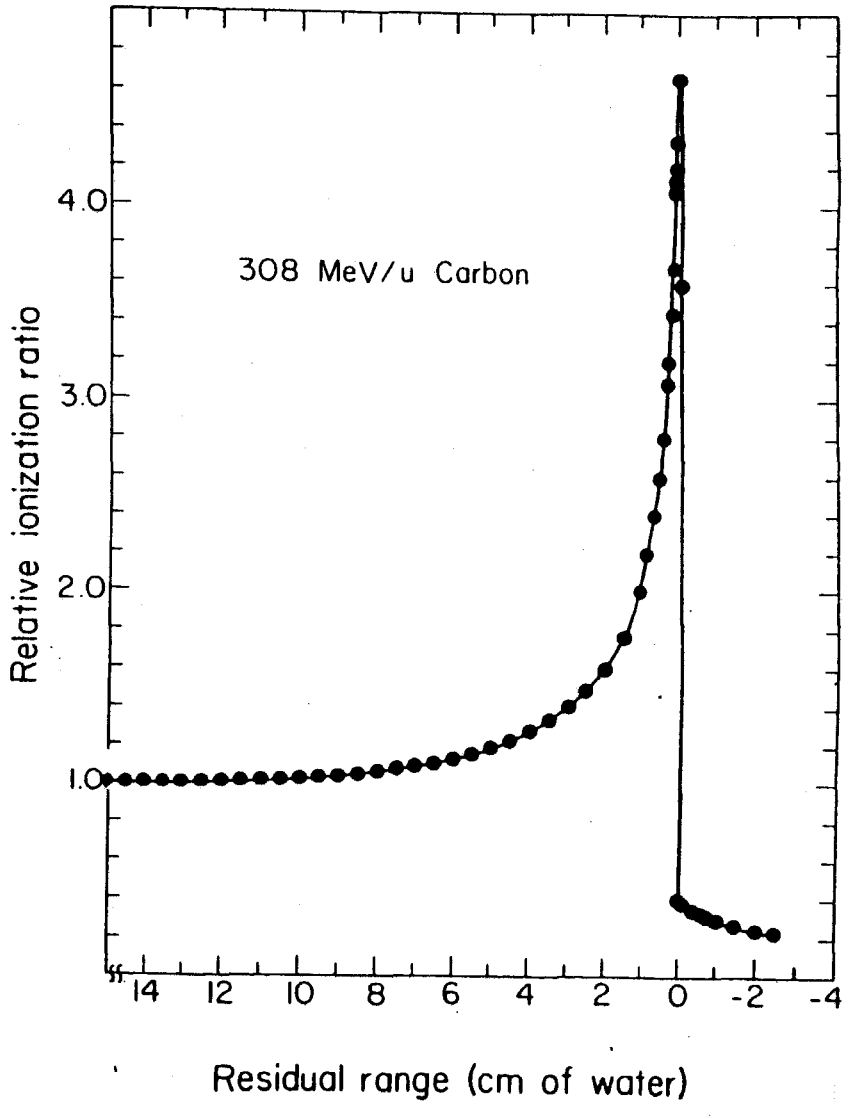

308 MeV/u Carbon
Relative ionization ratio
4.0
3.0
2.0
1.0
14
12
10
8
6
4
2
0
-2
-4
Residual range (cm of water)
XBL 833-8919-B

FIG. 4

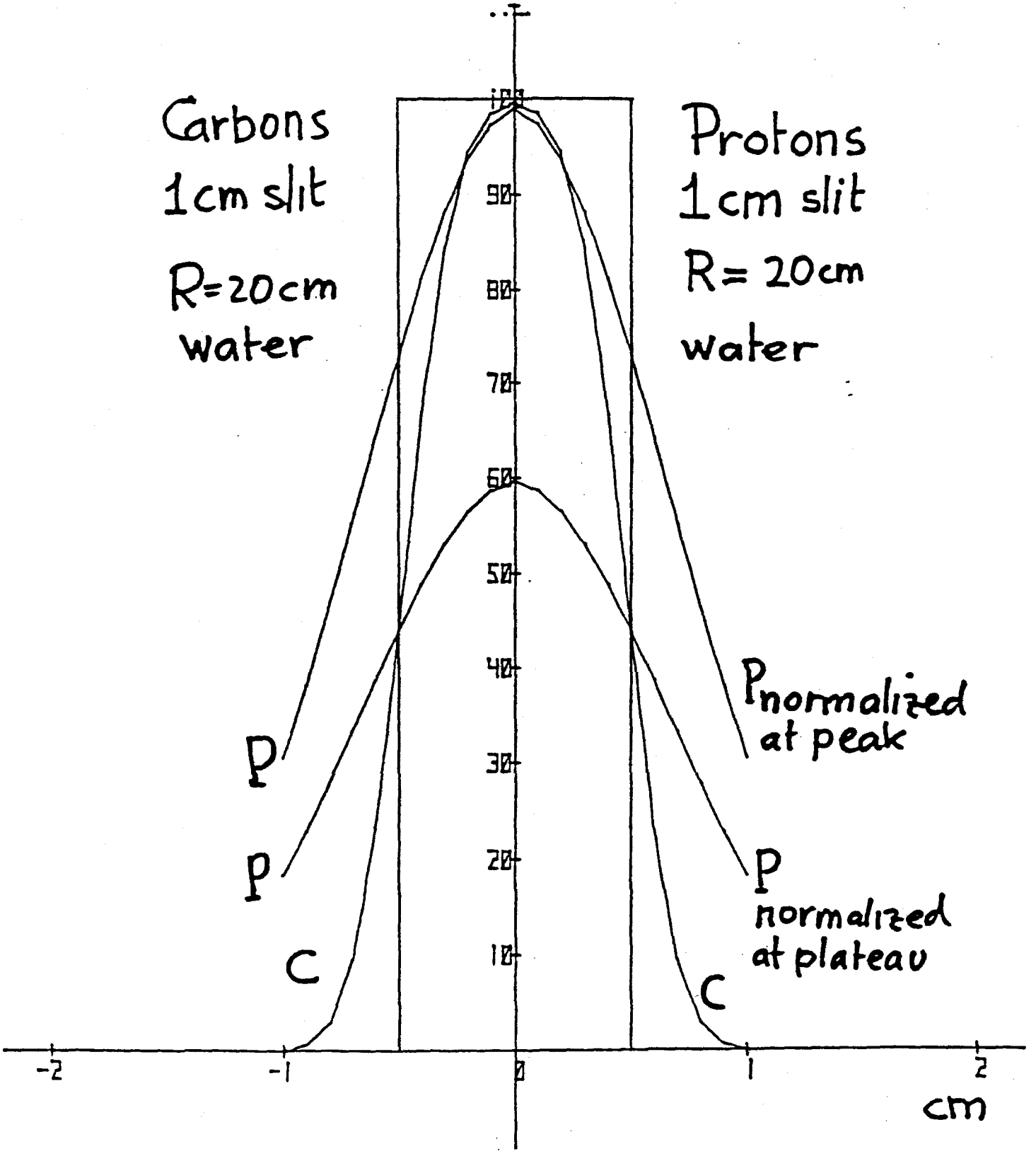
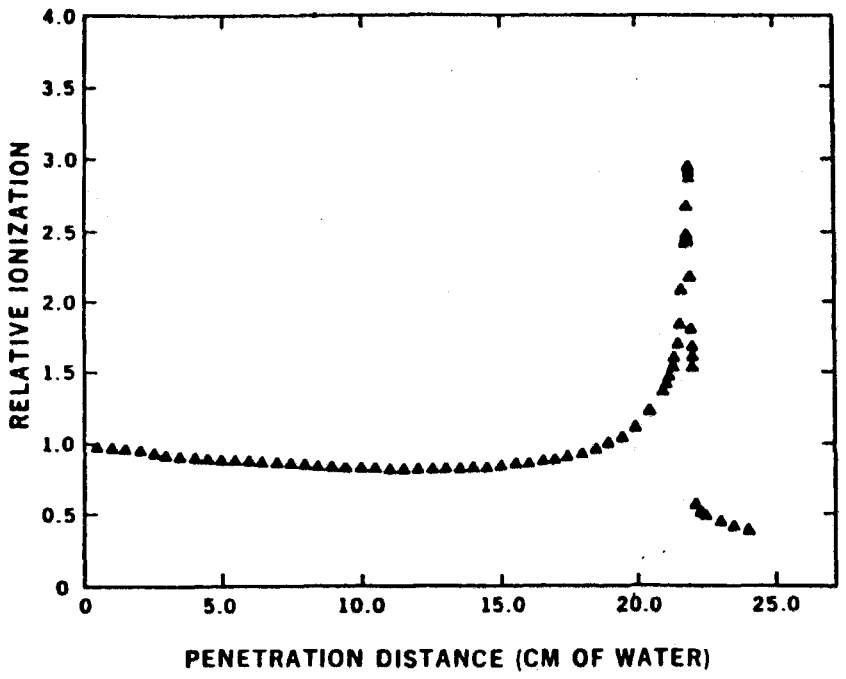
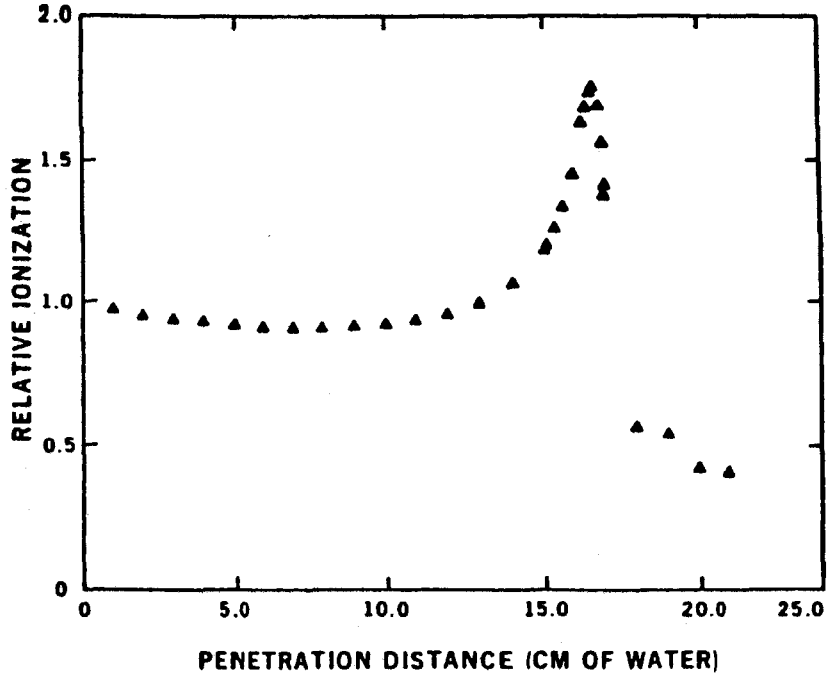

Carbons
1cm slit
R=20cm
water
Protons
1cm slit
R= 20cm
water
100
90
80
70
60
50
40
30
20
10
0
P
P
C
Pnormalized
at peak
P
normalized
at plateau
C
-2
-1
1
2
cm

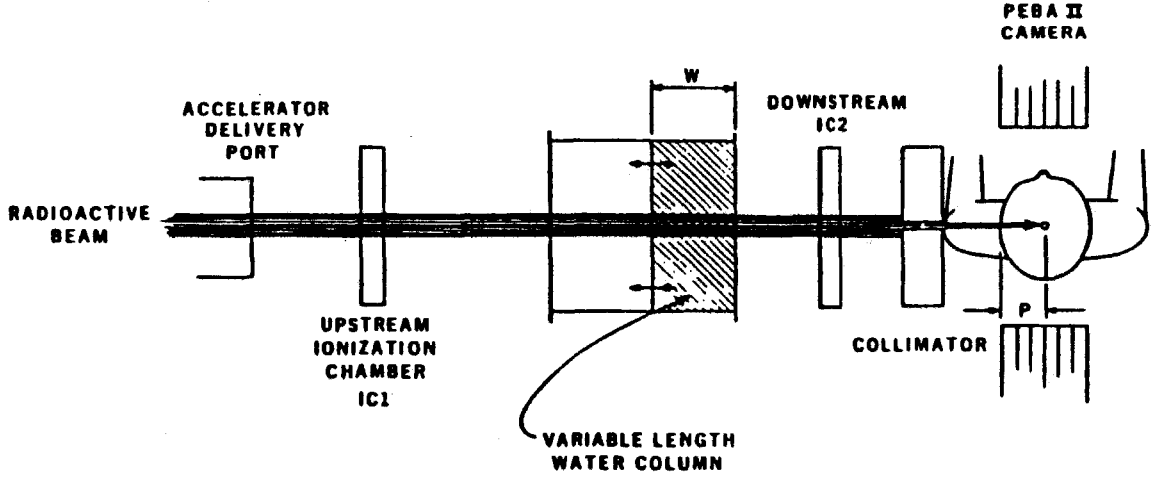
FIG. 5



(a) Bragg curve (rate of energy loss per unit path length) for a Ne-20 beam in water.



(b) Bragg curve for a Ne-19 beam obtained from the Ne-20 beam of (a) by letting the parent beam traverse a Be block and momentum analyzing the resulting fragments before delivery to a treatment room.



(c) Schematic diagram of a setup in a BEVALAC treatment room for end-of-range localization of a radioactive beam.

FIG. 6

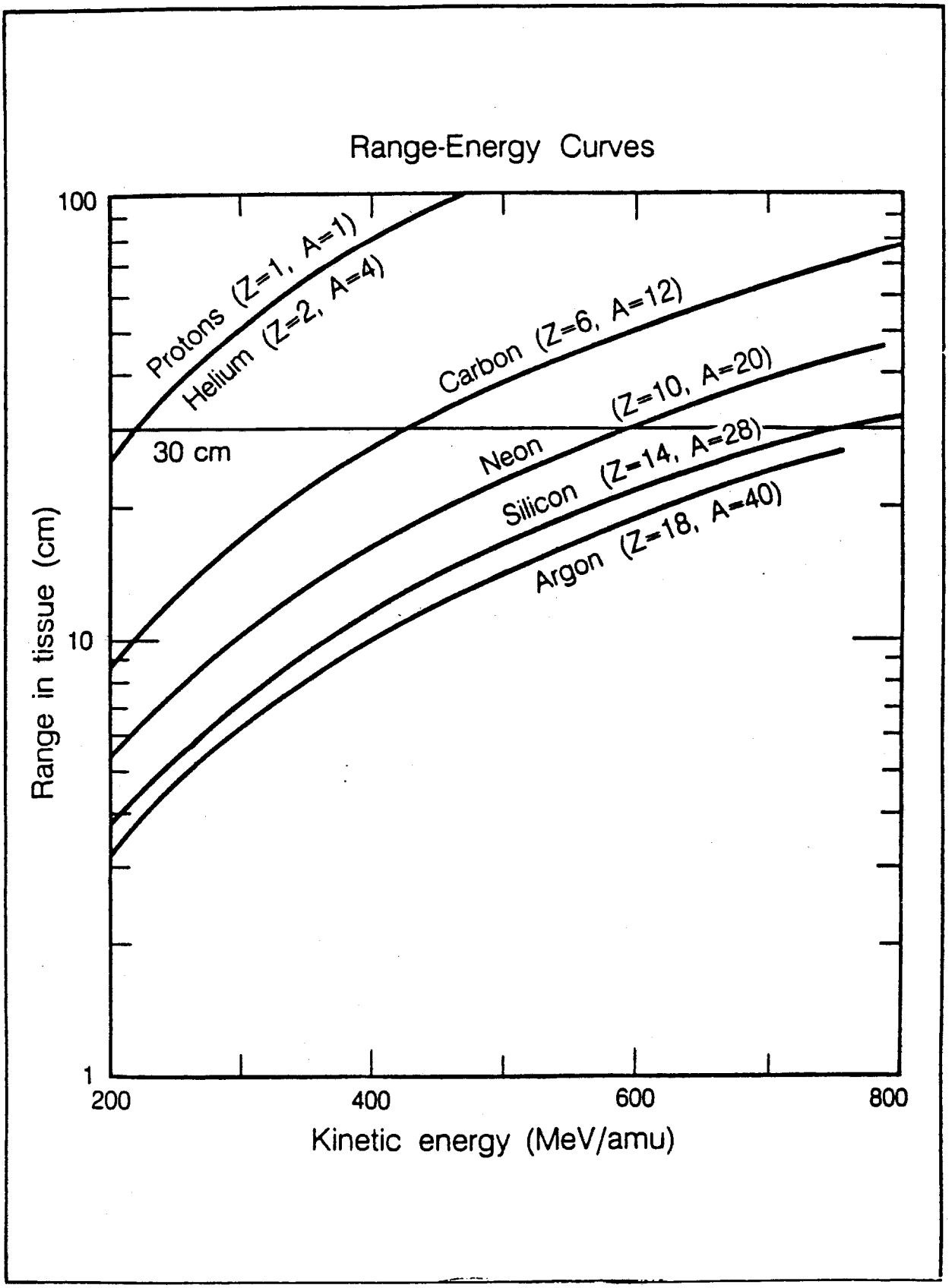


Fig. 7. Energy-range curves showing the depth to which various ions will penetrate in tissue.

Monoenergetic Particle Beams
at the Bevalac

Range 20 cm	Proton	Helium	Carbon
Large beam			
Peak to Plateau	2.9	3.9	3.8
Fragments	0.07	0.15	0.6
Scatter deflection cm	0.75	0.4	0.25
Straggling of range cm	0.8	0.4	0.27
Beam 1.0 cm wide peak to plateau	0.8	1.9	2.7
RBE peak to plateau	1.2	1.6	2.6
Merit factor	1	3	7

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TABLE 1. PHYSICAL CHARACTERISTICS OF PROTON, HE AND C ION BEAMS

TABLE 2.

Water Equivalent Thickness (cm) Using a Frozen Beagle

Location	Neon	Helium	CT Scanner
Brain	4.90 ± 0.10	4.85 ± 0.10	5.25 ± 0.10
Back	6.60 ± 0.10	6.68 ± 0.10	6.7 ± 0.15
Thorax (beam from left side)	no data yet	6.80 ± 0.10	7.0 ± 0.2
Thorax (beam from right side)	no data yet	4.60 ± 0.10	5.0 ± 0.2
Upper Abd.	7.65 ± 0.10	7.65 ± 0.10	7.8 ± 0.2
Lower Abd.	7.90 ± 0.10	7.85 ± 0.10	7.85 ± 0.1

TABLE 3.

MEDICAL ACCELERATOR REQUIREMENTS

Optimal/Minimal requirements

	Therapy	Focal lesion	Radioactive Beam	Radiological physics experiments
	- - - Radiation Biology - - -			
Ion species	He -- Si, Ar	He - Si C - Ne	C, Ne	C - Ne , Fe, La, to U C
Range (cm)	4 - 32 6 - 28	4 - 22 6 - 17	6 - 40 8 - 32	10 cm for breast 37 cm for body
Energy spread $\Delta E/E$ (% FWHM)	0.1 0.2	0.1 0.2	0.1 0.3	0.1
Pulse to pulse energy variation $\Delta E/E$ (% FWHM)	0.1 0.2	0.1 0.2	0.1 0.3	0.1 0.5
Intensity at target	600 rad-l/min	10^4 - 10^{10} / pulse 10^4 - 10^8 / pulse	10^6 - 10^7 /pulse 10^5 - 10^6 /pulse Secondary particles	10^3 - 10^5 /cm^2 pulse
Extracted flux (particles/sec)	He 2×10^{10} C 4×10^9 Ne 2×10^9		C^{12} 10^{11} Ne^{20} 10^{11}	
Repetition rate (Hz)	1 1/3	2 1/3	5 1/3	>1
Duty factor (%)	75 25	75 25	25 10	50 25
Emittance (m-rad)	10^{-4}	2×10^{-5} 6×10^{-5}	10^{-4}	$< 6 \times 10^{-4}$
Short pulse duration (msec)		>50		<1 50
Time required to switch ion species (sec)	20 120	20 120	20 120	20 120
Time required to change energies (sec)	20 120	20 120	20 120	20 120
Reliability (% machine up time)	99 95	99 95	99 95	99 95
Waiting time behind other users (minutes)	5	5	10	5

Table 4

Accelerator Requirements

Particle Species:	^{1}H or $^{4}He \rightarrow {}^{28}Si$, ^{40}Ar
Maximum energy:	30-cm-range ^{28}Si (800 MeV/amu)
Minimum energy:	4-cm-range ^{4}He (70 MeV/amu)
Intensity:	$\geq 3 \times 10^{7}$ Si ions/sec on target
Duty factor	20−50%
Reliability:	> 95%
Repetition Rate:	0.25 − 4 Hz
Emittance:	$< 2 \times 10^{-5}$ m-radians
Momentum spread	$\Delta p/p$: $1-2 \times 10^{-3}$

HEAVY ION MEDICAL ACCELERATOR OPTIONS

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Summary

This paper briefly explores the accelerator technology available for heavy ion medical accelerators in the mass range of 1 to 40 (protons through argon). Machines that are designed to produce the required intensities of a particular design ion, such as silicon (mass 28), can satisfy the intensity requirements for all lighter ions, and can produce beams with higher mass, such as argon, at somewhat reduced, but still useful intensity levels. They can also provide beams of radioactive ions, such as carbon-11 and neon-19, which are useful in diagnostic imaging and for directly verifiable treatments. These accelerators are all based on proven technology, and can be built at predictable costs. It is the conclusion of several design studies that they can be operated reliably in a hospital-based environment.

Background

There are presently at Berkeley a number of active programs in the application of energetic charged particles to research in biology and medicine. These programs, which include the development of appropriate accelerator technology and the operation of existing accelerators for clinical research, are the outgrowth of over 40 years of experience in these fields. While the present emphasis at Berkeley is focused on heavy ions ranging from mass 4 (helium) to mass 40 (argon), much of what has been learned concerning the design of these facilities is applicable to the design and operation of any charged-particle facility.

In 1977, a report was published summarizing the findings of a medical accelerator design study undertaken jointly by the Arizona Medical Center and the Lawrence Berkeley Laboratory[1]. This study surveyed the technical approaches for delivery of neutrons, pions, light, and heavy ions to a wide variety of medical applications, and provided an assessment of cost and performance on both an absolute and comparative basis. Because uniform costing practices were employed, these cost comparisons are extremely useful in the context of this workshop.

In 1984, another report was published summarizing a detailed LBL design study of a specific accelerator capable of providing a range of heavy ions from protons to argon[2]. The design ion in this case was silicon. The layout of a facility based on this design is shown in Figure 1. This study considered the construction of a complete, hospital-based facility that would support programs in community medicine together with research programs in clinical radiotherapy and in other biomedical applications of charged particle beams. It examined in detail the technical components required to meet specifications for a versatile, heavy ion accelerator. This machine

can also provide useful intensities of radioactive beams (such as carbon-11 and neon-19), and can be rapidly switched between different ion species and energies to provide efficient service to as many as 8 separate treatment areas.

In considering the heavy ion option, it is important to realize that it is really many options. A machine capable of producing protons, helium and carbon, for example, offers some advantages over a proton-only machine and would cost less than a machine designed for heavier ions such as silicon and argon. It is also important to realize that the cost of the accelerator itself is a relatively small fraction of the total cost for a new and complete facility. This fraction becomes very small if the capital costs are amortized over the productive life of the facility, which could easily be upwards of 30 years.

Requirements

Many of the requirements for charged particle medical accelerators can be expressed indepedent of the choice of particle species. Energy and intensity, for example, are set by the need for a range in tissue of about 30 cm, and for a treatment time of about 1 minute per 100 rad fraction. Momentum spreads of a few parts per thousand, and emittances less than about 2 pi cm-milliradians are required. All of these specifications pose little challenge to accelerator technology. Other requirements, however, such as patient safety, flexibility, simplicity of operation, and the achievement of ultra-high, clinical standards of reliability, including fast recovery from failures, are features that are absolutely essential for a successful medical program, but not normally found in accelerators designed for research in nuclear and high energy physics. These are areas that must not be overlooked in the design and construction of these machines. Many techniques that ensure component and system reliability are well known. One important principle is the use of proven and tested systems and components. In the construction of new accelerator systems that are pushing the technological frontiers, it is often necessary to obtain this field testing in R&D programs. In the case of medical accelerators, however, it is possible and desirable to avoid the cost and uncertainties of any R&D expenses, through the use of mature technology already tested in the field. Fortunately, all of the technology required to meet these specifications and reliability principles is available at synchrotron facilities now in operation. These machines can provide the energies, intensities, beam quality, flexibility and reliability needed for a successful medical program.

To summarize the basic technical requirements, we consider the specifications for a variety of synchrotron options, covering facilities where the heaviest ion can range from protons (mass 1) to silicon (mass 28). Table 1 presents a summary of some of these basic specifications. A very simple approach provides a means to generate a crude, first order description of design parameters. The machines in Table 1 can, in general, accelerate all ions up to and including the heaviest design ion with adequate intensities, and can typically provide some even heavier ions with reduced but still useful intensities. The maximum energy, determined by the 30 cm range, plus some small safety margin, sets the magnetic rigidity (Bp) of the beam which, in turn, determines the diameter of the synchrotron ring. The

swing of the synchrotron RF system should not exceed 10:1, allowing us to set a minimum energy for injection. This minimum injection energy is satisfactory for all these examples, except in the case of the silicon machine, where stripping efficiency considerations dictate a somewhat higher choice of injection energy. The last column gives the minimum intensities required to ensure that even large volumes can be treated in a reasonable period of time. For typical, modern synchrotrons, approximately 10^7 - 10^8 ions/pulse can be extracted for each particle microamp available at injection. This transmission, together with the synchrotron repetition rate, determines the performance requirements of the injector system. For machines designed for carbon or heavier ions, a cycle rate of 2 to 4 Hz is readily achievable, while for lighter ion machines, the lower stored energy in the magnet system should permit higher rep rates to be achieved.

Table 1

Summary of basic synchrotron requirements for various choices of heaviest ion

Heaviest Ion	Maximum energy (MeV/n)	Rigidity (kG-m)	Minimum injection energy (MeV/n)	Extracted beam Intensity (Ions/sec)
protons	250	25	1.8	2×10^{10}
helium	250	50	1.8	4×10^{9}
carbon	450	68	2.5	8×10^{8}
neon	670	86	3.1	4×10^{8}
silicon	800	97	7-8 *	3×10^{8}

* For silicon, injection energy set by stripping efficiency.

Accelerator Technology

Synchrotron

Previous studies [1,2] of both carbon and silicon synchrotrons have been completed, providing detailed descriptions for possible designs of two of the heavy ion options. Two somewhat different approaches were taken in these designs: the carbon option utilized a combined-function lattice design, while the silicon machine used a separated-function lattice. Combined-fuction types have been preferred for small machines to minimize the number of elements and machine size, though they often demand stricter fabrication and positioning tolerances. For heavier ion machines, however, a greater repertoire of ions is possible and more demand for fast ion switching is anticipated. In the silicon lattice, therefore, the separated function approach was adopted to ensure ease of tuning. In this case the ring diameter was kept small

by increasing the guide field from the 8 kG value used in the carbon lattice, to 16 kG. This, together with other differing goals of the two studies, makes direct comparisons and interpolations of the two designs more difficult, but serves to underscore that different approaches are often possible. Nevertheless, as we will see, costs scale very closely, despite these design differences. Parameter summaries for these two designs are given in Table 2.

Table 2

Summary of design parameters
for carbon and silicon synchrotrons

	415 MeV/n Carbon	800 MeV/n Silicon	
Maximum kinetic energy	415	800	MeV/n
Injection energy	2.9	8	MeV/n
Lattice type	comb. func.	sep. func.	
Mean radius	12	14.6	m
Repetition rate	2	2-4	Hz
Number of injected turns	4	1	
Dipoles			
Number of magnets	24	12	
Guide field	8	16	kG
Length	1.6-2.8	3.2	m
Quadrupoles			
Number of magnets	0	18	
Max. gradient	-	76.5	kG/m
Length	-	0.4	m

A layout of the silicon ring is given in Figure 2. The three superperiod symmetry is indicated by the dotted lines. The long straight sections are used for injection, extraction, RF, correcting elements and diagnostics. The 16 kG field requirement for the ring dipoles led to the development of a conservative, curved dipole design, capable of reliable operation at 4 Hz and 16 kG. The dipole magnets used in this lattice are illustrated schematically in Figure 3. They are of laminated construction, and have a 30 degree bend angle, a 3.2 meter length, a 4 cm gap, and a 10 cm aperture. Each dipole requires 46 kW at full excitation.

The synchrotron is a pulsed machine. Typical waveforms, shown in Figure 4, are taken from the silicon design study. Two operating modes are described. In each mode, the rate of rise is 160 kG/second, a conservative limit for what can be readily achieved with conventional power supplies. This can be applied, as shown at the top, to provide a 2 Hz rep rate and a duty factor of 60%, or, as shown at the bottom, to provide a 4 Hz rep rate with a 20% duty factor. Long duty factors are desirable from the viewpoint of beam delivery systems, as discussed later. A slow, RF-off, resonant extraction can be provided during flattop, keeping instantaneous dose rates from exceeding comfortable levels, and at the same time maintaining a uniform beam level, suitable for dynamic methods of beam delivery. Energy variability is achieved by programming the flattop at the level appropriate to the desired beam energy. Only a few pulses are required to change and verify the magnet excitation level.

Injection into the synchrotron can be readily achieved with septum magnets and ferrite-loaded fast kickers. These magnets are inserted in one of the long straight sections provided in the lattice as shown in Figure 5. The magnets shown here have modest dimensions and electrical requirements, and can be used to inject beams with Q/A of 1/2 at energies up to 8 MeV/n. In the carbon machine, a four turn injection scheme was developed to provide a conservative margin on the intensities. In the silicon design, single-turn injection was adopted - again to simplify the tuning. The use of single-turn injection has the additional advantage of reducing the magnet apertures, leading to lower projected power consumption and operating costs, but requires a higher level of injector performance to assure the needed conservative margin of available intensities.

Vacuum requirements for heavy ion synchrotrons in this mass range are typically in the low 10^{-7} Torr range. Most of the losses occur at low energy, and therefore the pressure requirements show some dependence on the acceleration rate. The required pressures can be readily achieved with conventional vacuum technology.

Injector

The task of the injector system is to provide an adequate intensity of the appropriate ion during the injection window of the synchrotron. This window is typically a few microseconds wide and occurs a few times per second, defining a very short duty factor for the injector of $\leq$ 0.1%. The traditional choice for a synchrotron injector is a linac, and for the higher-mass heavy ion options, is the accelerator of choice. The PIG source / RFQ / Alvarez linac combination, particularly for low duty factor, heavy-ion applications, offers proven and reliable technology with flexibility to switch rapidly between ion species. For proton and helium options, because the injection energy is so low, consideration should be given to duoplasmatron sources and to van de Graaffs or the RFQ linac for preacceleration.

A schematic layout for an injector developed for the silicon design study is shown in Figure 6. Because of the low duty factor, PIG source lifetimes of several weeks are expected. Depleted sources can be rebuilt and returned to operation in about 2 hours. Switching between multiple sources can be used to rapidly change ion species. The RFQ proposed here is identical in design to one designed and successfully operated for use at the Bevatron in Berkeley. The low beam energy at the RFQ entrance of only 8.4 keV/n, places the source on a dc platform of 60 kV, simplifying source access and eliminating the need for a Cockcroft-Walton preaccelerator. This RFQ accepts beams with Q/A as low as 1/7 and accelerates them to 200 keV/n. Two Alvarez tanks, each followed by a stripper, continue the acceleration to 1.75 and 8 MeV/n respectively. Each Alvarez uses pulsed quadrupoles for focusing; tank 1 operates on the two beta-lambda mode, and tank 2 operates on the fundamental. A bunch rotator cavity is specified in this design to ensure efficient matching to the injection requirements of the synchrotron. A parameter summary for the linac is given in Table 3.

Table 3

Parameter summary for silicon injector linacs

	RFQ Linac	Prestripper Alvarez Linac	Poststripper Alvarez Linac	
Input energy	8.4	200	1750	keV/n
Output energy	200	1750	8000	keV/n
Q/A	0.143	0.143	0.357	
Frequency	200	200	200	MHz
Aperture radius	2.5	5, 8	10, 12.5	mm
Length	2.24	10.7	11.3	m
Tank inside diameter	150	950	950	mm
Peak RF power	150	1000	1200	kW
Duty factor	0.001	0.001	0.001	
Stored energy	0.6	45	53	Joules

For a facility where carbon is the heaviest ion, an injector could be designed along similar lines. In this case, however, the source ion could be $^{12}C^{+4}$, leading to a more efficient acceleration than in the silicon design. An RFQ designed for Q/A = 1/3 ions would accelerate the beam to substantially higher energies than in the silicon example, and a short Alvarez tank, perhaps less than 5 meters in length, would boost the energy up to the level required for injection. This injector could also readily provide lighter ions, such as protons and helium, and could switch quickly among any of the ions in its repertoire, permitting the synchrotron to deliver the optimal ion for a given diagnostics or treatment situation - including radioactive beams of ^{11}C.

Power requirements for these injectors are modest because of the low duty factor. Commercially available vacuum equipment can be used to readily meet the pressure requirements of 10^{-7} - 10^{-6} Torr.

Controls

For any medical accelerator, the control system should be capable of storing and recalling tunes for each given energy. It is desirable that this be done very rapidly - on a time scale commensurate with scanning the beam energy during the course of a patient treatment. In the case of heavy ion machines, these tunes need to also include those required for different ions. In addition, to achieve the ultimate in machine reliability and simplicity of operation, it is highly desirable to provide a control system with enough sophistication to ensure precise fault diagnosis, together with easily-understood and conveniently-displayed graphics for the operator. Modern computer architechture makes it possible to provide this at reasonable cost.

Treatment Delivery

Preparation and delivery of a treatment beam needs careful study and will not be discussed at length here. However, it is important to review some of the requirements, as they impact other aspects of facility design. For heavy ions, it is appropriate to consider both fixed horizontal and fixed vertical treatment ports. It is also important to ensure that the external beam is free of time structure that would hinder the development of dynamic beam scanning. Methods for shaping the dose to conform to three-dimensional treatment volumes exist at presently operating facilities, but this is an area where new developments and improvements should be anticipated. Lateral or transverse spreading of the beam can be achieved with scattering techniques or by magnetic deflection methods. Axial spreading of the Bragg peak can be accomplished using degraders or by adjusting the energy of the beam delivered by the accelerator. The beam quality, and the precision with which the dose can be matched to the treatment volume are better if the material placed in the beam is minimized. This is important for all charged particle therapy, and its importance increases with the consideration of heavier ions. This argues in favor of magnetic deflection techniques, requiring uniform, structure-free beams, and for fast energy switching capability in the accelerator and beam lines.

Shielding

Shielding specifications can be prepared from data gathered at various operating accelerators. At the Bevalac Radiotherapy Facility, shown in Figure 7, concrete shielding blocks of normal density are arranged to provide radiation protection and permit access into the treatment room via a maze. A backstop thickness of approximately 3 to 4 meters, and sidewalls and roofs about 2 meters thick are required for 670 MeV/n neon treatments. These dimensions can be reduced through the use of high density concrete, but at most sites it would be prohibitively expensive to make extensive use of it. Considerable cost savings can be realized by using poured-in-place concrete. This is completely practical, but requires a well thought out use plan for all of the space, since much of the facility floorplan would be literally "cast in concrete". The severest need for radiation shielding is in the treatment room areas. Little beam loss is anticipated along the beam lines, and modest concrete walls should afford adequate radiation protection there. There is some energy dependence of the shield thickness on the beam energy but the overall difference in cost in the context of the total facility costs, is not that great. Further economies can be realized by careful arrangement of the facility on the site. By locating the treatment rooms slightly below grade, good advantage can be made of earth shielding.

Cost Analysis

Comparative cost analyses are difficult to make unless uniform costing practices are adopted, and unless there is a clear definition of what is included. The results of the 1977 LBL/Arizona study shown in Figure 8, provide such a comparison of accelerator base costs. These can be escalated to present-day dollars by multiplying by 1.92. They include all the hardware costs for an installed, working accelerator, but do not include the cost of the building, the shielding, beam transport or engineering. A striking feature of this graph for heavy ion synchrotron facilities, is the relative insensitivity to the choice of final energy. Curve B shows the cost vs energy for a heavy ion synchrotron using a cyclotron injector. (The cyclotron could also be used for isotope production.) Using this curve, and making some extrapolations, one projects the cost of a 415 MeV/n carbon synchrotron to be about 2/3 the cost of an 800 MeV/n silicon machine. The 1984 LBL study of a specific accelerator design for silicon with a linac injector scheme and no isotope production option, cites a base cost for the accelerator, converting to 1985 dollars, of approximately 18 - 20 M$, in good agreement with the value obtained by extrapolating from Figure 8. This would suggest that the base cost for a carbon synchrotron with a linac injector would be in the area of 12 - 14 M$. Projected accelerator-only operating costs for the silicon machine, including personnel, power and miscellaneous supplies and expenses, is less than 1 M$/year for five shift per week operation (exclusive of any applicable institutional overheads). For lighter ion machines, personnel costs would be about the same, but some reduction in power and miscellaneous expenses would be expected.

Our studies of facility requirements for charged particle radiotherapy have shown that the base accelerator costs, even for the heaviest ion considered, are not the dominant component of the total facilities costs. (Even for the silicon machine, the accelerator accounted for less than 30% of the total costs.) Therefore the choice of ion species and accelerator technology should not be driven solely by the accelerator cost, but one must also consider the need to maximize the potential scientific return on the total investment.

Conclusions

The accelerator technology required to meet the needs for heavy ion radiotherapy is well developed. Accelerators for charged particle radiotherapy are presently in existence, and several designs for new facilities are available. Heavy ion machines can, in general, provide beams of all ions, from protons to uranium; preliminary designs for various medical accelerator options up to mass 40 (argon) have been completed. These studies have determined that these machines can be built at predictable costs, and made to operate reliably in a hospital-based environment.

References

1) Dedicated Medical Ion Accelerator Design Study, Final Report, (December 1977) LBL 7230.

2) The Heavy Ion Medical Accelerator, Final Design Summary, (June 1984) LBL PUB 5122.

List of Figures

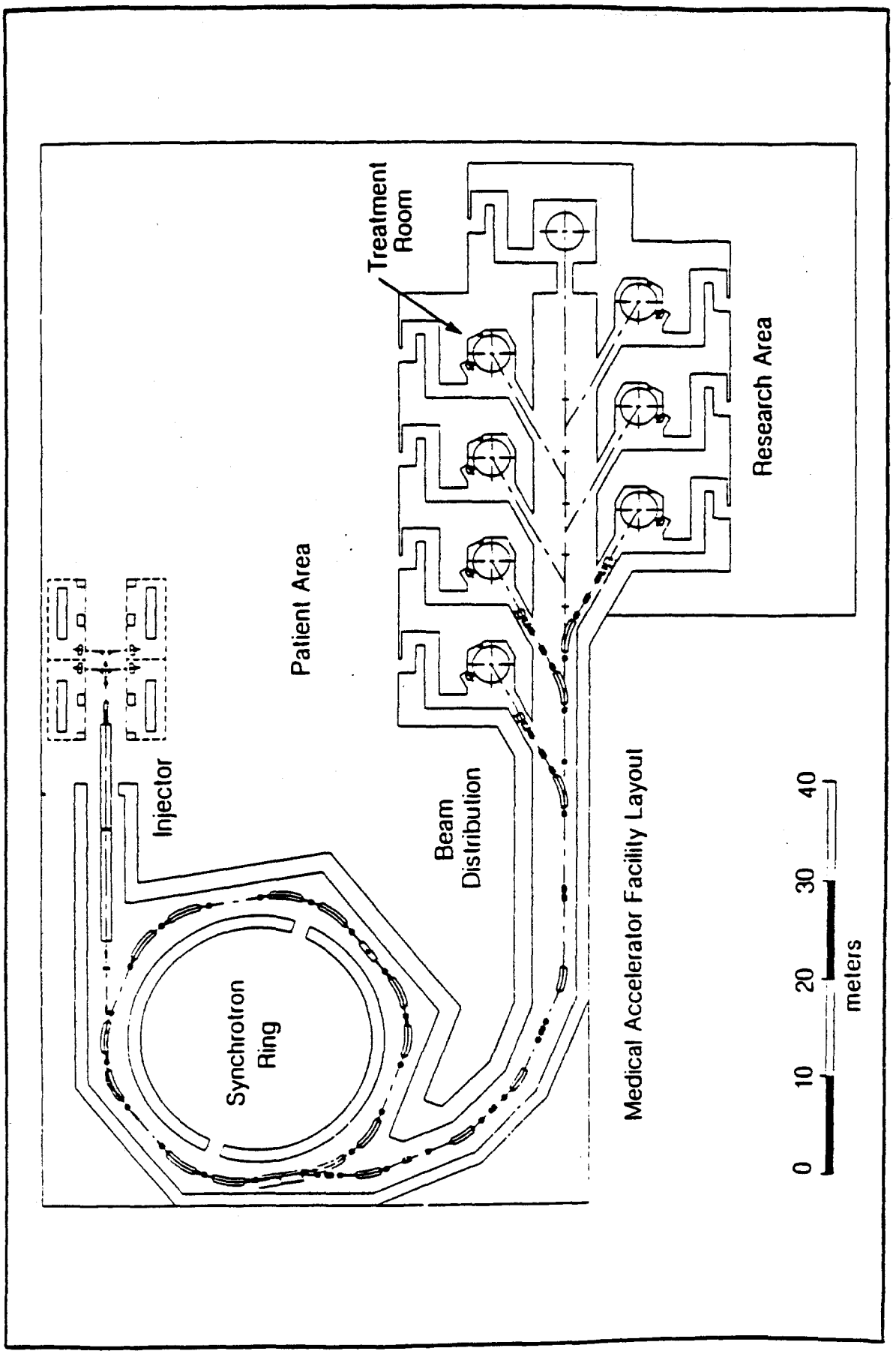

Fig. 1 Layout of a radiotherapy facility based on the silicon design study.

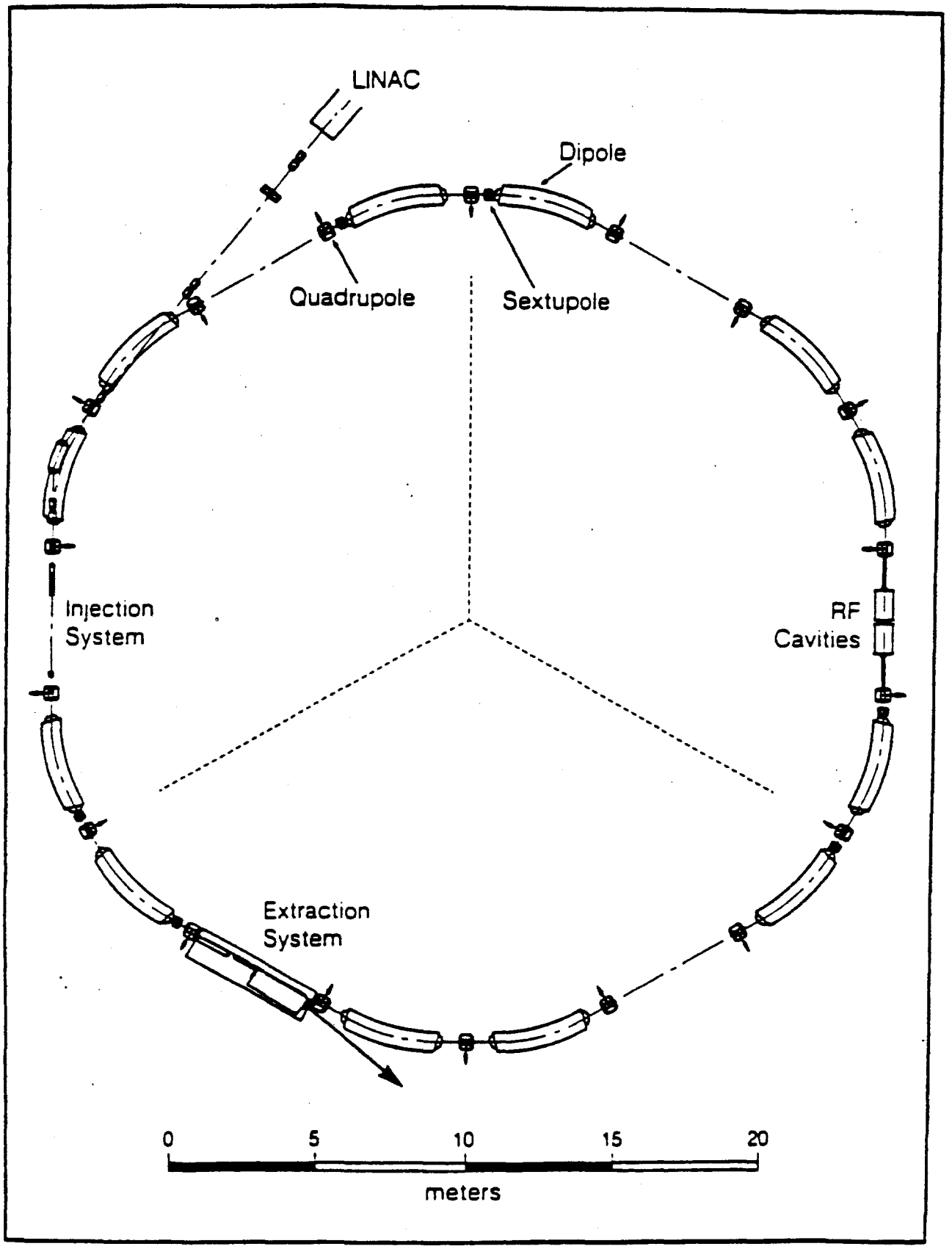

Fig. 2 Layout of a synchrotron ring designed for 800 MeV/n silicon.

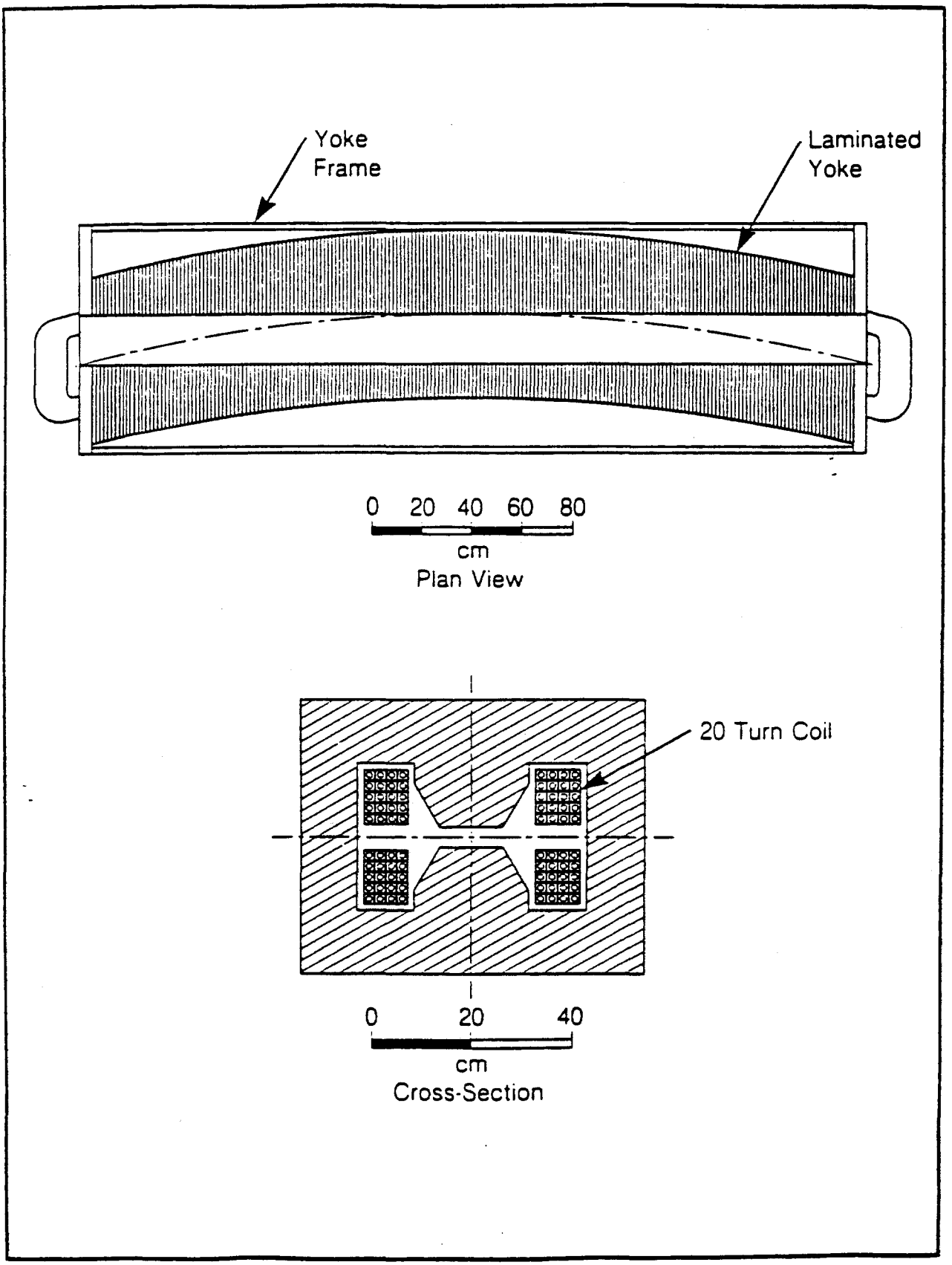

Fig. 3 Illustration of a ring dipole magnet from the silicon design study.

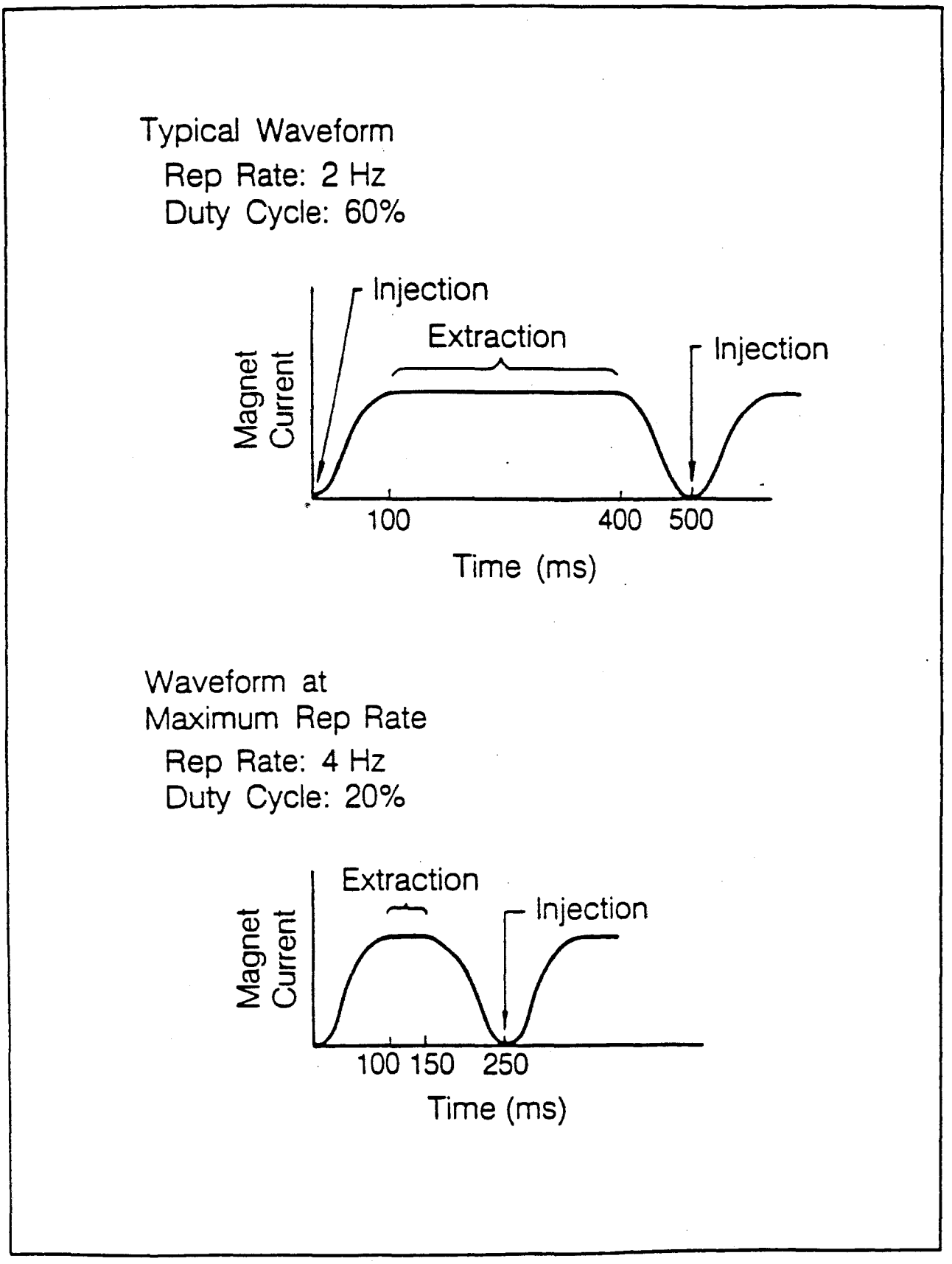

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Fig. 4 Typical waveforms showing 2 and 4 Hz operation.

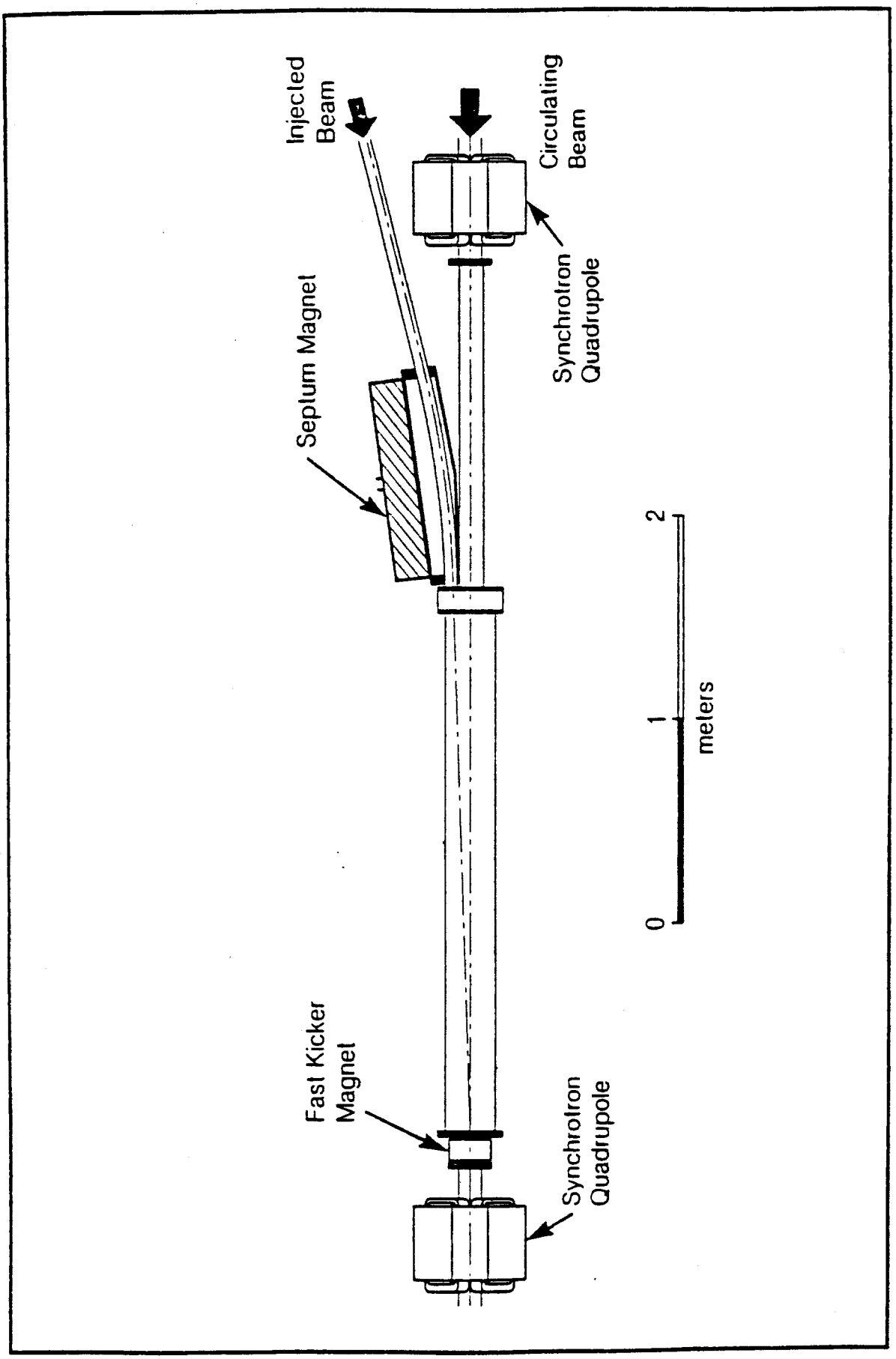
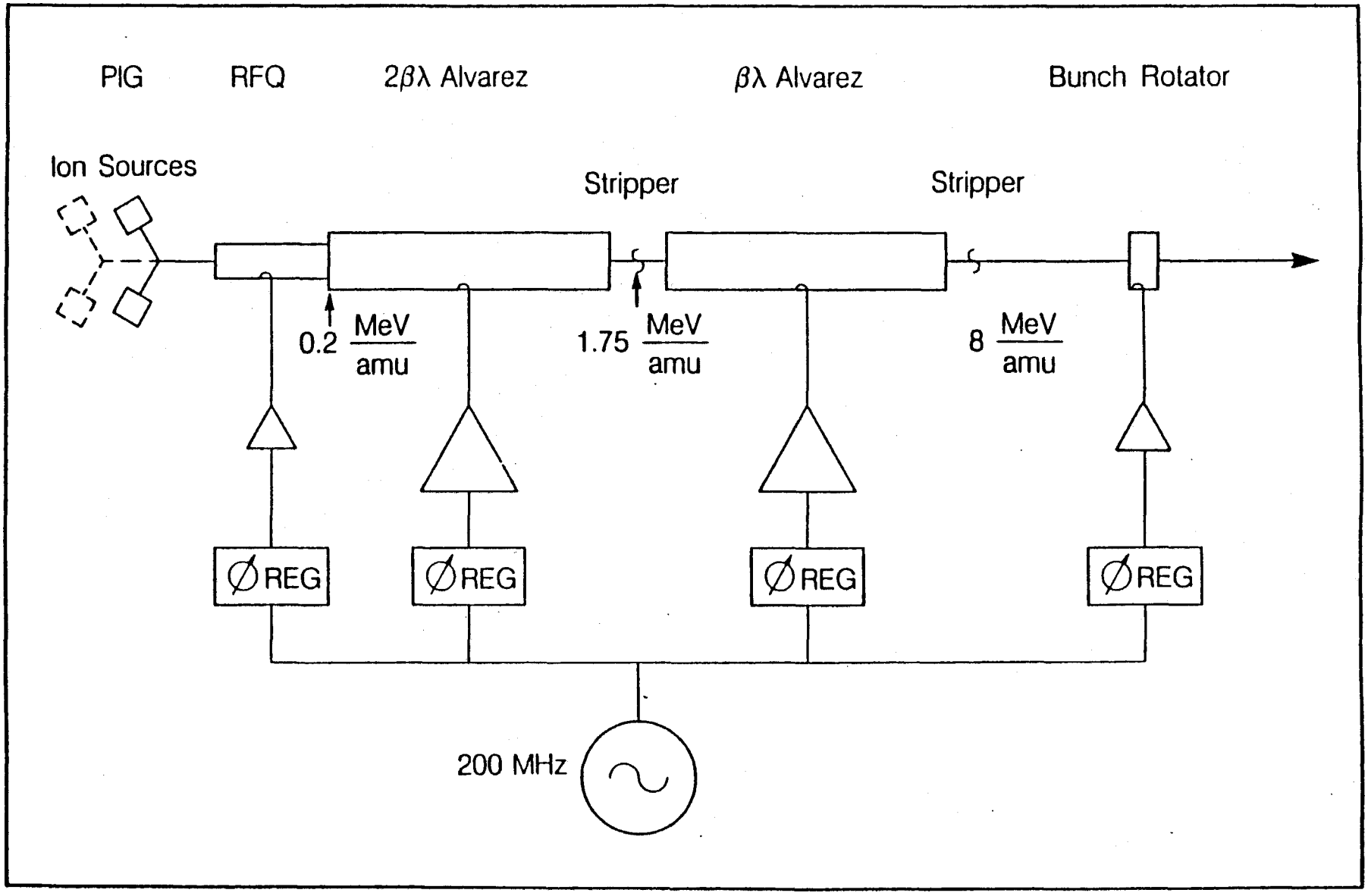


Fig. 5 Straight section of synchrotron ring showing injection magnets.



XBL 836-326A

Fig. 6 Injector schematic.

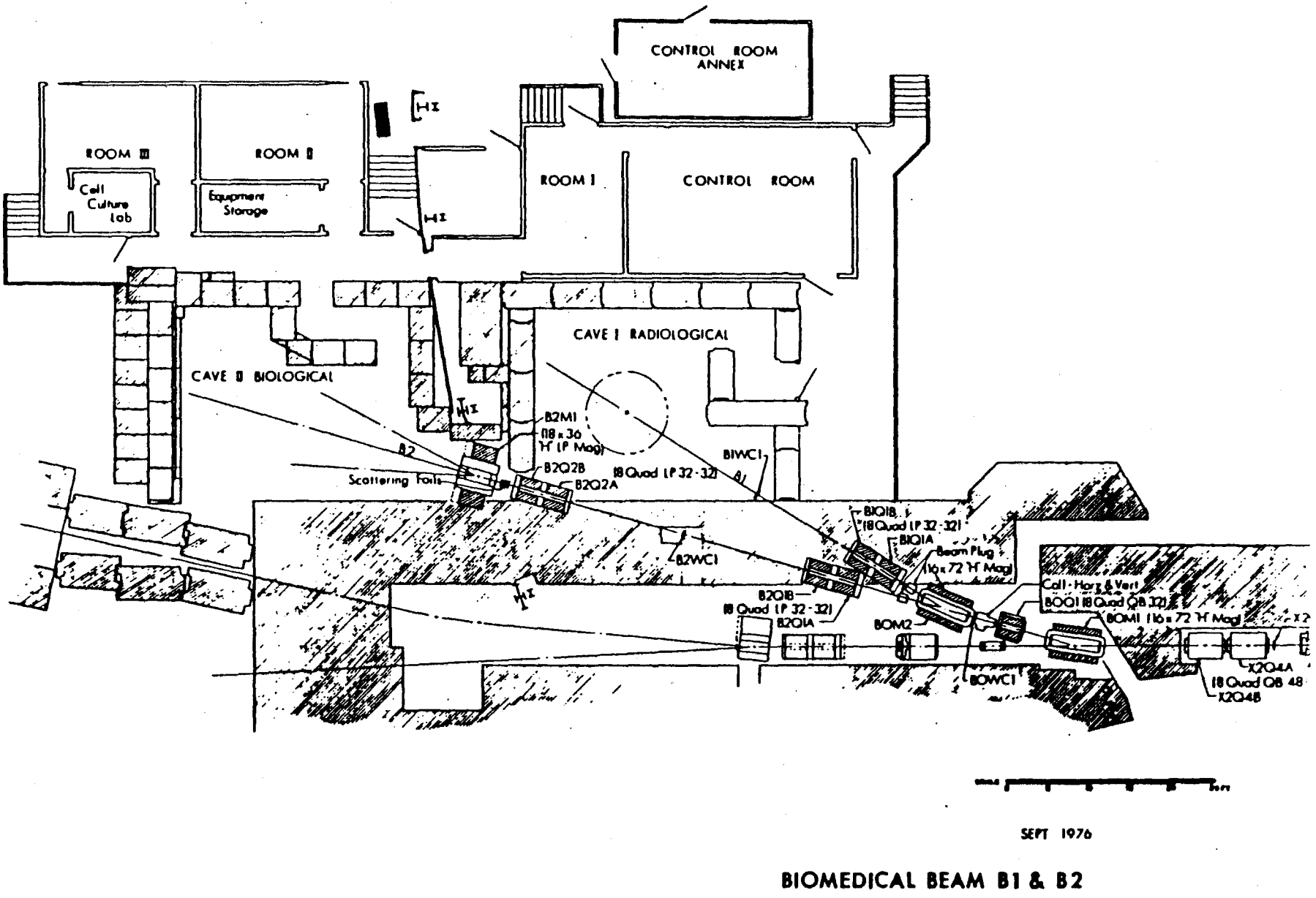


Fig. 7 Layout of treatment room at the Bevalac Radiotherapy Facility.

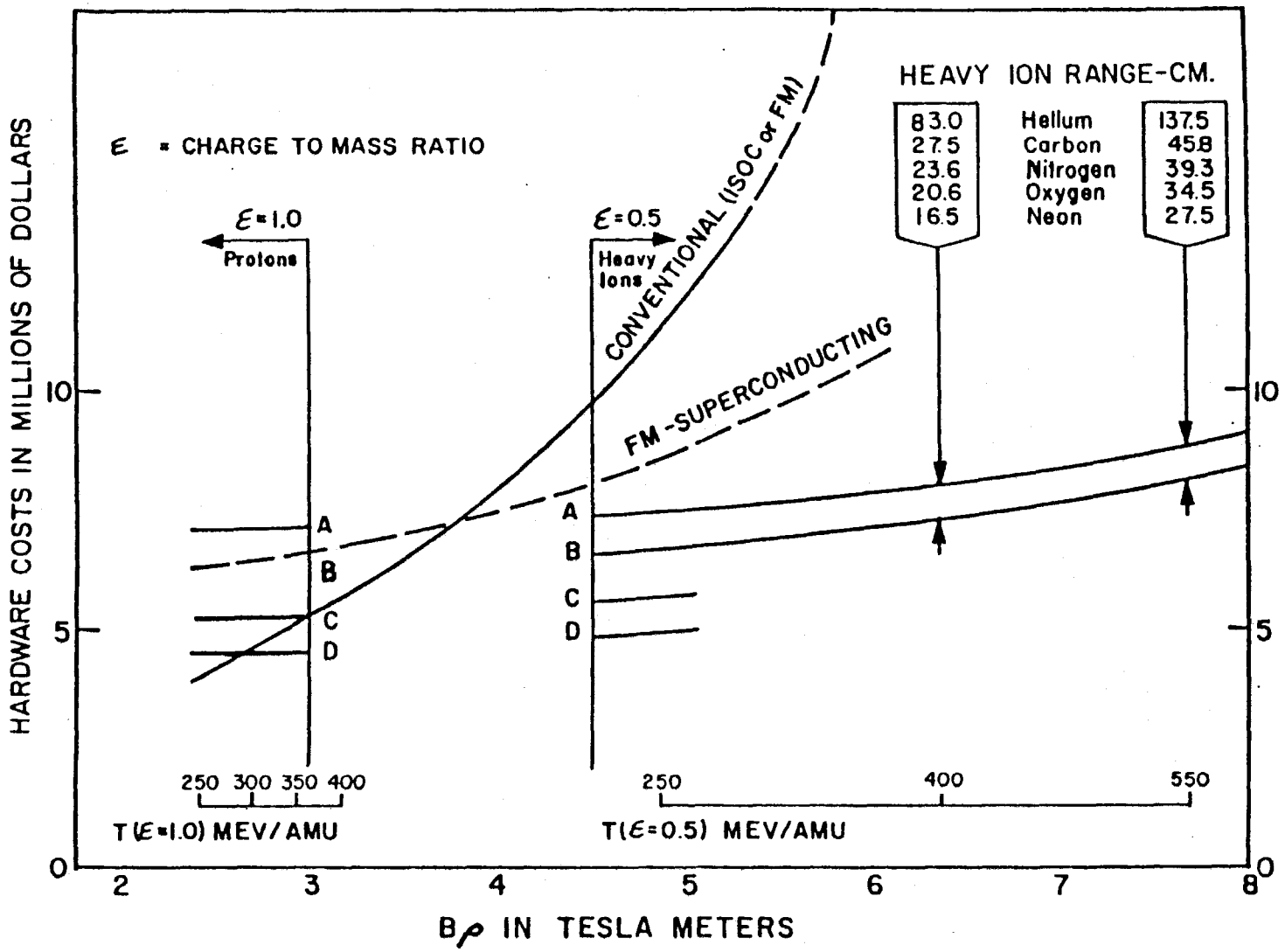


FIG. 22: Cost and performance summary of circular accelerators. Shown are base costs in FY 1977$ versus particle rigidity Bρ in Tm. Separate scales indicate the kinetic energies for ε=0.5 (heavy ions) and ε=1 (protons) corresponding to a given Bρ. The curves A,B,C & D show synchrotron costs vs. beam rigidity, with cost differences due to choice of injector.
A - heavy ion injector, neutron beam and isotope production capability
B - heavy ion injector, isotope production capability
C - p, α injector, isotope production capability
D - p, α injector only
Conventional cyclotrons are a good choice for protons, but prohibitively expensive for heavy ions. An FM-superconducting cyclotron is the cheapest heavy ion cyclotron.

Fig. 8 Cost and performance summary of circular accelerators.

CYCLOTRONS AND SYNCHROCYCLOTRONS FOR ONCOLOGY THERAPY

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I. Introduction

The use of cyclotrons and synchrocyclotrons to produce ionizing beams for oncology therapy is undergoing a major evolution as a consequence of recent progress in adapting superconducting techniques to each of these accelerator systems. These new devices, the so-called "superconducting" cyclotron or "superconducting" synchrocyclotron, are in fact simply an isochronous cyclotron or a synchrocyclotron with a superconducting main coil. The apparently simple step of making the main coil superconducting has a large impact on the overall accelerator design.

The direct effect of making the main coil superconducting is to rather fully free the design from the cost constraints related to main coil current. Cost optimization of the design with these constraints removed leads to much higher magnetic fields, typically in the range around 5 tesla versus the 1.4 to 2.0 tesla typical in room temperature cyclotrons and synchrocyclotrons. The higher magnetic field makes the accelerator smaller and lighter relative to a room temperature cyclotron or synchrocyclotron of the same energy. Typical linear dimensions of a superconducting design are about one-third as large as the corresponding dimensions for a room temperature system and typical weight of a superconducting cyclotron is about one-twentieth of the corresponding room temperature weight. The large decrease in size and weight more than off-sets the added costs which go with buying superconductor, constructing a low temperature vessel, installing super insulation, etc. Overall the superconducting cyclotron is then usually one-third to one-half the cost of a room temperature cyclotron of the same energy, and synchrocyclotrons would behave similarly.

At this time (March 1985) only one superconducting cyclotron is in operation in the world, this being the "K500" at the National Superconducting Cyclotron Laboratory in East Lansing and there are no superconducting synchrocyclotrons. The advantages of the superconducting technology are, however, broadly accepted in the physics community--five of eight major cyclotrons now in construction in the world are superconducting and the three which are not predate the introduction of the superconducting technology. (To the author's knowledge, no synchrocyclotrons are under construction at this time.)

The reduction in size and cost which makes superconducting accelerators attractive for physics applications is of course also highly important in medical applications. A first such project, a 50 MeV deuteron cyclotron for

neutron therapy is then already in process. In this application the characteristics of the superconducting cyclotron lead to a greatly simplified design in which the cyclotron is itself mounted in the head of an isocentric rotation system in much the same fashion as a modern electron linear accelerator therapy system. Neutrons are produced in an internal target so that extraction system, beam transport system and isocentric external magnet system are all eliminated. Major features of this project are described in Section II of this paper and in references 1 and 2.

Determining the optimum design for a medical proton therapy accelerator is unfortunately a significantly more complicated matter than the neutron application. Three different kinds of accelerators are likely choices namely the cyclotron, the synchrocyclotron, and the synchrotron, and for each both room temperature and superconducting options must be considered.

First of all the conventional room temperature isochronous cyclotron meets or exceeds all proton therapy requirements and the technology is firmly developed. Such a cyclotron provides easily variable energy and beam current up to 10 microamps, i.e. a thousand times higher than is conventionally used in therapy. A fairly well optimized version of such a cyclotron has been described in an earlier paper (ref 3).

A 250 MeV isochronous cyclotron can also be superconducting but, for protons, focussing and extraction limit the magnetic field which can be used to about 2.5 tesla (reference 4 explains the precise limiting phenomena in some detail). An increase in field to 2.5 tesla is a significant but not a dominating gain relative to the 1.4-1.8 tesla, which would be used in a room temperature cyclotron. The superconducting isochronous cyclotron is then not exceptionally attractive as a proton therapy system and detailed studies have not been pursued except to the degree of using scaling relationships to estimate some of the major parameters such as magnet size, cost, etc.

The room temperature synchrocyclotron is the accelerator used in presently operating proton therapy programs. It is fairly well matched to the therapy requirements except that energy variation must be accomplished by penetration through degraders, which also reduces beam quality. Room temperature synchrocyclotrons are also massive and bulky. Construction of a new such machine would involve large cost for both the accelerator and the associated building.

The synchrocyclotron can also be designed as a superconducting system and this concept is compatible with very high magnetic field values, possibly as high as 7 tesla. As with the room temperature synchrocyclotron the energy is fixed, but the beam current (10-100 na) substantially exceeds the therapy requirement so that energy variation by degrading is feasible. A design study for a superconducting synchrocyclotron is described in Section III of this paper.

The proton synchrotron is an accelerator system which easily achieves the desired proton energies. Energy variability is also straight forward. Careful design is required to achieve 10 nanoamps of beam current and the complexity of a synchrotron is a significant possible disadvantage (the need for an injector, the carefully synchronized time variations required by the magnet, the rf frequency, and the systems used to inject and extract, etc.). Synchrotrons of both room temperature and superconducting designs are

described in other papers at this conference and are therefore not discussed further here. Omitting the synchrotrons, Section IV of this paper undertakes to compare major attributes of a number of cyclotron and synchrocyclotron systems of interest in oncology therapy.

II. A Superconducting Cyclotron for Neutron Therapy

Figure 1 shows a cutaway view of the superconducting cyclotron which is being constructed at the National Superconducting Cyclotron Laboratory as a neutron therapy system for Detroit's Harper Hospital. The cyclotron uses a "pillbox" yoke so that the steel of the yoke functions as an integral part of the radiation shielding system, protecting the patient from primary neutrons except for the area of the tumor and also protecting personnel from residual radioactivity. Neutrons produced in the internal target are collimated in a conventional collimator system mounted in the yoke and directed at the tumor region. The acceleration system for the cyclotron is a "dee-in-valley" system in which a dee is mounted in each of the three valleys of a three hill, three valley magnet. An ion source is inserted along the axis of the magnet in a manner which gives accurate positioning relative to the acceleration structure. The cryostat for the main coil utilizes a novel, invertible, continuously vented structure and a simple bath cooling design holds cryogens sufficient to provide for a week of coil operation.

Figure 2 displays the isocentric mounting system for the Harper Hospital neutron therapy cyclotron. The 25 ton mass of the cyclotron plus a corresponding counterweight are easily supported by a pair of large steel rings which rest on below-the-floor rollers. With box rings constructed of 3/4 inch plates, maximum stress in the rings is 5,800 lbs/sq. inch and stress deflection of the neutron aiming point as the cyclotron is rotated is small. (The aiming error introduced by the deflection is 0.7 mm.) The location of the counterweight--at zero degrees relative to the direction of the deuteron beam as it strikes the target--also means that the counterweight plays an important role in shielding the most penetrating component of the neutron spectrum. The thickness of shielding walls can then be sizably reduced.

Figure 3 shows the overall system as seen by the physician and patient. The patient table mounts outside the ring system on a fixed concrete floor with a canterlevered extension to support the patient. The table system includes all conventional table position adjustments. The floor includes a special custom designed moveable section which moves aside as the cyclotron shifts to the angular region immediately below the table. When the cyclotron is at any of the upward angular locations the special floor provides a convenient and comfortable footing for patient and physician access. The system includes arrangements for quickly and conveniently changing collimators and for verifying patient position.

The complete cyclotron and support system should undergo Laboratory tests in the summer of 1986. Patient treatment using the facility should begin at Harper Hospital early in 1987.

III. Superconducting Synchrocyclotron

Historically, the synchrocyclotron has been the dominant proton therapy accelerator. Discussion at this conference has focused on a 250 MeV proton beam with intensity of 10 nanoamperes as meeting the requirements for proton radiotherapy. Capability for lowering the beam energy to values as low as 70 MeV is also important. The synchrocyclotron in fact usually achieves much higher extracted currents, up to levels of a few microamperes in recently modified synchrocyclotrons, which gives a comfortable margin to cover intensity losses associated with the process of degrading the energy to lower values in situations where lower energy is needed.

The room temperature synchrocyclotron has the disadvantage of being quite massive. The Rochester synchrocyclotron, for example, produced 240 MeV protons and used a 1000 ton magnet (ref 5). The Harvard synchrocyclotron reaches 165 MeV, with a 640 ton magnet. Noting that the cost of machined steel is typically $1-$1.25/lb, the cost of steel for a conventional synchrocyclotron is then of itself an almost prohibitive expense in today's economy. From the point of view of building construction, it is also clearly desirable to reduce the weight of the cyclotron magnet as much as possible. Achieving a weight reduction which would permit isocentric mounting of the cyclotron in much the same manner as the previously described neutron system would offer many significant theraputic advantages, as well as reducing cost.

Application of superconducting techniques to the synchrocyclotron leads to structures which are much more compact than the conventional synchrocyclotron and much lighter. Assuming that focussing is derived from the average field gradient in the customary synchrocyclotron way there is in fact no clear limit on the maximum field strength which might be used, and the higher the field the lighter the magnet. In particular, superconducting magnets of this general type and size have been successfully constructed in the range of fields up to and beyond 10 tesla. There is however a general consensus to the effect that the overall cost optimum for such magnets is at somewhat lower fields and the studies described here have therefore used 5 tesla and 7 tesla as illustrative cases. For 250 MeV, the magnet would weigh 80 tons at 5 tesla and 60 tons at 7 tesla both of which are light enough to be compatible with isocentric mounting.

Figure 4 and 5 give a plan view and a vertical section view of such a synchrocyclotron and generally illustrate these features. The design assumes a one dee accelerating structure as is normal in synchrocyclotrons, but the high frequency (84 mhz at a central field of 5.5 tesla and 120 mhz at 7.7 tesla) leads to resonators which end within the magnet if built with the normal "quarter wave" design and for these two cases one then needs "three-quarter" and "five-quarter lambda" systems, respectively, to bring the tuning elements outside the magnet yoke. Designs of this type are however straightforward, the synchrocyclotrons at Berkeley (ref 6) and Cern (ref 7) being examples of three-quarter lambda systems which have functioned smoothly for many years.

Beam extraction from the superconducting synchrocyclotron is assumed to be accomplished by a "peeler" induced regenerative system in the fashion which is basically standard for synchrocyclotrons. Since this extraction is accomplished by means of magnetic perturbations one qualitatively expects the behavior of the extraction process to scale with the magnetic field, i.e. that behavior at high fields will be similar to behavior at low fields.

Calculations checking this point have however not been made. Such calculations should clearly be an early element in any further design study.

Other elements of the superconducting synchrocyclotron system are reasonably evident in the figures. The ion source enters axially through the magnet, the main superconducting coil is in an annular cryostat, room temperature penetrations through this cryostat provide for the dee stem and the extraction path, etc. The superconducting coil is supported by a network of thermally insulating tension links as is normal for such coils, the coil is electrically driven thru a standard cryogenic lead system, a normal superinsulated radiation shield is provided, etc. Since the stored magnetic energy of such a system is fairly high--seven megajoules, for example, for the 5 tesla system--the coil would be designed to be cryogenically stable to avoid the possibility of damage to the coil in an inadvertent quench.

Overall, a synchrocyclotron such as described would be categorized as a new application of existing technology rather than as requiring development of new technology. Information on other details of the design is available.

IV. System Comparisons

Given the studies of superconducting synchrocyclotrons described in the previous section and utilizing an earlier study of a room temperature variable energy isochronous cyclotron (ref 3), it is possible to assemble a summary list of proton cyclotrons and synchrocyclotrons which might be of interest for the medical application. Table I lists some of the important parameters which result. In this table Case #1 is based on the 1972 engineering study of a room temperature isochronous cyclotron. Cases 7 and 8 are based on the less complete recent studies of the superconducting synchrocyclotron, described in section III above. Other entries in the Table are interpolated, or estimated on the basis of experience, using applicable scaling rules for cyclotrons.

Costs given in Table I are intended to represent the accelerator system only, where the accelerator system is taken to include all necessary controls, power supplies, etc. The accelerator also includes a beam extraction system out to a first beam stop at the exit port of the magnet but does not include beam transport elements beyond that point. Costs do not include buildings, shielding, patient facilities, normal utilities such as cooling water, primary electric service disconnects, etc. Prices do include, for the superconducting systems, a refrigerator-liquifier of capacity adequate to cool down the coil in a 10 day period and to maintain the cold mass at liquid helium temperature on an indefinite basis.

The absolute value of costs in Table I are undoubtedly laboratory dependent and any serious consideration of an actual project should obviously involve a careful engineering re-estimate based on the cost structure of the site at which the work would be done. The relative comparisons between different types of accelerators should have much broader general validity and from these comparisons one sees that the superconducting synchrocyclotron would have a very substantial cost advantage relative to the isochronous cyclotron. A similar conclusion of course also holds relative to the room temperature synchrocyclotron (case 6).

It should be noted that the "isochronous cyclotrons" in the Table produce very much higher beams than are required, i.e. external beams of up to 10 microamps. A variable energy isochronous cyclotron, such as in Cases 1, 2, and 3, also provides beams whose energy can be arbitrarily selected at any value within the specified range. The high current of the isochronous cyclotron is, of course, largely of no help in the therapy application and variable energy is useful but perhaps not to a sufficient degree to justify the sizeable additional cost.

With respect to the superconducting synchrocyclotron one notes from the Table that the 7 tesla design (case 8) is slightly less expensive than the 5 tesla design (case 7) and slightly lighter, but the differences are small enough that one might well prefer the more conservative 5 tesla choice, this being the field used in the present generation of superconducting research cyclotrons.

Case 9 of Table I is the neutron therapy cyclotron described in Section II, while Cases 10, 11, and 12 are possible cyclotrons for so-called "stripped nucleus" therapy, a therapy modality which, though expensive, is expected to combine the benefits of both proton and neutron modalities. Case 10, in particular, is the cyclotron now under construction at NSCL for physics applications, except with the variable energy feature suppressed. This cyclotron is expected to come into operation early in 1987 and as a national user facility could be available for biological and medical studies if appropriately persuasive proposals were submitted to the Program Advisory Committee.

In conclusion, we note from Table I that a number of the accelerator options are apparently now in a cost range comparable to modern photon therapy units. If this conclusion is confirmed, a major change in the direction of oncology therapy would seem an expected consequence. This expectation follows from the observation that if neutrons, protons, and photons were equal in cost, the photon would never be selected as the radiation of choice, since the proton matches the photon in biological characteristics but is much better in physical characteristics, while the neutron matches the photon in physical characteristics but is significantly better in biological characteristics. There is then no situation in which the photon is superior overall. (In this statement, "physical characteristics" refers to the fraction of dose delivered to the tumor area relative to the fraction delivered to normal tissue, while "biological characteristics" refers to the ability to lethally damage tumor cells relative to the number of normal cells which are lethally damaged.) We then may well be at the beginning of a period of quite significant change in radiation oncology therapy.

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[2]H. Blosser, D. Johnson, E. Kashy, B. Milton, and J. Riedel, Proceedings of the Tenth International Conference on Cyclotrons (1984)436.

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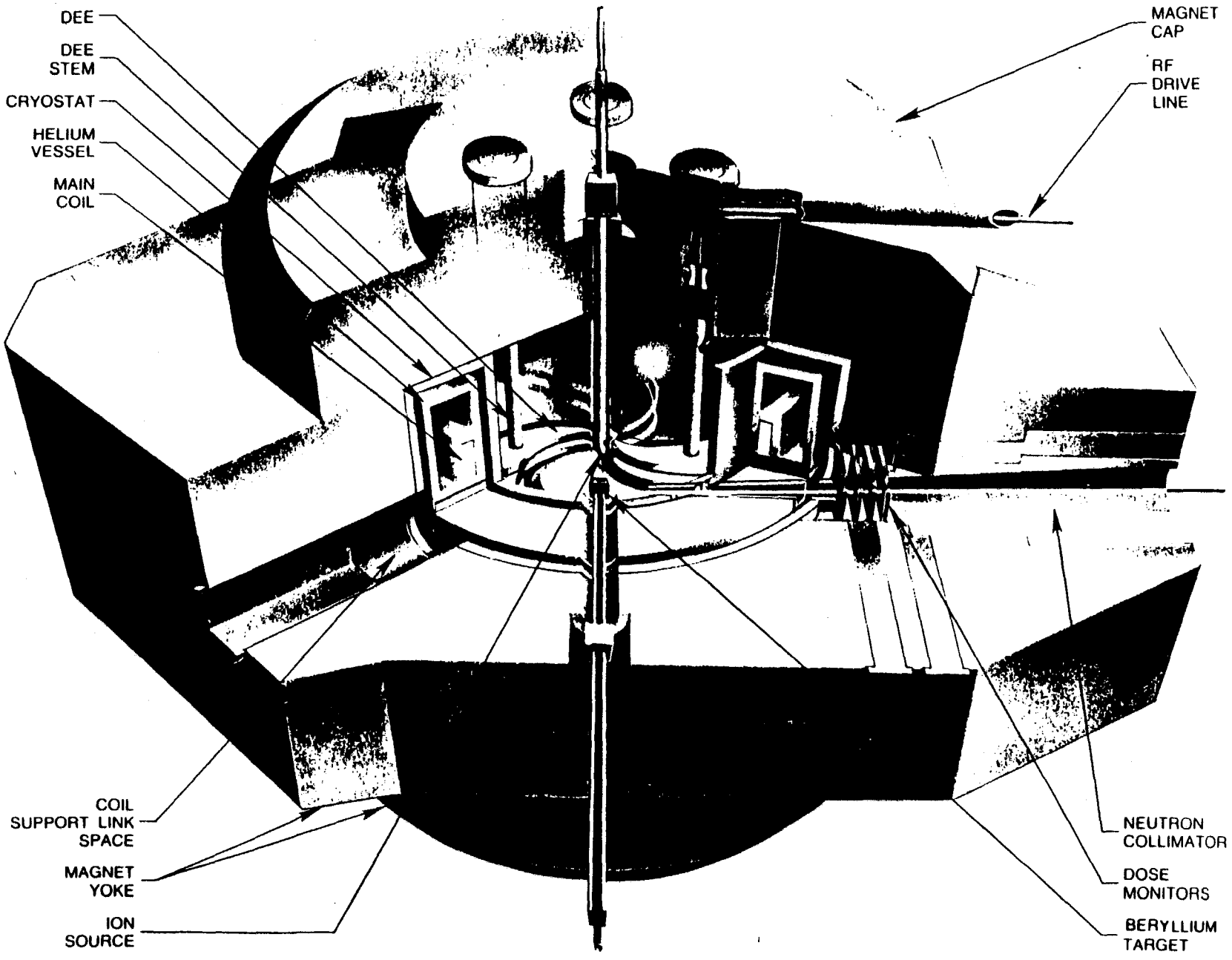
DEE
DEE STEM
CRYOSTAT
HELIUM VESSEL
MAIN COIL
MAGNET CAP
RF DRIVE LINE
COIL SUPPORT LINK SPACE
MAGNET YOKE
ION SOURCE
NEUTRON COLLIMATOR
DOSE MONITORS
BERYLLIUM TARGET

Figure 1

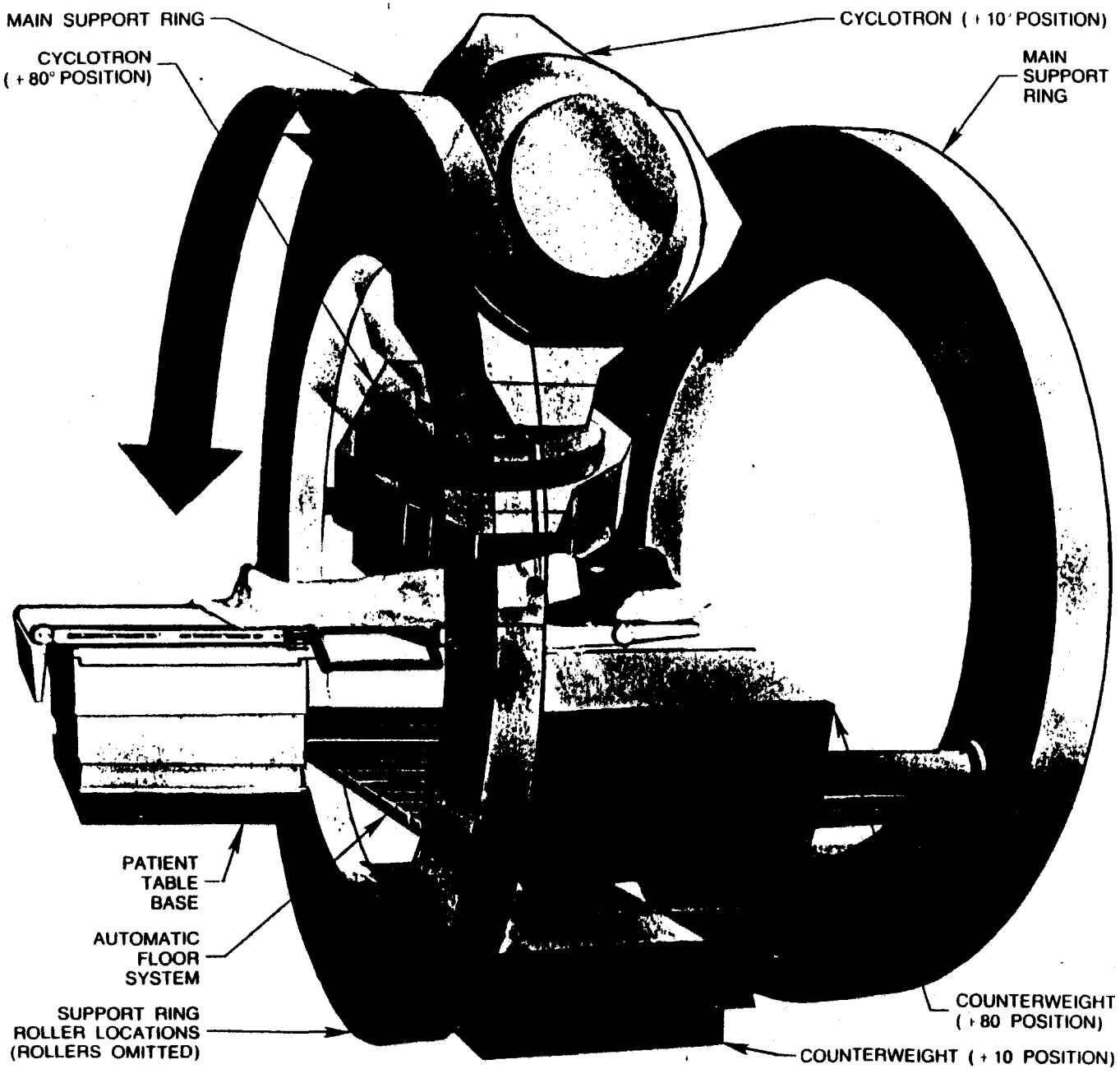
MAIN SUPPORT RING
CYCLOTRON (+ 80° POSITION)
CYCLOTRON (+ 10° POSITION)
MAIN SUPPORT RING
PATIENT TABLE BASE
AUTOMATIC FLOOR SYSTEM
SUPPORT RING ROLLER LOCATIONS (ROLLERS OMITTED)
COUNTERWEIGHT (+ 80 POSITION)
COUNTERWEIGHT (+ 10 POSITION)

Figure 2

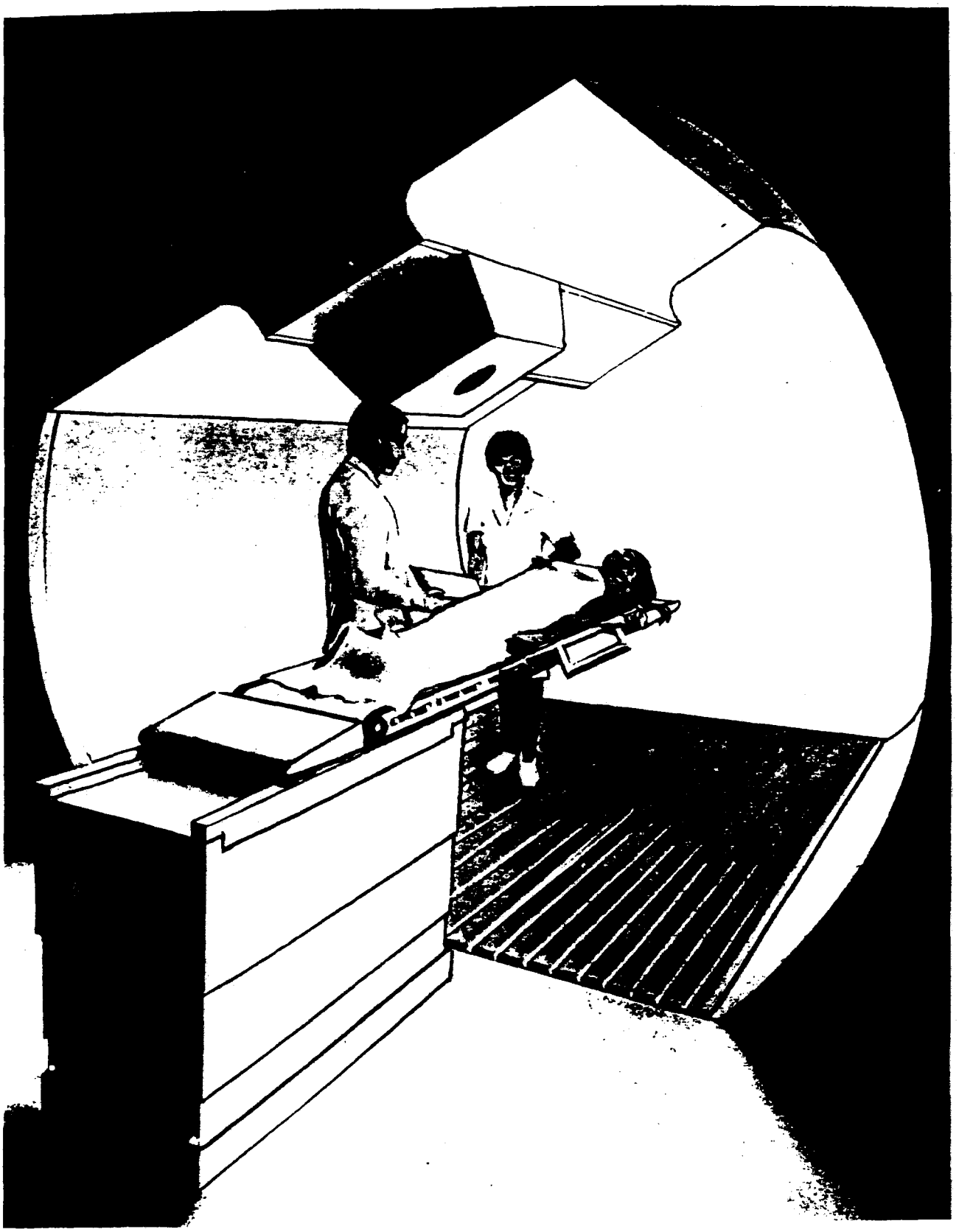

Figure 3

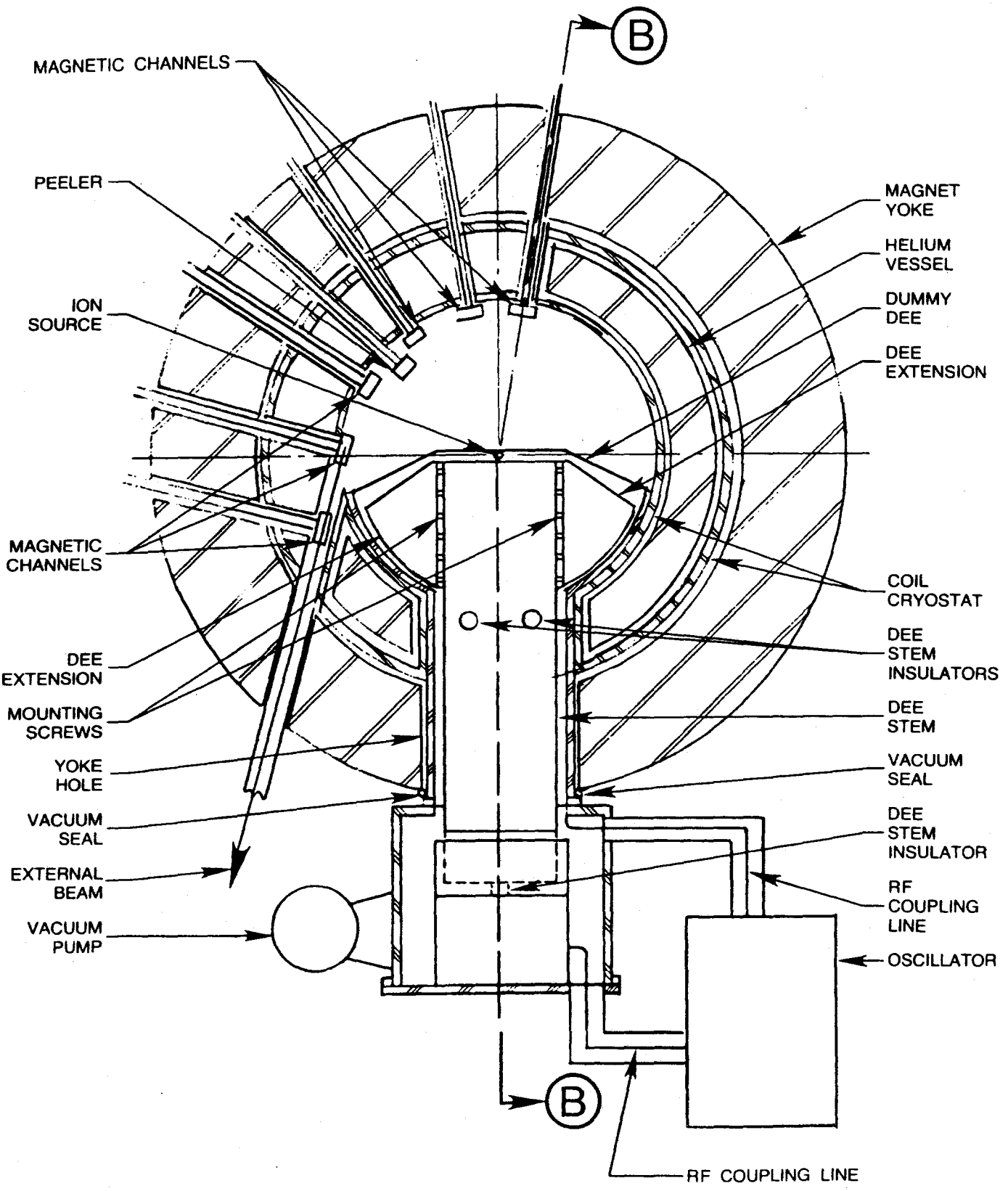
B
MAGNETIC CHANNELS
PEELER
ION SOURCE
MAGNETIC CHANNELS
DEE EXTENSION
MOUNTING SCREWS
YOKE HOLE
VACUUM SEAL
EXTERNAL BEAM
VACUUM PUMP
MAGNET YOKE
HELIUM VESSEL
DUMMY DEE
DEE EXTENSION
COIL CRYOSTAT
DEE STEM INSULATORS
DEE STEM
VACUUM SEAL
DEE STEM INSULATOR
RF COUPLING LINE
OSCILLATOR
B
RF COUPLING LINE

Figure 4

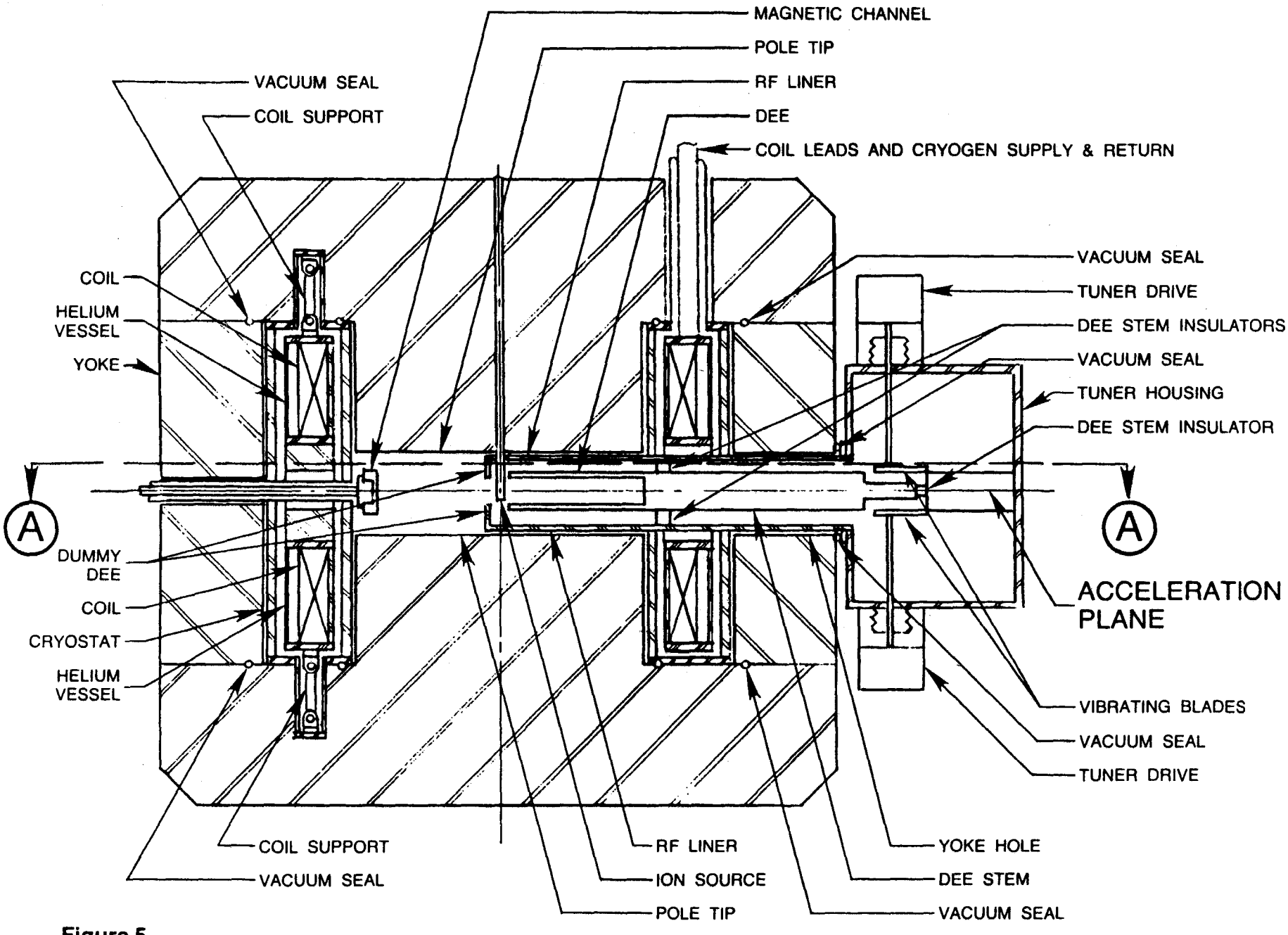
MAGNETIC CHANNEL
POLE TIP
RF LINER
DEE
COIL LEADS AND CRYOGEN SUPPLY & RETURN
VACUUM SEAL
COIL SUPPORT
COIL
HELIUM VESSEL
YOKE
VACUUM SEAL
TUNER DRIVE
DEE STEM INSULATORS
VACUUM SEAL
TUNER HOUSING
DEE STEM INSULATOR
A
A
DUMMY DEE
COIL
CRYOSTAT
HELIUM VESSEL
ACCELERATION PLANE
VIBRATING BLADES
VACUUM SEAL
TUNER DRIVE
COIL SUPPORT
VACUUM SEAL
RF LINER
ION SOURCE
POLE TIP
YOKE HOLE
DEE STEM
VACUUM SEAL

Figure 5

Fig. 1.--Cutaway view of 50 MeV, internal target, deuteron cyclotron for neutron therapy.

Fig. 2.--Isocentric mounting system for neutron therapy cyclotron. The system provides full 360 degree rotation of the cyclotron.

Fig. 3.--The neutron therapy cyclotron system as seen by the physician and patient. The floor below the patient automatically moves aside when the cyclotron moves to locations in the lower quadrant.

Fig. 4.--Plan view of a 250 MeV superconducting proton therapy synchrocyclotron (view as seen from Section A-A Fig. 5). For a magnetic field of 5 tesla at the extraction radius, the overall outer diameter of the yoke is 100", the extraction radius is 19" and the central magnetic field is approximately 5.5 tesla (corresponding to a maximum rf frequency of 84 mhz).

Fig. 5.--Vertical section view through 250 MeV superconducting synchrocyclotron (view as seen from Section B-B Fig. 4). For a magnetic field of 5 tesla at the extraction radius, the overall yoke height is approximately 90".

TABLE I: CYCLOTRONS AND SYNCHROCYCLOTRONS FOR ONCOLOGY THERAPY

Case#	Par.	Energy (MeV)	External Beam Current (nanoamps)	Cyclotron Type	Accelerating System	Magnet	B° (tesla)	Iron Wt. tons	Pole diam.	Cost M$(85)
1	p	40-210	10,000	Isochronous	dees in gap	conventional	1.4	325	125"	5.0
2	p	60-250	10,000	"	" " "	"	"	390	136"	5.5
3	p	"	10,000	"	dees in valley	"	"	300	126"	4.6
4	p	250	10,000	"	" " "	"	"	280	125"	3.2
5	p	"	2,000	"	" " "	Superconducting	2.6	150	76"	2.5
6	p	"	1,000	Synchro-cyc	dees in gap λ/4	Conventional	1.6	1000	130"	7.0
7	p	"	500	Synchro-cyc	" " " 3/4λ	Superconducting	5.0	80	44"	1.6
8	p	"	500	Synchro-cyc	" " " 5/4λ	"	7.0	60	33"	1.5
9	d	50	(20,000 internal)	Isochronous	dees in valley	"	4.6	25	26"	0.9***
10	^{12}C	2,400*	100	"		"	4.0	240	82"	4.2
11	^{12}C	3,000**	100	"		"				≈4.7
12	^{20}Ne	6,800**	20	"		"				≈5.9

* range 9 cm
** range 12 cm
*** 360° gantry add 0.5

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Neutron Therapy Department

July 1, 1985

Re: Medical Workshop on Accelerators
for Charged-Particle Beam Therapy
held at Fermilab, January, 1985.

We have just learned that Table I from "Cyclotrons and Synchrocyclotrons for Oncology Therapy" by H. Blosser, et al., has been unintentionally omitted.

A copy of this table is enclosed. Please add it to your proceedings after page 114.

If you did not pick up a copy of the Fermilab Proton Beam Therapy Facility Proposal at the workshop, they are available upon request.

Phone: (312) 840-3865 • From Chicago: 261-1910/ext. 3865 • FTS: 370-3865 • From Suburbs: 231-6040/ext. 3865

250 MeV SYNCHROTRON FOR PROTON THERAPY

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I. SPECIFICATIONS

These were discussed yesterday by Michael. Let's review them:

In principle, alpha particles can give a sharper dose distribution than protons. However, for equal penetration an alpha beam must have four times the energy and twice the magnetic rigidity; therefore the machine is twice as large as the already-large p machine. Other items such as the main power supply scale accordingly. One has to show that the advantage gained in practice is worth this substantial additional effort, for a significant number of patients. Of course one can design for protons and then use that machine for alphas as far as it will go; for instance the 250 MeV proton machine could be used to treat eyes with alphas, and this might be very sensible. For now, let's confine ourselves to protons.

An energy of 250 MeV penetrates 37.6 cm of water; this is more than adequate. Degrading from here down to 60 MeV would produce a rather sloppy Bragg peak, so the energy ought to be variable, even if it is held fixed for any given treatment.

An accelerated current of about 20 nAmp is indicated to meet the goal of 1 Gr../minute for large fields with some safety margin. Assume for instance that we wish to treat a 30 cm diameter field to a depth of 15 cm (a fairly extreme example):

$$i = \frac{1\ \text{Gray}}{\text{min}} \times \frac{1.2\times10^{9}\ \text{proton}}{\text{Gray}\cdot\text{cm}^2} \times 707\ \text{cm}^2 \times \frac{\text{min}}{60\ \text{sec}} \times \frac{1.6\times10^{-19}\ \text{coul}}{\text{proton}} = 2.3\ \text{nAmps}$$

However, if we use the passive double-scattering technique to get a flat field, we lose a factor of five, and the extraction/beam transport process could cost us another factor of two, so 20 nAmps seems about right.

This unfortunately exhausts the list of absolute requirements. Michael quite properly pointed out that the clinician is interested in a complete facility, not a machine. But this does not mean that the designer has to consider the entire facility ab initio, and I shall not do so, except to try to arrive at a machine which will not be incompatible with any reasonable clinical goals. Hospital based is the overriding requirement. This means reasonable size and weight; however, we are talking about a pretty large facility so there is no point in taking heroic measures to make the machine extra small. Compatibility with an isocentric gantry mainly means keeping the emittances under control, and scanned beams demand a reasonable duty factor, say 50% or better. The most serious shielding problems will arise in connection with the gantry.

Another class of requirements: reliability, maintainability and ease of operation will get no arguments from anyone; of course the question is how to achieve them. The LBL/Arizona study appears to assume that the very first machine will have to meet all these requirements within a short time after construction, and

PTA 1/22/85

concludes that this can only be done by a combination of the obvious techniques (i.e. conservative design choices, use of proven commercial components where possible ...) with an intensive application of reliability analysis. I could not disagree more strongly here. In the long run, reliability can only be guaranteed by gradual progress through a series of prototypes.

Finally, cost is obviously an important factor. Although I have been foolish enough to fling cost estimates about from time to time, our design is not really complete enough yet, nor are its less conventional aspects sufficiently well tested, to allow an accurate estimate. The numbers that have been quoted perhaps reflect our hopes more than a true assessment of what can be done. A study done by Andy and Kris Johnson a few years ago indicates that a machine costing under $2,000,000 ought to break even on a fee-for-service basis. This goal does not seem impossible.

II. TYPE OF MACHINE

A 250 MeV proton linac is a very large machine. Proton linacs are not easily tunable, and perhaps most important, one is unable to trade off the low current requirement for cost savings.

The FM cyclotron is well-proven technology and features a simple control system and no injector. However, we are talking about a 400-ton object which would certainly have to be built in situ. Output energy is fixed and extraction efficiency is good only with extremely careful engineering of the central region.

An alternating-gradient synchrotron seems the best choice by far. The current requirement can be met and money can be saved by keeping the aperture just large enough to meet it. Output energy is easily variable. The machine weighs a few tons. It should be relatively easy to shield since extraction efficiency is high and it is possible to control where the beam losses occur. Construction is intrinsically modular and (if the machine is ever commercialized) it is reasonable to envision building and testing a machine at the factory and then shipping it out to be reassembled and commissioned in a matter of weeks. The control system is more complicated but this is precisely where technology has made its greatest strides. Finding a reliable and economical injector may be the greatest problem.

III. PTA250 REFERENCE DESIGN

I have attached a reference design. Please don't take it too literally. For instance, it wasn't really made with the 50% duty factor in mind. This will increase the cycle time, reducing the beam, but with scanned beams one ought at least to recoup the factor of five lost in generating a flat field by passive means. The reference design is only meant to convey the general scale of the machine we are discussing. Let me go into just a few of the design decisions and tradeoffs.

The overall size of about 7.5 meters is determined by how much field one can get in the laminated magnets plus the length of straight sections one needs to fit in the RF, extraction gear, internal beam monitors etc. I started off with a quadrant design; one could go to more superperiods but there does not seem to be any special advantage to this. 1.2 Tesla max field is certainly a conservative assumption; one may be able to go to 1.5 with a corresponding reduction in size.

The next choice is the lattice. By the basic rules (90^{o} betatron phase shift per superperiod) any reasonable machine in this energy range will have a tune near 1, making it a weak-focusing machine in some sense even though it is alternating gradient. The lattice should achieve this with minimal gradients; also, the beta functions should be reasonably flat. The 4 x (OFDFO) lattice, which is a variant of the quadrupole triplet idea, seems to meet these goals. Perhaps the most important goal is that, if possible, the machine stay below transition. This appears to be just possible at 250 MeV.

The next major choice is the aperture. This will impact not only the magnet weight but also the size of the power supply, since the gap height determines the current and the volume determines the inductance. First, we had to pick a repetition rate to determine how many protons need to be packed into a pulse. There is no sharp optimum, but 10/sec seems clinically convenient and is not far from the figures suggested by the LBL/Arizona study. Given the number of protons per pulse, the aperture size is determined either by the size of the matched beam at injection or by the tune shift at injection. Assuming injection at 300 KeV (which choice is justified later), the two criteria are comparable for the aperture (about 1 x 3 inches) we have chosen.

Having picked the aperture, one has a number of choices revolving around fabrication. Putting the entire magnet under vacuum has been done at a number of synchrotrons, and takes advantage of the rather modest vacuum requirement. It allows one to utilize the aperture more efficiently, and circumvents the need for a beam pipe with its eddy-current problems. A more debatable (but also less far-reaching) decision is to try foil-wound coil construction rather than the more conventional hollow-conductor. This would permit a slightly smaller magnet (since the packing factor is higher) and eliminate the water manifold which, given the proportions of the coil, would have to be extensive. The foil-wound design cools well enough on paper, but thermal resistance at interfaces tends to be greater under vacuum; this will have to be tested.

The last decision I shall have time to cover is the choice of RF system. The frequency swing is prodigious (24/1). However, the energy gain/turn is a modest 1.2 KV, and it looks as though we can get by with a drift tube (filling one of the straight sections) loaded with 50 ohms. This solution is brute-force (14 KW of RF) but exceedingly simple, and should make for reliability.

IV. THE INJECTOR

The choice of injector may take the longest to settle down. One school of thought seems to revolve around injecting at a few MeV using one of a variety of off-the shelf machines (Dynamitron, Pelletron...). If we are thinking of single-turn injection (for simplicity) we require some tens of mA for about a microsecond, ten times per second - a very low duty factor. The standard machines are greatly overqualified for average current, somewhat underqualified for peak current, and all quite large.

If the aperture estimates are right, and if we can indeed get away with a broad-band RF system, injection at a few hundred KeV looks OK. This makes it possible to use one of a number of smaller machines: small pulsed RFQ, DC accelerating column powered by a Cockroft-Walton supply, pulsed accelerating column powered by a high-voltage pulse transformer. The last takes advantage of klystron modulating technology. The voltage is certainly no problem; the main question is whether the pulse-to-pulse repeatability and the flattop accuracy are adequate. We have started looking into this only recently.

We have studied the RFQ option (certainly the trendiest choice if nothing else) in some detail. Proton RFQ's have been operated to 3 MeV, but these are very large machines and produce monstrous peak currents which we do not need. A pulsed 700 KeV RFQ has been working well at Brookhaven for some time now, and some of the technology could be taken over. What distinguishes a 300 KeV RFQ qualitatively from a much larger one is that, even with full matching at both ends, the device need only be about half a wavelength long which makes it far easier to obtain the desired longitudinal voltage distribution.

V. THE HCL MACHINE DEVELOPMENT PROGRAM

Let me close with some remarks on where we stand. In the near term we plan to concentrate on two things: a) Fill in some gaping holes in the conceptual design (extraction mechanism, control system ...) to produce a well-rounded design which we can try to sell; b) Begin constructing and testing a short magnet section to investigate durability, field accuracy, fringe fields, behavior under vacuum etc. The second project is appropriate at this time because the magnet requirements are sufficiently well defined, because the magnet is by far the single largest component, and because the cycle time for specifying, procuring and testing a magnet prototype is fairly long.

Our longer range plans are also two-pronged: a) Prepare a proposal for a full facility. This will include all the ancillary items listed by Michael. Of course the prime movers in such a proposal will have to be the clinicians at some major center, but it would certainly help if we had a better idea of the machine by then. b) At the same time, construct a 70 MeV "eye machine" at HCL. This makes sense in our particular situation: it fits into real estate we control, it would be very useful in the treatment program, and it would serve as a test bed for the larger machine.

Let us hope that, after nearly a decade of dedicated-machine proposals, something will actually happen this time.

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PTA250 REFERENCE DESIGN A

I. INPUT PARAMETERS

particle	protons
energy range (main ring)	.3 - 250 MeV
average accelerated current	20 nanoamperes
pulse spacing	.1 second
max field	1.2 Tesla
coil type	foil wound, edge cooled
copper packing fraction	.8
coil window (HxW)	3.46 x 6.92 cm
# turns in coil	40
aperture (HxW)	2.6 x 7.8 cm (1 x 3 in)
lattice	4 x (OFDFO)
field index	approx. .8
circumference factor	2

II. LATTICE CHARACTERISTICS

bend radius	2.02 meter
tune (H,V)	1.2, .8 (approx.)
transition energy	250 MeV (approx.)
max beta functions (H,V)	3.9, 6.8 meter
max dispersion function	2.8 meter

III. ELECTRICAL

field range	.039 - 1.2 Tesla
current range	20 - 620 Amperes
coil resistance	.42 Ohms
coil inductance	77 milliHenry
I*R max	260 Volts
L*dI/dT max	920 Volts
average power	56 KiloWatt
stored energy	15 KiloJoule

IV. MISCELLANEOUS

tuneshift at injection	-.2 (bunch fact. = 5)
H x W of matched beam at 300 KeV	2.2 x 1.6 cm (LASL ion source)
weight (steel, copper)	3.8, .5 tons
operating temp. (steel, copper)	40, 50 degr. C
side of circumscribed square	7.5 meter (25 feet)
energy gain/turn	1.2 KiloVolts
RF power (50 ohm broadband system)	14 KiloWatts
time per turn	3.4 - .14 microsecond

A HOSPITAL-BASED PROTON MEDICAL ACCELERATOR*

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(Presented at the joint FNAL/ANL Workshop on Charged Particle Accelerators for Cancer Therapy, Fermilab, January 24-25, 1985)

My goal in the design of a medical accelerator is to focus on one that would be suitable for general use in a hospital or clinical setting rather than one that might be more appropriate for large dedicated medical centers. This choice is based on the belief that if protons were generally available in hospitals, and as convenient to use as any other method of radiation treatment of cancer, then protons would prove effective for treatment of many more cancer sites than is the case today. I am under no illusion about the amount of R&D and length of time required to demonstrate that protons are at least as good as present methods for treatment of tumor sites for which they have not yet been used. In the long run, however, I think protons will take their place in hospitals along with electron beams to give the physician a wider choice in the treatment of cancer.

To achieve this goal, minimizing the construction and operating cost of the accelerator and its transport and beam delivery system is very important, simplicity and reliability are essential, and the flexibility and ease of use of the entire system are very important. The latter places a strong emphasis on being able to safely and inexpensively transport 250 MeV proton beams in order to provide for several different treatment rooms, each of which might have different characteristics, including at least one with beams from more than one direction.

It would be highly desirable to be able to scan the proton beam across the two transverse dimensions of the treatment volume, and to scan in depth by varying the proton energy from the accelerator on a pulse-pulse basis. This procedure would not only allow 3-D contouring of the volume treated but could, theoretically, make use of 100% of the accelerated beam for treatment. If so, it would reduce the cost of the accelerator, and also reduce the amount of shielding required around the accelerator, the

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transport lines, and the treatment areas. It would, however, require slow extracted beams with uniform and precisely-controlled current. I believethe latter can be achieved in a reliable way by accelerating H^- ions and extracting protons by stripping the electrons from the proton in a very thin foil. This charge-exchange extraction technique will be explained later.

Another very significant advantage of a slow extracted beam relates to the resulting high beam quality. The required aperture and number of focusing elements in the transport system are reduced. In addition, the low average beam current leads to reduced shielding requirements on the transport line. These points will be discussed further in a later section.

Simplicity and reliability of the accelerator system are enhanced by the following choices:

1. Single turn injection.
2. Slow acceleration of H^- ions to 250 MeV.
3. Low space charge tune shifts.
4. Currents considerably below instability thresholds.
5. Utilizing charge-exchange extraction.
6. Conservative design of all components.
7. Avoiding technology unsuited for hospital operation.
8. Good diagnostics, control, and alignment procedures and equipment.

The process of transmitting H^- beams through very thin foils to remove the 2 electrons and change the ions into protons is quite common in the worldwide accelerator community today. The technique is in daily use (when the accelerators are operating) at Argonne, Fermilab, Brookhaven, KEK (Japan), and Rutherford (England). At all of these laboratories charge-exchange is used at injection into a circular machine in order to overcome, in a simple way, a fundamental injection limitation. It seems essential in order to achieve high circulating currents in small accelerators (the practical development of this technique was undertaken to accomplish this with the Argonne Rapid-Cycling Synchrotron, a 500 MeV, 30 Hz, proton accelerator with an average current of 12 μA, operating with the Intense Pulsed Neutron Source). However, the performance of larger accelerators has sometimes been improved by this technique, resulting in increased beam currents and greater reproduceability on a pulse-pulse basis.

For the proton accelerator concept presented here, however, injection is very straightforward and simple. On the other hand, achieving an extracted beam of uniform current over a long period of time (the ions circulate about 2 million times around the ring in 0.4 second) is more difficult. Here I propose that H^- charge-exchange extraction will simplify achieving this goal, and perhaps lead to the equivalent in improved performance already seen with charge-exchange injection.

The acceleration of H^- ions, which appears highly advantageous for the extraction process, introduces two technical requirements that are quite different than if protons were accelerated. The first of these is a much higher vacuum requirement (estimated at 10^{-10} torr) in order that the ions not lose their electrons in collisions with residual gas atoms. I believe that this vacuum requirement can be met in a reliable and straightforward way by the use of newly-developed Zr-Al getters. The vacuum system will be discussed in more detail later.

The second technical requirement related to the choice of H^- ions is the limitation to a maximum magnetic field in the accelerator of 6 kG or less. At higher fields, at the full proton energy of 250 MeV, the magnetic field would be sufficient to separate the electrons, and the ions would be lost. The relatively low peak field implies a diameter of approximately 40' for the main accelerator. This size could appear to be a serious drawback to the proposal of retrofitting proton therapy facilities into existing hospital space. However, if one can achieve transport of the proton beam as simply and inexpensively as appears possible, then locating the accelerator in any available space, such as in a basement or under a parking lot, would be feasible. Such transport systems are simplified by high beam quality (to minimize both the number and aperture of transport elements) and the low peak currents of slow extracted beams (to minimize shielding requirements). Both of these beam characteristics can be achieved in a simple manner by charge-exchange extraction of circulating H^- ions.

This method of extraction is so simple, requiring only a properly-placed foil and a pair of orbit-controlling magnets, that extraction from many points around the ring is feasible. In my design, I propose to provide for extraction from all 8 straight-sections of the ring, and to utilize extraction at any desired energy, including the injection energy, as a

diagnostic tool to measure the properties of the circulating beam. These individual extracted beams can terminate in a shielded beam dump, or they can be transported for treatment or other use. Figure 1 shows a possible layout of several extracted beams. The beams at the top and bottom of the sketch might be bent upward (e.g., if the accelerator were in the basement) for directing the beam into one of any number of treatment rooms. The number of treatment rooms is only limited by the number that can be efficiently utilized, which might most strongly depend on how much setup time is required for a given treatment. If this time can be reduced by improved beam characteristics, then more efficient use of the accelerator might result in lower cost treatment. The 3 beams (from 2 extraction points) in the lower left of the sketch are intended to illustrate a possible layout to provide 3 radiation fields, at least 1 of which should be vertical, in a single treatment room. The desirability of the latter was pointed out to me by John Archambeau of Loma Linda Univ. The 3 beams in the upper right would be provided for a number of purposes. One important use would be to have the accelerator operating continually, even when not delivering beam for treatment. Thus the operational status of the accelerator would be known at all times. Other uses of these test beams might be to develop new techniques, improved characteristics, or other development of the medical capability. In addition, there could be other important physics uses of the beams, such as proton-induced x-ray studies.

Also shown in Figure 1 are a few of the parameters of the accelerator design. Note the low requirements on the H^- source, 1 mA for 1 μsec, the small space charge tune shift at injection, and the low RF voltage requirements. These low values might indicate that the design is not optimized; no attempt has been made to optimize the parameters, or to produce an engineering design. The maximum beam amplitude (the beam diameter is twice this value) decreases from about 1 cm at injection to 3 mm at the full energy of 250 MeV.

As an injector for the accelerator I would choose one on which the performance and reliability have already been demonstrated, and the cost is known and reasonable for the purpose. One such accelerator is the Model 5SDH Pelletron Accelerator produced by the National Electrostatics Corp. It is a small tandem accelerator with 1.6 MeV on the terminal. It is a proven machine, having been used industrially for a few years, and the

price of the accelerator without source was quoted in August, 1984, as $100K. While it is normally run with much lower currents on a DC basis, there seems little doubt that it could handle the short duration beam currents suggested here. The H^- ion source would have to be mounted in the terminal, but I do not believe there would be any problem with source reliability at the low duty cycles required.

Protons could also be provided by this injector system (and at higher injection energy) for direct proton acceleration. An H^- source at the input end of the Pelletron, with stripping in the terminal, would produce proton beams of 3 MeV. The accelerated current with this injection energy could be 2 times higher, but a different technique for extraction would be required.

Initial ideas of the magnet cross-section are shown in Figure 2. I have chosen a large number of short magnets (8 per octant, or 64 total for the ring) in order that they can be straight magnets for ease of fabrication, and because only a short magnet length can be tolerated after the stripping foil. Other choices could be made and might be better for different reasons. The low required magnet power and cooling for this magnet at 1 Hz means that the magnet could easily be designed to operate at 10 Hz.

A sketch of the vacuum chamber design is shown in Figure 3. Here the octant chamber would be curved to avoid a large number of welds, which seems prudent since the required vacuum is high. The 8 straight magnets would fit over this curved vacuum chamber with a sagitta of about 1/2 cm, quite adequate in view of the large horizontal dimensions of the chamber. The circulating beam does not use a very large part of the horizontal aperture. The proton beam after the foil, however, moves outward by 4 cm in the final magnet before the straight section. The key to attaining a very high vacuum in a reliable way are the Zr-Al getter strips shown here on the inside radius of the vacuum chamber, out of the way of the circulating beam. Properly conditioned, a 2 cm wide strip will have a pumping speed of 200 liters/sec/meter of length. This should be adequate to hold the pressure of the chamber shown (baked before installation) below 10^{-10} torr with sufficient margin of safety. The system needs ion pumps at the straight sections to pump methane and the noble gases. The eddy current fields and heating in the 1/8" stainless steel chamber will not be a problem at the 1 Hz repetition rate. At higher repetition rates such questions will have to be examined more carefully.

As an exercise, because the vacuum system is one of the more expensive parts of this accelerator concept, an initial estimate of the cost of the vacuum system equipment is also shown in Figure 3. This estimate does not include contingency or EDIA (engineering, design, installation, and administration).

Figure 4 shows the variation of the horizontal (x) and vertical (y) amplitude around the ring at injection (1.5 MeV). Also shown is the horizontal displacement for a momentum error of 10^{-3}. The abscissa goes from the center of one octant at the left, through 4 bending magnets, a straight section containing a horizontally-focusing quadrupole followed by a defocusing quadrupole, and 4 bending magnets to the center of the next octant. This arrangement is shown schematically at the bottom of the Figure.

A schematic of the stripping extraction is shown in Figure 5. The foil, of thickness of perhaps 100 $\mu g/cm^2$ (Argonne uses foils of 50 $\mu g/cm^2$ for injection at 50 MeV; Fermilab uses thicker foils for injection at 200 MeV.), is located between the last two bending magnets of the octant. The horizontal position of the beam at this position is precisely controlled by two weak magnets, located in straight sections before and after the extraction straight section, with feedback from extracted beam current monitors. Only the extreme outer edge of the circulating H^- beam is brought onto the foil. Ions which penetrate the foil lose their 2 electrons (with very high efficiency, approaching 100%). The protons then bend the opposite direction from the ions in the following magnet and come out of the machine in the straight section. They receive an additional angular kick from the quadrupole, which was horizontally focusing for the H^- ions, but is horizontally defocusing for the oppositely-charged protons. The effect from the quadrupole is relatively small, however. The foil need not be very high in the vertical direction if it can support itself. Here I have shown it with 1 mm height that would have a probability of 1/4 of intercepting the ions vertically if they were at the right horizontal position. The differences in the two planes are shown in the phase space plots, where the cross-hatched area is the foil and the primes refer to angles in the x and y direction.

The table of Figure 5 shows a comparison of the rms coulomb scattering angle introduced by the foil and the maximum beam divergences of the circulating beam for different beam energies. Used as a diagnostic technique, it is clear that a correction is required to determine the characteristics of the circulating beam from measurements on the extracted beam at the lower energies, but that multiple coulomb scattering is negligible at 70 MeV and above. One conclusion from these calculations is that considerably thicker foils could be utilized for the extracted beams for therapy, so there should be no problems with foil lifetime or reliability.

One possible advantage of the low-current, long beam duration of the slow extraction might be in minimizing the shielding required in the transport of this beam. For example, if the total beam pulse containing 6×10^9 protons were extracted uniformly in 0.4 sec, then the peak current would only be 2.5 nA. If an accident occurred such that protons were striking the beam pipe or transport magnets, then strategically placed neutron detectors could turn the beam off in perhaps 1 μsec. In this case only 1.5×10^4 protons would have been unintentionally lost, and this would not present a difficult shielding problem for the transport line.

The simplicity of the transport line can be understood by considering the emittances of the extracted beam. These might be 0.3 mm-mrad in the vertical plane and extremely small in the horizontal plane. Dealing with the vertical plane, it would be possible to maintain the beam diameter below 1 cm with a quadrupole pair every 30 m. These might then be permanent magnet quadrupoles with a 1 cm bore placed inside the vacuum pipe. They would require no power, cooling, or maintenance. What is not so well known is that such a transport system could be arranged to efficiently transport any proton energy from 50 to 250 MeV by simply adjusting the matching conditions at each end of the transport line, however long, for the energy to be transported.

The bending magnets in the transport line are no longer restricted to low fields, so it is proposed that they would be the ring magnets (for cost effectiveness) with pole face inserts to reduce the vertical gap to 1 cm and increase the field to 20 kG. At this field, the radius of curvature of 250 MeV protons would be 1.2 m. The bending magnet field, as well as that in the matching quadrupoles, the switching magnets, and the scanning magnets would have to track the beam energy on a pulse-pulse basis.

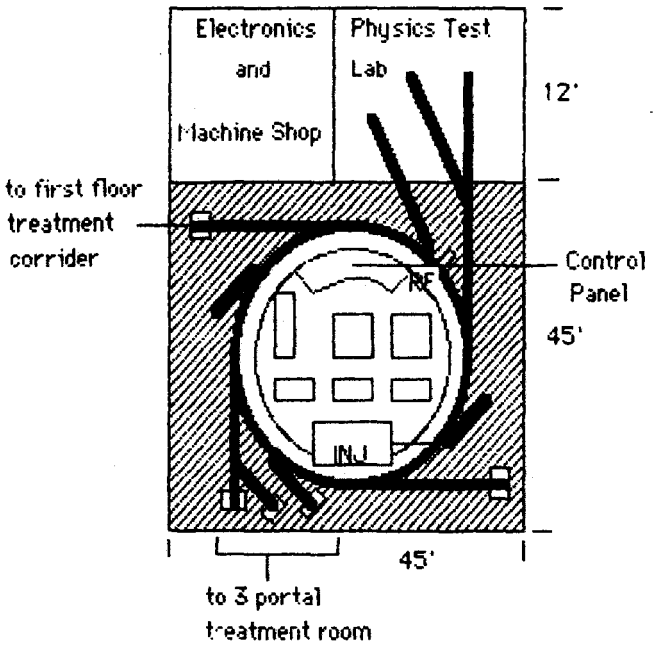
I consider the possibility of scanning beams to be one of the most attractive features of the design concept presented here. To deliver a uniform dose with scanning requires beams of high quality, long duration, and precisely-controlled current. The latter requires active feedback from beam current monitors. I don't believe beams with suitable characteristics exist in any facility today, but they can be produced with the stripping extraction of H^- ions. This is partly due to the fast and very direct relationship between the extracted beam current and the currents in a pair of bump magnets in the ring that control the beam position at the stripping foil.

One possible scenario for scanning beams is shown in Figure 6. If the goal is to scan an area of 30 x 30 cm with horizontal and vertical deflecting magnets 3 m away, the deflecting magnets must have an integrated field strength of $\pm$0.12 Tm for 250 MeV protons. A possible choice would be 20 cm long magnets excited with AC currents to fields of $\pm$ 6 kG. Each horizontal scan could cover the same width, and the beam turned on and off to cover only the desired contour for that position (with perhaps a small current left on outside this contour to monitor the beam position when it is nominally off). When the beam is at the extreme position it would be moved 1mm vertically and scanning resumed on the opposite swing of the sine wave. The total scan at one depth would then take 300 horizontal sweeps (for 30 cm vertical height), and, in a beam time of 0.4 sec, the required magnet AC excitation would be about 400 Hz. The power supply might be a well-controlled AC generator. For smaller fields, say 10 x 10 cm, one might want a slower scanning rate. A generator that could be connected to produce current at either 125 or 375 Hz might be suitable. This area scan would be repeated at a different penetration depth (proton energy) on each pulse until the desired volume was covered. As an example, with 1 mm difference in penetration/pulse (implying considerable overlap due to range straggling, which can be adjusted to any value desired to produce uniformity), a 10 cm depth could be irradiated in less than 2 min. Greater overlap, hence longer irradiation times for a given volume, would result in higher delivered dose.

At the fastest scanning rate, the beam is moving horizontally only 1 mm in 4.4 µsec. This time is more than that of 20 revolutions of the beam around the ring. Therefore there is no need to turn off the RF accelerating voltage and debunch the circulating beam. Retaining the RF fields can be useful for beam control in the ring, and the bunch structure on the extracted beam (about 5 MHz) can be of advantage to monitor the precise energy of the beam.

The beam size incident on the patient should be optimally adjusted, taking into account the unavoidable coulomb scattering of the protons in the patient. To scan with a "pencil" beam would produce an unnecessarily high skin dose. Fortunately, this type of matching is easy to do, and the optimum size depends upon the depth of penetration. A table of the rms beam spread due to multiple coulomb scattering as a function of the energy (or range) of the protons is shown in Figure 6. The effect can be quite significant for very deep-seated tumors, and must be included in the treatment planning.

In conclusion, I believe that achieving uniform radiation doses utilizing scanning beams is possible, and that this technique should increase the efficiency of treatment. It would result in a higher efficiency in the use of the accelerated beam, thereby requiring less accelerator intensity, less shielding around the accelerator, transport lines, and treatment rooms, and simplifying the problem of beam transport and delivery. The latter factor appears to make it possible to locate the accelerator in nearly any available space and safely transport the protons to any desired area. While one can clearly build medical accelerators with any desired current (at a cost that may be proportional to the cube root of the current), may accelerate protons rather than H^- ions, and may utilize conventional beam delivery techniques, the advantages I have outlined of accelerating H^- ions and using charge-exchange extraction and scanning beams seem to outweigh the disadvantage of the larger radius required.

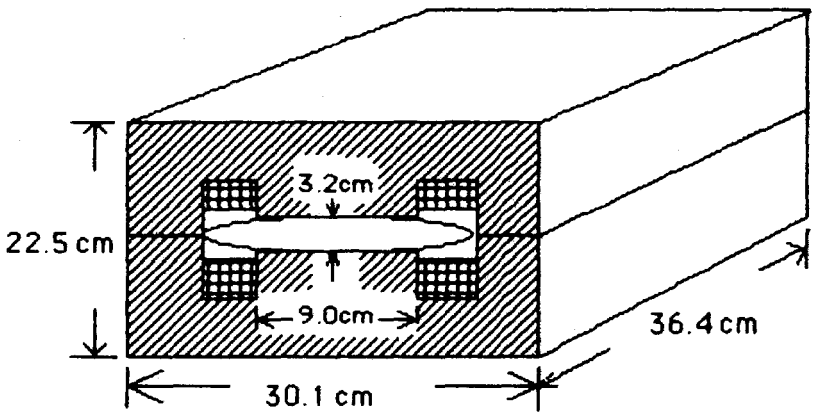


POSSIBLE BASEMENT FLOOR PLAN

PARAMETERS

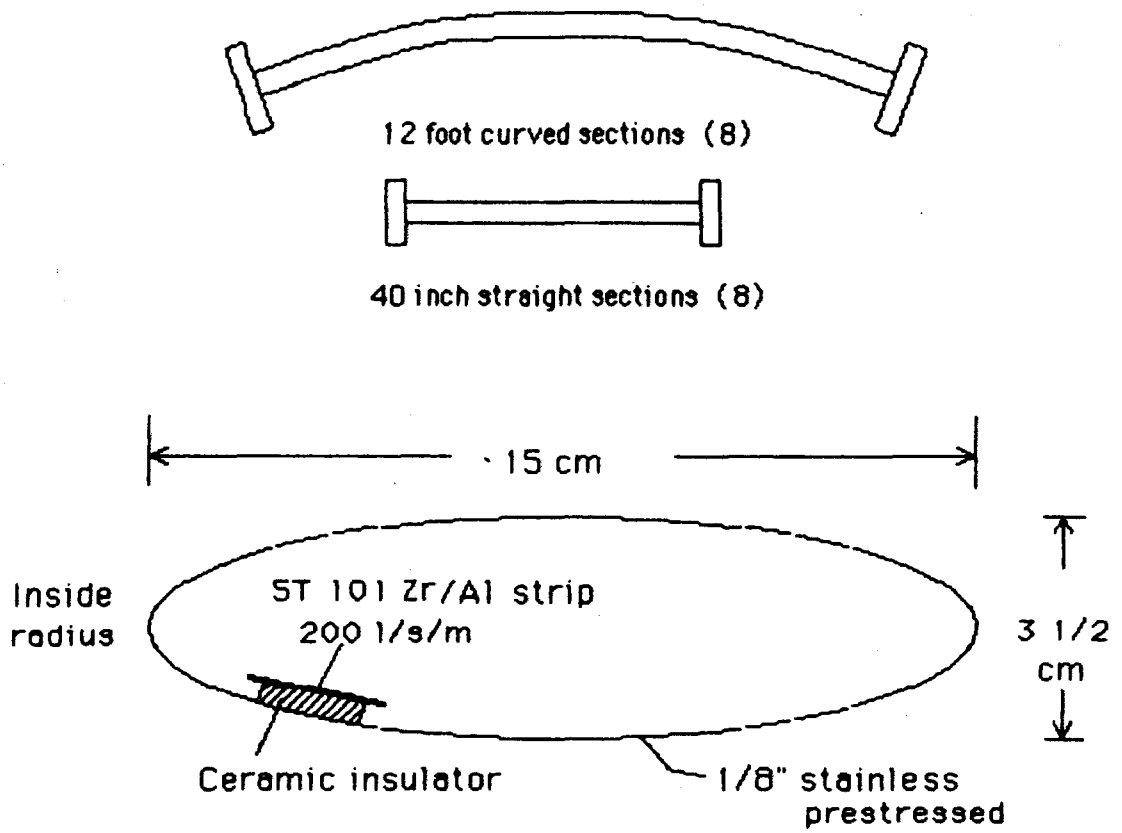
Injection	Acceleration	Extraction
1.5 MeV	f_i = 500 kHz	250 MeV
440 G	f_f = 5.4 MHz	6000 G
1 mA-1 μs	ΔE = 280 V/turn	t ~ 100 nsec
c = A/π = 1.9 cm-mr	V_{RF} =560 V	c = 1.36 mm-mr
x_{max} = 1.10 cm	Rep. Rate = 1 Hz	x_{max} = 3.0 mm
y_{max} = 1.02 cm	Field Rise = 0.3 sec	y_{max} =2.75 mm
N = 6 x 10^9 ions	Constant Field = 0.4 sec	
ΔQ = 0.1	Field Fall = 0.3 sec	

FIGURE 1. POSSIBLE LAYOUT AND PARAMETERS



0.231" sq. Cu conductor - 1/8" dia. hole
5 turns/layer x 4 layers/pole
424 A at 1.22 V =476 watts (DC)
x 64 magnets = 30.5 kW
185 kg/magnet (96.5 kg w/12 kG in yoke)

FIGURE 2. Magnet Cross Section



VACUUM CHAMBER CROSS SECTION

Preliminary Estimate of Vacuum System Cost

1.	38 m of ST101 Zr/Al strip	$75/m	$ 2,850
2.	12 -11 l/s ion pumps	$2500 ea.	30,000
3.	1 - 280 l/s turbo pump pack	$7725 ea.	7,725
4.	4 - 6" metal isolation valves	$10,000 ea.	40,000
5.	4 - 4" metal isolation valves	$6500 ea.	26,000
6.	4 - ion guages and controls	$1000 ea.	4, 000
7.	Chamber (design, fab, clean, inst)	$500/ft.	60,000
		Total	$170,575

Figure 3. Vacuum System

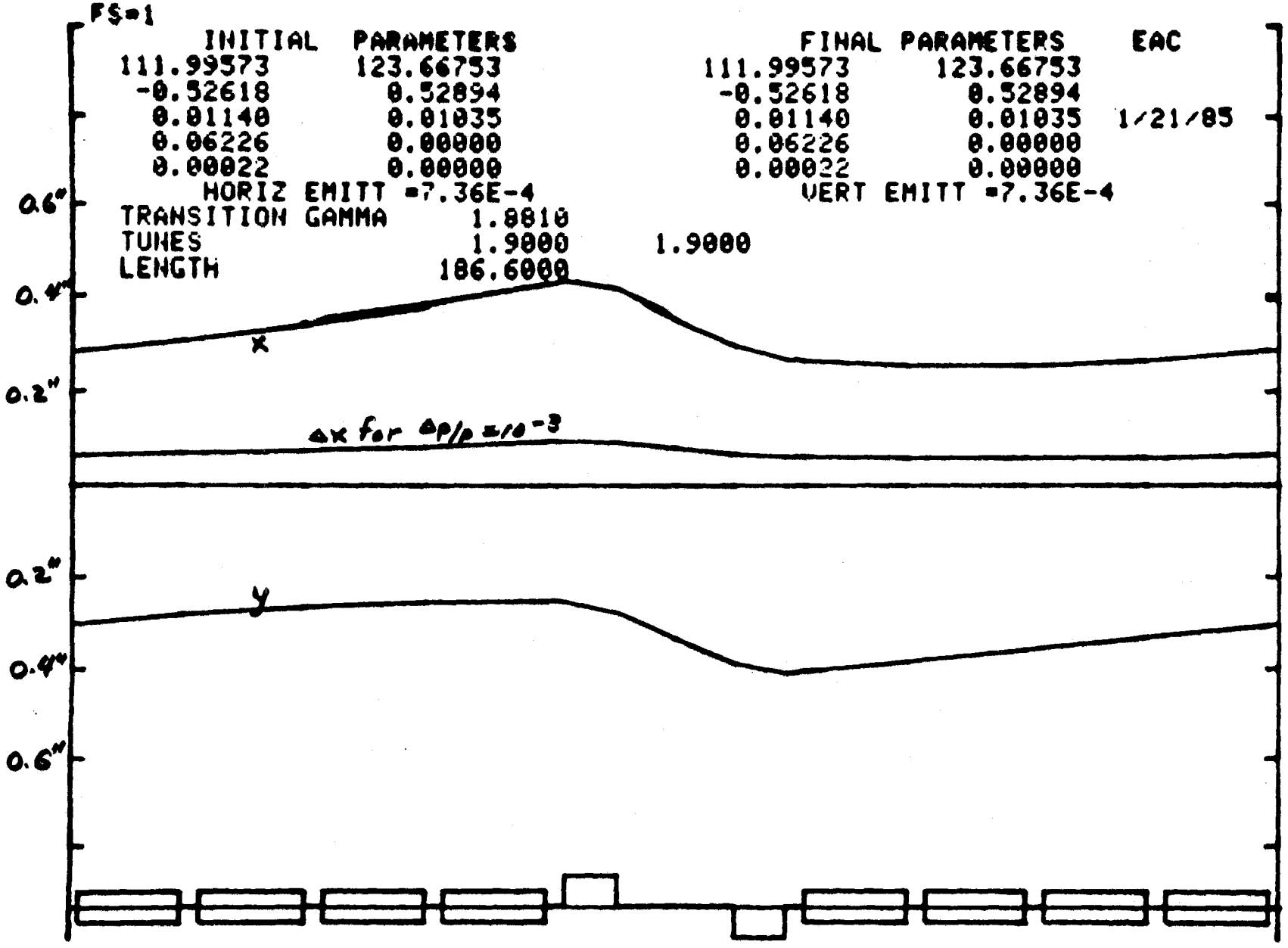
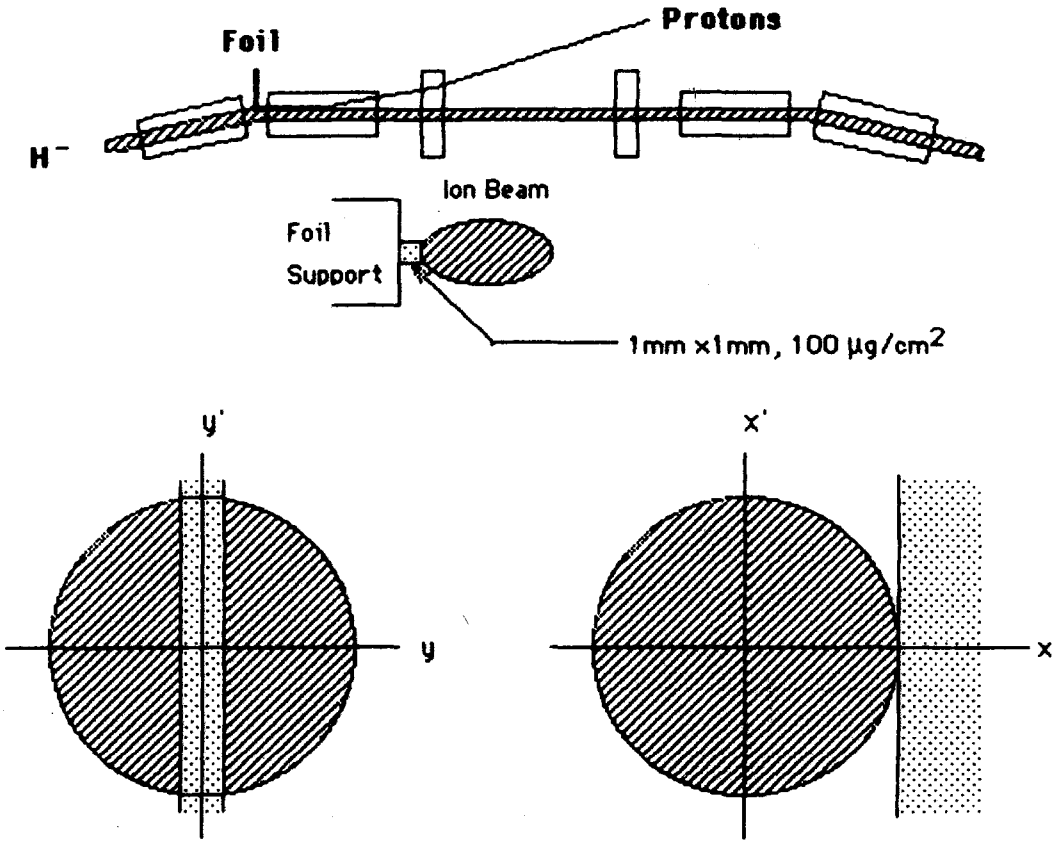


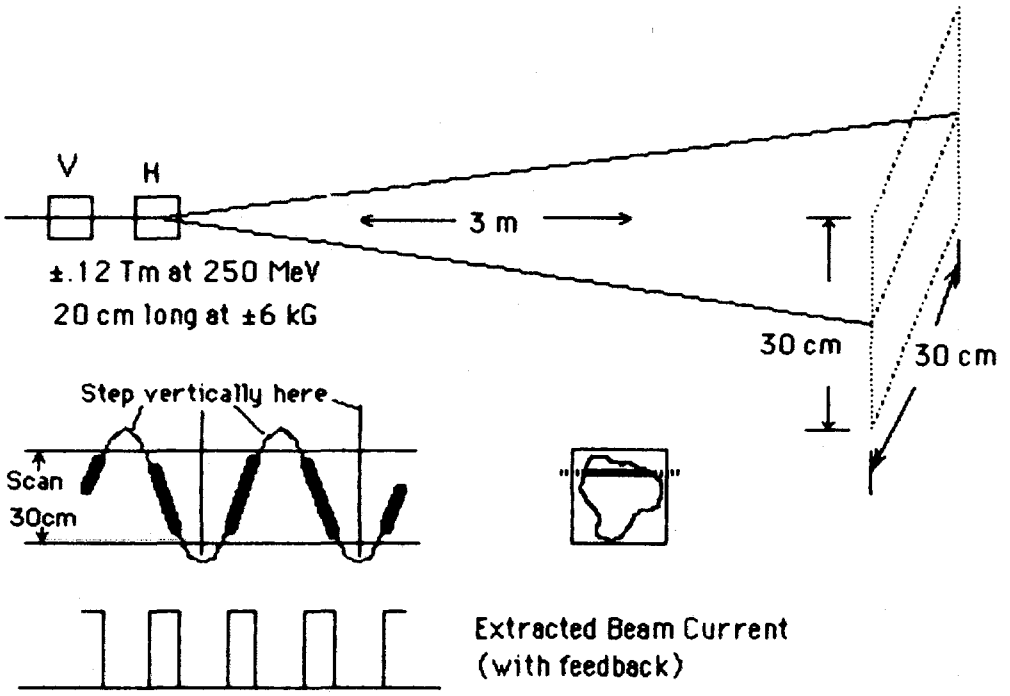
FIGURE 4. BEAM AMPLITUDES



Foil Scattering

E(MeV)	ø (circ-mr)	ø (foil-mr)
1.5	1.63	0.80
3.0	1.37	0.40
10.	1.01	0.12
70	0.62	0.02
200	0.47	0.007
250	0.44	0.005

Figure 5. Stripping Extraction



Multiple Scattering of Protons in Tissue

Energy (MeV)	Range (g/cm^2)	Y (rms-mm)
100	7.5	1.9
137	13	3.15
153	16	3.85
201	26	6.05
226	32	7.4

Figure 6. Scanning Beams