HIGH ENERGY MEDICAL ACCELERATORS

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Abstract : The treatment of tumours with charged particles, ranging from protons to "light ions" (Carbon, Oxygen, Neon), has many advantages, but up to now has been little used because of the absence of facilities. After the successful pioneering work carried out with accelerators built for physics research, machines dedicated to this new radiotherapy are planned or already in construction. These high energy medical accelerators are presented in this paper.

Introduction

It was Robert Wilson in 1946 at Harvard [1] who realised that protons of a given energy travel in almost straight lines, all with roughly equal range and that this property could lead to a new radiotherapeutic tool for targeting deep seated tumours while preserving the surrounding healthy tissues. Almost 45 years later, the first hospital based dedicated proton accelerator is preparing to treat 1000 patients per year. This machine which is installed at the Loma Linda University Medical Center, was designed and fabricated at Fermilab, where Robert Wilson was director from 1967 to 1978. In this sense a loop has been completed.

The use of charged particles has three major advantages over the photon or electron beams which are used for conventional radiotherapy :

- first, a physical selectivity : in contrast to x-rays and electrons the beam does not spread sideways inside the body and has a very well defined range (cf Fig 1 and Fig 2) for a given energy. This is true for protons and even better for heavier ions.

- secondly, the so called Bragg curve : the ionization increases as the particles slows down giving a greater dose at depth than on the surface. Fig 2 shows the relative dose as a function of depth in tissue for different types of classical radiation compared to a light ion (Neon).

- thirdly, heavier ions ranging from Carbon up to Argon, produce a high ionization density, known in the trade as high LET. The so called RBE (Relative Biological Efficiency [2]) increases and the OER (Oxygen Enhancement Ratio [2] decreases). This latter effect is a serious limiting factor in radiotherapy of large tumours which are poorly vascularised and whose cells are less oxygenated and therefore less sensitive to radiations. These two factors which magnify the effect of the Bragg peak are shown on Fig 3 which presents typical variations or RBE and OER and characteristic LET bands for several charged particle beams. Hence a modification of quality of the radiation received by the patient becomes possible.

These biological and physical advantages of high-energy charged particle beams in cancer therapy have been established over a number of years in a series of biomedical experiments and clinical trials carried out in institutions whose accelerators were designed for nuclear physics research : Berkeley and Harvard in the United States, Uppsala in Sweden, Dubna and Moscow in the USSR, Tsukuba and Chiba in Japan, PSI in Switzerland. The total number of patients treated in 35 years is about 9000 throughout the world.

Following theses good results, physicians are now asking for dedicated facilities which include not only a specific accelerator but also sophisticated beam delivery systems in order to treat a large number of patients. Several projects, both for protons and light ions, in the United States, Japan and plans in Europe will be discussed in this paper.

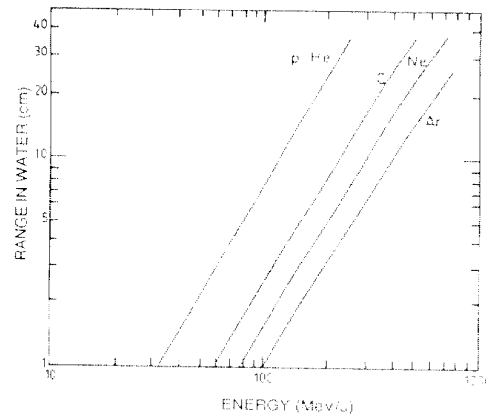

Fig 1 : Range of ions in water as a function of kinetic energy

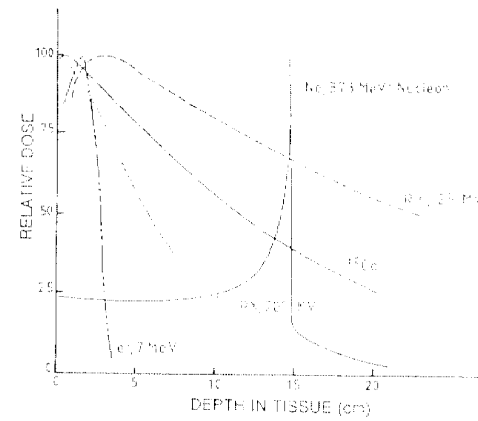

Fig 2 : Depth dose distribution for different radiation

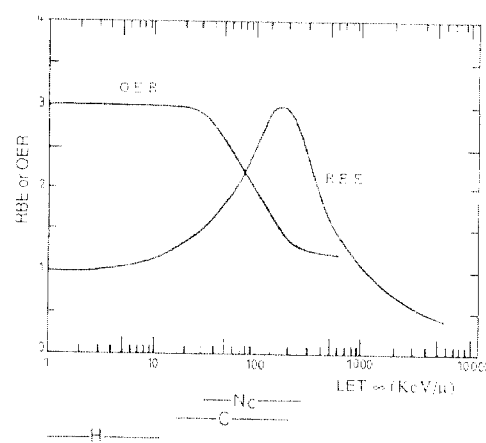

Fig 3 : RBE and OER as a function of LET for several ions

Medical constraints

The main requirements for a new radiotherapy facility are as follows :

1- Installed in a large hospital in order to get an adequate supply of medical and scientific staff for developing high technical level diagnosis and treatment systems.

2- Accelerator highly reliable and easy to operate.

3- Beam delivery system permitting to scan the beam over the tumour volume.

4- Avoiding to move the patient, i.e. possibility to use different directions for the beam : horizontal and vertical beams, either above or below the couch. An isocentric gantry is suitable if the maximum beam rigidity makes this requirement realistic (possible for protons, massive for ions...).

5- Maximum range in tissues : 25 cm. This fixes the maximum energy for the beam ; 200 MeV for protons and several hundred MeV per nucleon for the ions.

6- Maximum dose rate at the tumour : 5 Gray/minute in a 2 litre volume. This fixes the beam intensity (cf. Table 3)

7- Maximum irradiated field : 30 x 30 cm^2.

8- Possibility to check the treatment plans by PET verification of the irradiated volume.

The accelerator

Imposing a range in tissue of 25 cm, the maximum kinetic energy and magnetic rigidity of proton and fully stripped ion beams are given in Table 1. From these figures it is clear that the proton machines and light ions machines will be quite different in size and cost. Two kinds of accelerators are feasible and the choice is not simple because these machines lie in the overlap of large isochronous cyclotrons and small synchrotrons.

Table 1

	Protons	Carbon	Oxygen	Neon
Energy (MeV/nucleon)	200	380	430	520
$B\rho$ (T.m.)	2,15	6,16	6,62	7,42

Isochronous cyclotrons

A fixed frequency isochronous cyclotron, giving a fixed energy for accelerating ions at a given harmonic number of the radiofrequency, is certainly the simplest accelerator to operate. A simple Programmable Logic Controller is enough to tune and control such an accelerator.

Neutrontherapy machines

This simplicity and the ability to accelerate large intensity has made the medium energy cyclotron the working horse of high energy fast neutron therapy programmes. Fast neutrons are classified as high LET particles because of the high ionization density of the recoil protons giving biological advantages over the conventional radiations for radioresistant tumours with the drawback of poor localisation. In order to get the required flux, a proton beam is accelerated up to 50-65 MeV onto a thick beryllium target. A high intensity is requested (15 microamps) and therefore several isochronous cyclotrons have been designed for neutrontherapy. Fig 4 shows the 65 MeV proton isochronous cyclotron designed and installed in Nice. Use has been made of H^- acceleration to facilitate the extraction system, avoiding a cumbersome, power consuming and difficult to construct extraction channel [3]. A compact superconducting cyclotron (K100) rotating around the patient has been constructed by H.G. Blosser [4] and is being installed in the Harper Hospital in Detroit (USA). The 40 Mev deuteron maximum energy orbit of this cyclotron has a radius of only 30 cm.

Iontherapy machines

For the higher energies requested for protons and light ions therapy, the design of the machine becomes more difficult. For protons the use of superconducting coils for the magnetic field is an open question and recently two interesting designs have been proposed : IBA [5] has chosen a high field design (2.15 Tesla on the extraction radius) produced by conventional coils (cf. Fig. 5) and a compact superconducting synchrocycloton has been proposed by H. G. Blosser [6](cf Fig 6).

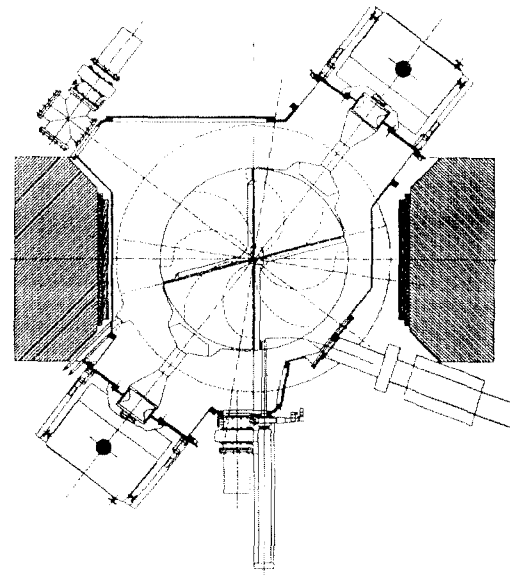

Fig 4 : Median plane view of the 65 MeV H^- MEDICYC cyclotron installed in Nice

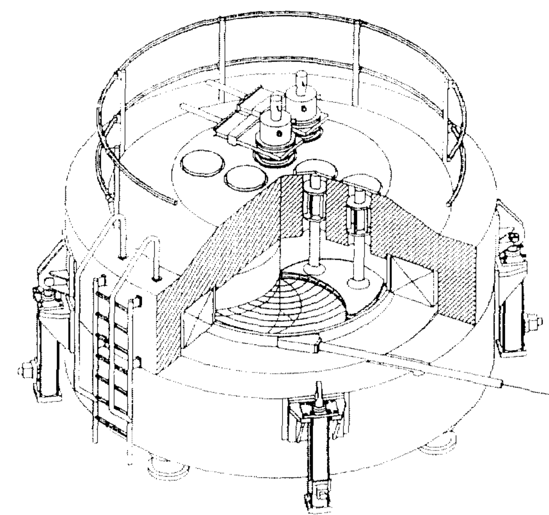

Fig 5 : The "CYCLONE 230" proposed by IBA

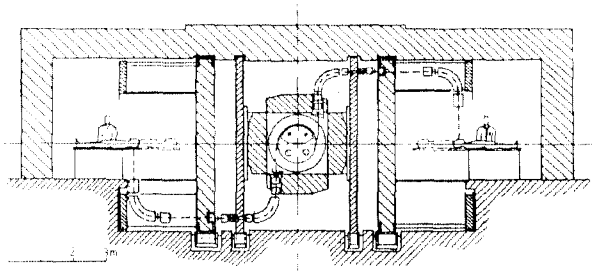

Fig 6 : 250 MeV Superconducting Synchrocyclotron proposed by H.G. Blosser, rotating around the patient.

Nevertheless for light ion acceleration the high magnetic field required is in favor of a superconducting solution.

Preliminary studies of the EULIMA project [7] concentrated on a superconducting separated-sector cyclotron accelerating fully stripped light ions axially injected from a high voltage platform located on the vertical axis of the machine. The magnet consists of four tightly spiraled sectors spanning 35° that are driven into saturation by a common cylindrical superconducting coil. The accelerating system comprises of two spiraled cavities located inside the vacuum chamber. The layout of the machine is shown in Fig 7 and the major parameters are given in Table 2.

Table 2

Particle frequency	17.4 Mhz
Max. energy fully stripped light ions	430 MeV/nucleon
Number of magnet sectors	4
Iron weight per sector	155 tons
Sector gap	50 mm
Sector angular width	35°
Average sector spiral	30°/m
Sector height	4.80 m
Sector maximum radius	2.20 m
Coil internal radius	2.31 m
Coil external radius	2.61 m
Coil current density	2850 A/cm2
Number of RF cavities	2
RF frequency	69.6 Mhz
RF harmonic number	4
RF peak voltage at extraction	250 kV
RF peak voltage at injection	125 kV

Details of this machine are described in several papers presented at this conference [8].

The common feature of all these high energy cyclotrons is the fixed energy. Hence scanning of the beam in depth is necessary to reduce the energy by using a degrader. Extensive calculations of the effect on the beam quality of such systems are then necessary to assess the performances of such systems [9].

Synchrotrons

The Table 3 presents for the same particles as Table 2, the required minimum current to give 5 Gray over a volume 20 x 20 x 5 cm^3 for different ions in one minute.

Table 3

	Proton	Carbon	Oxygen	Neon
Intensity (pps)	2×10^{10}	10^9	7×10^8	5×10^8

These intensities are of course within the reach of a classical synchrotron and several projects have been proposed.

Protontherapy machines

Fig 8 presents the first high energy medical facility based in a large hospital located on the Loma Linda University campus in southern California. This facility houses a proton synchrotron giving a variable energy from 70 Mev up to 250 MeV. Three treatment rooms with isocentric gantries and one room with a fixed horizontal beam are presently being installed [10].

The zero gradient synchrotron has eight 45 degree dipole magnets arranged to have four straight sections providing space for injection, acceleration and extraction systems. The 30 KeV proton beam from the duoplasmatron system is injected into a 2 MeV-RFQ operating at 425 Mhz. A debuncher reduces the momentum spread form 1 % to 0.3 % at injection. Acceleration to 250 MeV is made via simple ferrite loaded RF cavity operating on the first harmonic. The beam is extracted from the synchrotron by using half-integral resonance. The cycle time is 2,4 or 8 seconds and the extraction time is variable from 0.4 sec to 10 sec. The design intensity is 10^{11} protons/sec. This design is a result of a collaboration between the Loma Linda University Medical Centre, the Fermi National Laboratory and the Science Applications International Corporation (SAIC) Company.

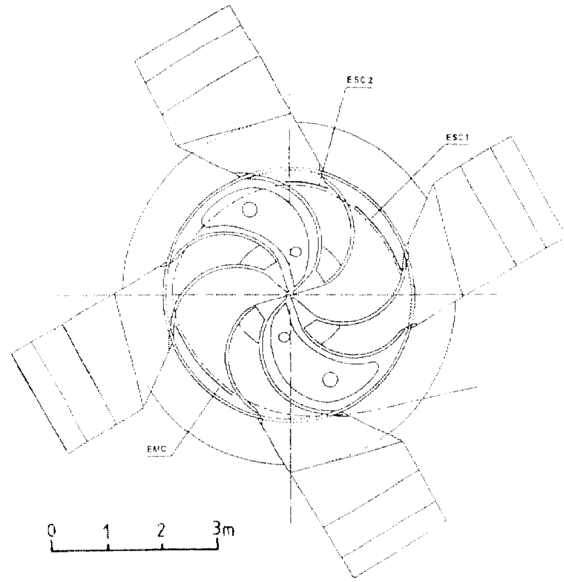

Fig 7 : Top view of the EULIMA superconducting cyclotron

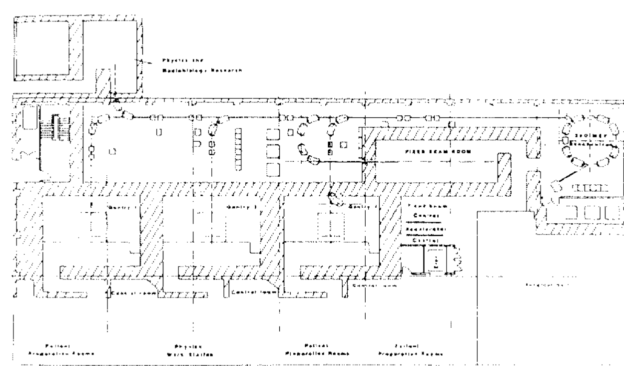

Fig 8 : The Loma Linda facility

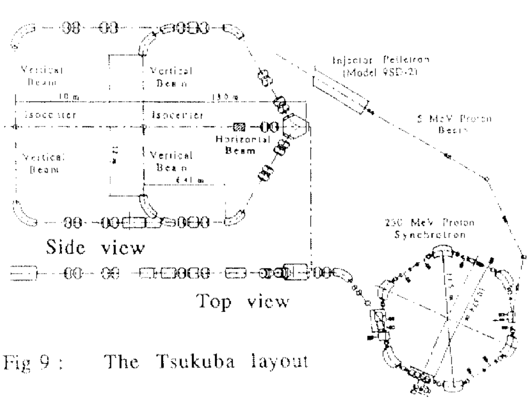

Fig 9 : The Tsukuba layout

Following the pioneering work at the Particle Radiation Medical Science Centre (PARMS) of the University of Tsukuba which started to treat patients with a 250 MeV proton beam provided from the degraded beam of the 500 Mev booster synchrotron of KEK, a dedicated 230 MeV proton facility [11] will be build next to the conventional radiotherapy department at the University Hospital. Fig 9 shows the proposed facility which has two treatment rooms, the first will be equipped with three beams : one horizontal beam and two vertical beams for upper and lower directions. The second room with two vertical beams in opposite directions. The synchrotron is a 6 superperiods machine accelerating 5 MeV protons from an injection up to 230 MeV in 0.5 sec. The main parameters of this machine are summarized in Table 4.

Table 4

Energy range	5 - 230 MeV
Circumference	34.9 m
Structure	DOFB
6 Bending magnets	B_{max}=1.5 T
12 Q-poles magnets	G_{max}=6.0 T/m
Ion source	Multicusp H^-
Injection energy	5 MeV Tandem
Acceleration	f=0.88 - 5.11 Mhz V=450-300 Volts
Ejection spill	up to 1 s, half-integer resonance slow ejection

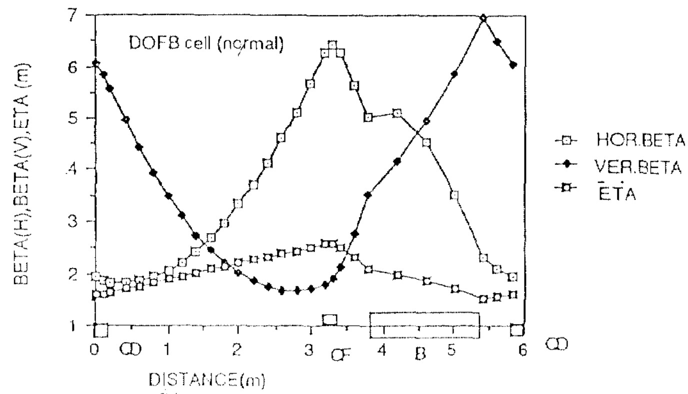

Fig 10 : β an η functions in the unit cell of the 230 MeV Tsukuba proton synchrotron

Light ions therapy machines

Following the stimulative results of the BEVALAC research and clinical trials with ions [12], the HIMAC project proceeds along a 10 year strategy for cancer treatment launched in Japan in 1983. The National Institute of Radiological Sciences (NIRS) in Chiba started in 1987 the construction of a facility for radiotherapy with ions up to Ar. Based on a two ring large synchrotron, the completion of the facility is foreseen for 1993 and will be the first ion-therapy facility in the world [13]. Three irradiation rooms will be constructed : one, equipped with a horizontal and vertical beams. and two rooms with a single beam direction (horizontal and vertical). Extra rooms will be available for radiobiology, secondary beams experiments and general purpose research. The main parameters of this accelerators complex are given in Table 5.

Table 5

Energy range	100-800 MeV/n
Average diameter	41 m
Structure	FODO
12 Bending magnets	B_{max}=1.5 T
24 Q-poles magnets	G_{max}=7.0 T/m
Ion source	PIG + ECR
Injection energy	6 MeV/n Alvarez linac
Acceleration	f=1.0 - 7.5 Mhz V=6KV
Ejection spill	0.4 s, 1/3 integer resonance slow ejection

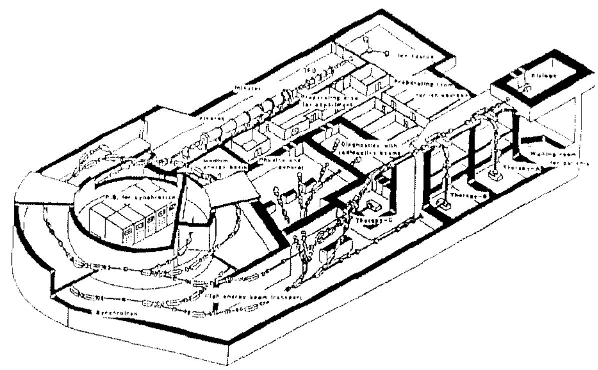

Fig 11 : Bird-eye-view of the HIMAC facility in construction in Chiba

Following similar ideas of other light-ion radiotherapy facilities, a synchrotron solution has been also studied for EULIMA. The beam energy interval from 100 to 450 MeV/n was considered, corresponding to the magnetic rigidity of 6.8 Tm, which is very similar to LEAR at CERN. The circumference of the EULIMA synchrotron is estimated at about 60 m, and the machine could be designed in a form of a ring or a racetrack, depending on the site conditions and the design of insertion devices. In Table 6, the preliminary parameters of this design are given, and its possible layout is depicted in Fig 12.

Table 6

Energy range	100-450 MeV/n
Circumference	60 m
Structure	FODO
8 Bending magnets	B_{max}=1.2 T
18 Q-poles magnets	G_{max}=10. T/m
Ion source	ECR
Injection energy	2-5 MeV/n (RFQ or linac)
Acceleration	f=0.5 - 4 Mhz V=10 KV
Ejection spill	0.5 - 1 s, 1/3 integer resonance ultra slow ejection

This basic design could be refined to include better monitoring of the extracted beam, and beam storage and cooling facility with a higher repetition rate injector. Hence, modulation of the beam intensity and programming of dose across the irradiation volume, as well as storage of radioactive beams could become possible.

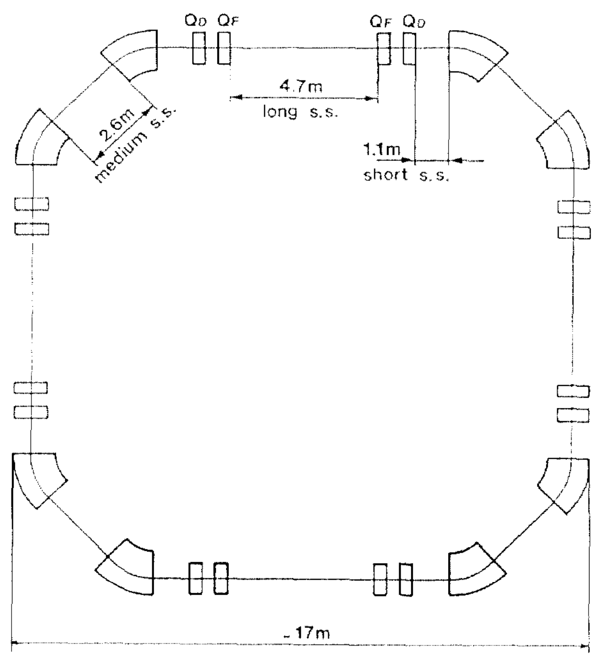

Fig 12 : An arrangement of EULIMA synchrotron lattice

Emphasis has been put on dedicated full time facilities to medical treatment but significant par time therapy programs are also planned at GSI in Darmstadt using the SIS synchrotron which accelerates light ions up to 2 GeV/nucleon. In order to use this accelerator complex in an efficient way for radiotherapy , it is proposed [14] to add a dedicated injector for light ions (3 MeV/nucleon) and to install a separated area for patient treatment.

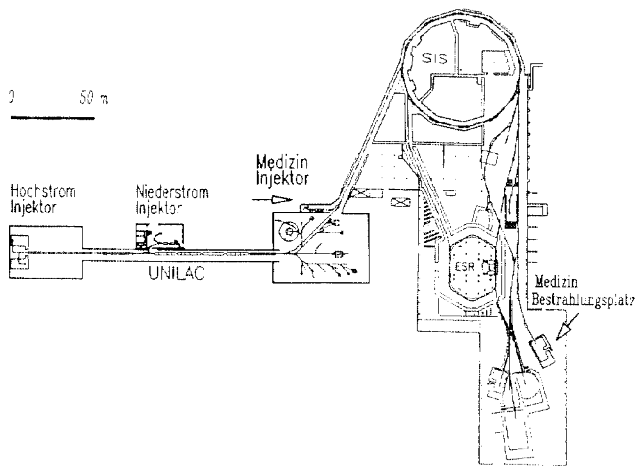

Fig 13 : GSI accelerator complex with the medical injector and the radiotherapy facility

It is very well known that the radiotherapy with light ions was started in LBL using the BEVALAC part time (1/3 therapy, 2/3 physics) and they now have 15 years of experience on which to base the next step which will be a dedicated medical accelerator to replace the Bevatron when it shuts down in the mid 1990's [15]. The design parameters of this machine are presented in Table 7.

Table 7

Range	30 cm
Beams	From proton to neon
Intensities	5×10^{11}/sec for proton, helium
	4×10^{9}/sec for carbon, neon

Fig 14 shows the proposed layout which uses as much of the present BEVALAC infrastructure as possible, hence a large circumference (120 m) synchrotron.

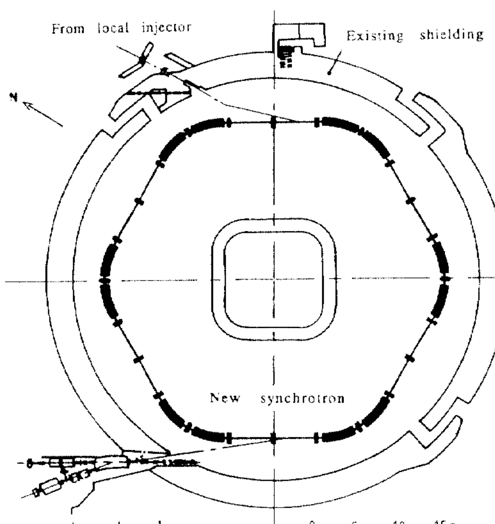

Fig 14 : The proposed LBL Heavy Medical Accelerator to replace the Bevatron

Synchrotron versus Cyclotron

I have presented designs for cyclotrons and synchrotrons but it is difficult to choose between the two because the energy requested by the physicians is high for a cyclotron and somewhat low for a synchrotron : the cyclotron needs a large magnet which requires a superconducting coil, particularly for light ions. On the other hand with a small synchrotron it is hard to reach the desired intensity due to space charge limitation at injection, particularly for protons. The cyclotron gives a continuous beam of fixed energy with plenty of intensity to spare ; the synchrotron beam is pulsed, variable energy. All these characteristics have implications for the beam delivery system and treatment planning [9]. Some important features that may influence the final choice of the facility are presented in Table 8.

Table 8

	Cyclotron	Synchrotron
Energy variation	degrader	machine adjustable
Beam Intensity	High (CW mode)	Low (Pulsed mode)
Injection energy	0.01-0.1 MeV/n	1-5 MeV/n
Typical diameter		
ions	8 m	18 m
protons	3 m	6 m
Operation	simple PLC control	computer controls
Beam delivery system	Raster and Pixel	Raster

Conclusion

The development of sophisticated diagnosis methods (CT-scans, MRI, PET cameras), together with the high level of accelerator technology are now in favor of the development of new radiotherapeutic tools using protons and ions. In the next five years the Loma Linda proton facility will have treated a large number of patients and the HIMAC accelerator complex will start treatment with high LET particles, new medical experience with this type of radiations will be available. Several other projects both for protons and ions will probably be funded. Hence the applications of accelerators in radiotherapy will continue to be a major spin-off of high energy research technology outside big science, and a challenge for accelerator engineering.

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