Synchrotrons for Cancer Therapy

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Abstract

The need for improved radiotherapy modalities and so far gained experience with particle beam treatment is outlined briefly. The choice of an appropriate accelerator is discussed for protons and light ions. Studies on a light ion machine, performed at GSI are reported. In an appendix a brief review on earlier proposals is included.

1 INTRODUCTION

The cancer case: it is reported [1] that in the year 1980 were 1.2 million new cancer incidents in the countries of the European Community. The cure rate is arount 45 % [2] , 22 % by surgery, 12 % by radiotherapy, 6% by the combination of both, 5 % by chemotherapy. Radiotherapy so far includes electron beam, x-ray, γ-ray and neutron irradiation. All have an exponential intensity decay when penetrating the tissue and suffer from lateral scattering as well. Therefore deep seated tumors, even when well localized, cannot be cured by conventional radiotherapy. The damage to the healthy tissue in front of the tumor or to sensitive organs near or behind the tumor exclude this modality, though any conceivable effort was made to rotate the radiation source around the patient, or more precisely, around the tumor as an isocenter. The above mentioned cure rate by radiotherapy is not this low, because it fails, rather becaue it is only applicable in a low percentage of cases. An equivalent comment might be given on the cure rate of surgery: a large number of tumors, even if well localized, are not accessible by invasive methods, because they are seated near sensitive organs or nerves, like in the eye, brain or close to the spinal cord.

The above mentioned restrictions against a substantial increase in cure rate can be overcome when proton or light ion beams would be included widely in radiotherapeutic modalities. These beams are highly ballistic with nearly negligible side scattering and they depose most of their energy in the Bragg peak at the end of their range, the latter can be selected by adjusting the particle energy. The advantage of light ion beams (carbon to neon ions) over the certainly cheaper proton beams lies in the fact that their lateral scattering in tissue is still smaller and that the biological efficiency of cell killing in the Bragg peak region is up to 3 times higher than for protons.

One medical dedicated proton synchrotron with a macimum energy of 250 MeV was recently commissioned at the Loma Linda Medical Center in the USA [3].

Only one nuclear physic machine is partly in use for light ion therapy beams: the BEVALAC at Berkeley, USA. 435 patients have been treated at this accelerator mostly with neon beams. A still older machine at Berkeley, the synchro-cyclotron treated around 2050 patients with helium beams, but was shut down in 1987. Thus limited clinical experience exists for light ion beams. But biophysical experiments performed over the last 15 years at Berkeley and Darmstadt, strongly bore evidence for the physical and biological superiority of light ions over proton beams [4]. A very comfortable light ion accelerator complex is under construction at NIRS, Chiba, Japan [5].

Besides the BEVALAC at Berkeley, there is one more machine with the appropriate particle energy for light ion beam therapy: the SIS at Darmstadt. It was proposed to use this nuclear physics facility for patient treatment, as well. However, this machine and the associated experimental facilities are totally overburdened by beam time demands from the nuclear physics community. A conceivable beamtime share for treating around 100 patients per year would not satisfy the overall demand for patient treatment but it would definitively contribute to early clinical experience.

2 THE CHOICE OF THE MACHINE TYPE

The literature review of various studies and proposals of the last 15 years is given in a table in the appendix. The beam requirements for medical machines kept fairly stable over the years with fluctuations of 20 % in energy and a factor of 5 in intensity. A typical figure is 5 Gy per liter and minute, which corresponds to 10^8 particles per second for Ne ions spread over a one liter target volume. This number is easy to meet for various choices of the machine.

For the design of medical accelerators, there are few issues not relevant for nuclear physics machines: the extreme care in beam control in respect to patient safety. This implies the fast beam switch-off capability and monitoring redundancy. The time structure of the beam extraction needs some concern in case of a synchrotron when combined with a magnetic scanning system.

For the accelerator builder the question of protons or light ions strongly folds into the choice between cyclotron and synchrotron. This comes not this much from the difference of charge-to-mass ratio, this is a matter of bending power, hence a matter of cost. It comes from the fact that for the same penetration depth in tissue, say 25 cm, a beam energy of 230 MeV is required for protons and around 500 MeV/u for neon ions. The latter value presents focusing difficulties for an isochronous cyclotron.

For proton beams, the required maximum energy lies well in the domain of normal conducting [6] and superconducting [7] cyclotrons. Of course, a synchrotron can be chosen [8] as well. For both machine types examples exist and both choices are likely to be available from commercial manufacturers.

The tumor occupies a large volume compared to the primary beam size and his stopping depth. So far, the volume was covered by defocusing or scattering the beam transversely and masking out a tumor conform slice shape by fixed or programmable collimators. This method by no means takes advantage of the good beam quality of the accelerator and it does not allow for adjustable island shaping inside of the slice contour. A sizable fraction of the beam is lost on the masking aperture with consequences on activation and neutron production. Develeopments in several laboratories [9] have the promise to avoid the above mentioned disadvantages by a magnetic scanning system, for which line length and writing speed are freely programmable and the sharp beam spot is really used for obtaining the contour precision in a loss-free way.

Going one step further in the desire for a clean and flexible beam delivery, the depth control must be considered. Since isochronous cyclotrons with maximum energies mentioned earlier, are not energy variable and synchrotrons, though being energy variable in principle, were not operated in this way, the beam energy had to be trimmed by degraders with fixed thickness for coarse depth adjustment and additionally by a device with modulated thickness for Bragg peak lengthening. Again, the consequences of this passive approach are intensity and quality losses of the beam and limited flexibility in depth control. For light ions, with their inherent susceptibility to nuclear fragmentation, the passive depth control is still more questionable. Only the choice of a modern synchrotron can avoid the above outlined disadvantages. It has been shown, in the meantime [10] that it is energy varaible in coarse and fine steps from pulse to pulse, and the associated beam line setting follows accordingly.

In conclusion: for protons there definitively exists the choice between the cyclotron and the synchrotron. The former being more compact, the latter providing variable energy. For a light ion facility only the synchrotron is at present a realistic choice. In the following the proton option is neglected and design considerations are presented for a light ion synchrotron. Of course, it can accelerate protons as well.

3 SYNCHROTRON DESIGN STUDIES AT GSI

At the GSI a heavy ion synchrotron SIS is in operation since 1990 [11] , having a maximum energy of 2 GeV/u, much higher than necessary for therapy. SIS is designed for a 3 orders of magnitude higher beam intensity than necessary for cancer irradiation. The demand for the acceleration of very heavy ions, up to Uranium, implies a long injector linac, which existed before and it implies an ultra high vacuum system in the ring as well. These and many other features necessary for a maximum of flexibility requested by the nuclear physics community do not constitute a model situation for a medical machine opterating at lower energies and lighter particles. However, the perfectly available energy variation from pulse to pulse was demonstrated routinely and is an indispensable feature for a therapy facility.

Unlike the usual design goal, saying that high beam intensities are beneficial for what reason so ever, here the approach of low, but still sufficient intensities is followed as an exercise. The 10^8. neon ions per second are taken as a specification, assuming no losses in the high energy beam transport and beam delivery system. In the rare event that the tumor volume exceeds one litre, the irradiation time will then be more than one minute. The usual sources of beam losses in the linac and the ring are well considered. But any additional intensity reserve, which then would have to be accounted for in the shielding dimensioning, is deliberately excluded. This restrictive philosophy on intensity management allows one to resort to a short linac and single turn injection, the latter reducing substantially the magnet and power supply cost. The low emittance of the circulating beam simplifies the extraction adjustment.

3.1 The injector

Aside of the synchrotron ring itself, the injector linac is a major subsystem of the accelerator complex, and contributes one third of the total hardware cost. Moreover, linacs were responsible for a regretably large fraction of lost beam time. In the past 20 years progress in the layout and the components of the synchrotron rings was rather slow. But major progress was made in the linac design. Three items of this development should be mentioned in particular.

(a) After a development time of 20 years, the Penning sources are now replaced by ECR sources, yielding adequate currents in much higher charge states [12], [13] . Operation experience is largely available and the expected long life time, stable current yield and good emittance was proven. The ECR source is basically a DC source and is particularly advantageous for cyclotrons. For a pulsed mode, typical for a synchrotron, a current increase of a factor of two was veryfied. The mysterious "afterglow mode", yielding a factor of 5 - 10 more current for short pulses of heavy ions, does not exist for light ions.

(b) The RFQ structure [14] has replaced the bulky and unreliable high voltage DC preinjector at all modern proton and heavy ion linacs. Developments are still going on, aiming for an improved RF efficiency and mechanical stability. The RFQ structure becomes less efficient with increasing particle energy and at 300 - 600 keV/u it is advisable to switch over to some other linac structure, still suitable for low particle velocities.

(c) A novel RF accelerating structure, the Interdigital H-Type (IH) structure [15] is now replacing the traditional Alvarez structure. In the energy range considered here, the IH structure has a 3 times higher RF efficiency, is 2 times shorter for the same energy gain and is smaller in diameter and simpler in its mechanical characteristics.

For an injector of the medical synchrotron all three above outlined developments should be fully applied.

But even with these improvements the linac still represents a substantial fraction of the cost of the facility and should be as short as possible, or more precisely, the injection energy should be as low as possible. There are some conflicting laws involved.

For the high intensities of nuclear physics machines the space charge limit at injection is the limiting factor which can be improved by higher injection energy. For a medical facility we can ignore the space charge limit.

Another important issue is the stripping efficiency which increases up to saturation at 8 MeV/u. But the benefit of higher energy is partly offset by the fact that for higher particle velocities, hence shorter filling time for one single turn, less particles are transferred from the ion source in the ring.

Thus, the injection energy should lie between 3 and 5 MeV/u, giving a 1.6 times larger beam intensity for the higher value. The importance of this factor is by far outweighted by present uncertainties of source abundance and stripping efficiency. Considerations on the practicability of the large rf swing of 1:9.9 and the evaluation of electron capture at 10^{-9}mb during the early ramp start did not reveal objections against the lower injection energy. A final decision will be made during the detailed design of the linac, because linac cost goes up somewhat stepwise with energy, depending on an appropriate choice of tank and amplifier numbers.

3.2 *The ring*

The following design of a medical synchrotron was based to a smaller extend on the heavy ion synchrotron SIS. Older studies and proposals, tabulated as a literature review in the apendix were not used either as a starting point: These rings were too large and contained inherent features of high intensity machines.

Advantage was taken from the design progress of a Japanese proposal for a 250 MeV medical proton synchrotron [8]. The key issue of this proposal was an extensive study, how the machine size could be reduced by various options of the ring optics, or more precisely termed: lattice layout. In this context the length of straight sections, density of focussing elements, edge angles of dipoles, magnet apertures, value of the transition energy etc. are weighted against each other under the constraints of injection and extraction requirement.

The GSI design, as given in Fig. 1 and Table I, is not just a scaling-up from protons to neon, i.e. by a 2.5 times larger beam stiffness, but contains new elements: single

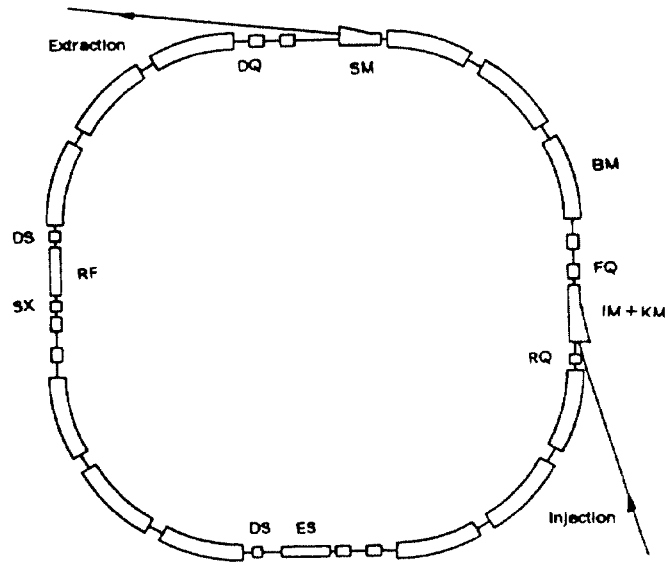

Figure 1: Layout of a light ion synchrotron with 4-fold symmetry. BM = bending magnet. FQ DQ = focussing and defocussing quadrupoles. RQ = resonant quadrupole. DS = extraction bumper magnets. SX = sextupole. ES = electrostatic septum. SM = septum magnet. IM = inflector magnet. KM = kicker magnet. RF = accelerating cavity.

turn injection, and doublet focussing further reduces the ring size.

The relatively low beam intensity is a favourable option allowing for a decently small dipole aperture of 80 times 40 mm. This aperture size provides generous real space for closed orbit distortions. It helps evidently to reduce the magnet weight and eases the design of the dipole vacuum chamber. The weight of the individual magnets is low enough that no crane for assembly and repair is required, nor a particular basement or floor slab fortification. The total magnet weight is about 90 tons, compared to a superconducting cyclotron with an iron mass of around 600 tons.

Particular attention has been given to the beam extraction performance, because at the SIS, low extraction efficiency and poor time structure of the external beam was found initially. In order to avoid the delicate resonant extraction scheme, stripping extraction of partially stripped circulating ions was studied, but it was given up because of the increased ring size and a much more complicated vacuum system. In fact, most of the shortcomings of the resonant extraction, i.e. the enhanced stability requirements for power supplies, would have persisted even for stripping ejection.

In view of the encouraging experience at SIS over the last two years the third order resonance extraction was selected for the medical synchrotron as well. However, the

Table 1: Selected Parameters of the GSI Design Study

Particle Species	p,He,C,O,Ne
Final Energy	var. 50-480 MeV/u
Energy Definition	~ 0.3 %
Beam Int. in 10^8pps	He:9.5, C:4.2, N:3.7, O:2.0, Ne:1.0
Repetition Rate	1 Hz
Beam Burst	var., typic. 400 ms
Beam Emittance norm.	vert. 0.5π mm · mrad hor. 0.1π mm · mrad
Beam rigid. $B \cdot \rho$	max. 7 T·m
Injection	single turn at 3 MeV/u
Extraction	slow (1/3 integer reson.)
Ring size	squared 17 x 17 m
Lattice periodicity	4 focussing doublets
Straight sections	2.9 m
Magnets:	12 dip. 2.7 m long, B_{max} 1.4 T 8 quad. 0.46 m long 1 sextupole
Aperture	dipoles: 40 x 80 mm quad.: 100 mm diam.
Vacuum	10^{-9}mb, not bakable
RF	first harmonic 0.44-4.13 MHz 1 cavity 0.85 kV

structure of the external beam must be much cleaner and repeatable for a medical synchrotron associated with a magnetic scanning beam delivery, compared to the tolerance of nuclear physics targeting. This was not emphasized in the earlier proposals, perhaps because a final decision on the tumor conform beam delivery was never included.

Presently a development program is underway at GSI, aiming for an extracted beam pulse of rectangular time shape, with steep leading and trailing edges and a flat top level regulated in the range of a few percent. The technical measures for reaching these properties allow, at the same time, any fast turn-off of the external beam for ending a scan pattern or for other interlock purposes.

If the desired pulse shape is not reached and the ordinary bell-shaped time structure with fluctuating height must be accepted, the problem is transferred to the realisation of a much wider dynamical range of the speed control in the rasterscan electronics.

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APPENDIX

Light Ion Medical Accelerator Proposals

1	**Proposal**	**1977**[16] **LBL** LBL-Arizona	**1984**[17] **LBL** H.I.Medic.Acc.	**1987**[18] **LBL** LIBRA	**1980**[19] MARIA	**1987**[5] HIMAC	**1988**[20] **EULIMA** Cyclotron	**1991**[21] **EULIMA** Synchrotron
2	**Particle Intensity in pp/s**	He $2\cdot10^9$ C $4\cdot10^8$ Ne $2\cdot10^8$	He Si $3\cdot10^7$	He C $6\cdot10^9$ Ne	P 10^{11} Si $2\cdot10^9$ Ar 10^9	He 10^{10} Ne $3.4\cdot10^8$ Ar $2.7\cdot10^7$	O $5\cdot10^{11}$ Ne $5\cdot10^{10}$	O $1\cdot10^9$
3	**Energy in MeV/u Range in cm**	250 415 28cm 550	30cm 800	500 38cm	250 35cm 1000	30cm 800	400	400 22cm
4	**Energy Switching**	pulse to pulse	slow	slow	slow pulse to pulse?	slow (5min)	not included	pulse to pulse
5	**Beam Broadening**	Raster Scan	Scattering Wobler	Raster Scan Wobler	?	Scattering Wobler	Raster Scan	Raster Scan
6	**Treatment Rooms Vertical Beams**	3 3	6 1	6 2	4 1 up & down	4 2	3 1	2 1
7	**Other Purpose**	none	Rad. Physics Biology	Rad. Physics Chemistry Biology	Nuclear Sci. Atom. Phys. Biomed.	Physics and General	Biomed.	none
8	**Accelerator**	Synchrotron	Synchrotron	Synchrotron	Synchrotron	Synchrotron	Cyclotron	Synchrotron
9	**Other Accel. Consid.?**	Cycl./SCCycl. Linacs	none	none	Cyclotrons Linacs	none	none	none
10	**B·ρ**	6.5 Tm	9.7 Tm		12.5 Tm	9.7 Tm	6 Tm	6.3 Tm
11	**Diameter**	25m	30m		34.5m	41m	9m	19m
12	**Rep. Rate**	2 Hz	2 Hz	2 Hz	1 Hz	0.5 Hz	continuous	1 Hz
13	**Source**	PIG, C^{3+}	PIG, Si^{4+}	PIG EBIS?	PIG, Ar^{5+} ECR	PIG, C^{2+} ECR, O^{8+}	ECR, O^{6+}	
14	**Injector**	Alv.2MeV/u	RFQ. 8MeV/u Alv.	RFQ. 1.5 MeV/u Alv.	RFQ. 10 MeV/u Alv.	RFQ. 6 MeV/u Alv.	optional:Cycl.	RFQ. 5 MeV/u Alv.?
15	**Cost**	7 M$ tot.	Inj. 8 M$ Syn. 6 M$	22.4 M$	?	120 M$	18 MECU	13.9 MECU Hardware

Legend to Table II

1. Short term of proposal title and year of publication.

2. Design particles and beam intensities of the accelerator in particles per second.

3. Maximum energy for the particles of line 2 and penetration depth in tissue.

4. Comment on energy variability. Slow means from treatment to treatment, pulse to pulse means that the dose monitor of the raster scan determines the next energy step in increments of about 3%, but not faster than from cycle to cycle.

5. Beam broadening indicates how the beam covers a target area of about 15x15 cm. The traditional method is scattering, the most advanced is the raster scanning.

6. The first line gives the number of treatment rooms with horizontal beams, the second line gives the number of those rooms, which have a vertical beam, as well.

7. Other purpose means, whether research and application fields, other than cancer therapy, have been considered in the parameter table and facility lay-out.

8. This line denotes the accelerator type which was chosen finally.

9. Indications are given, which other accelerator types have also been studied as alternatives to the final choice.

10. Bending power of the dipole magnets.

11. Geometrical machine diameter.

12. Repetition rate is the number of beam bursts per second.

13. Type of ion source and charge state extracted from the source. PIG means the classical Penning source. ECR means the modern Electron Cyclotron Resonance source.

14. The traditional synchrotron injector is the Alvarez structure. Modern injectors definitively include a radio Frequency Quadrupole structure in front of an Alvarez structure or, more recently, an Interdigital H-Type structure.

15. Cost figures are vague in a sense that only a lengthy tabulation can give evidence about what is included.

For References, see end of main paper.