Review of accelerator technologies for ion beam therapy

Titus Dascalu

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Abstract

The current accelerator technologies designed for proton and ion beam therapy have experienced gradual improvements driven by the need to reduce the cost of treatment. This report presents an overview of the main operational properties of cyclotrons and synchrotrons, the only types of accelerator currently used in active treatment facilities. The major developments are highlighted in contrast with the challenges to be overcome in order to match the novel advances in beam delivery. Laser-driven accelerators are proposed as the main alternative for a step-change in cost, size and speed of treatment. Their major potential lies in enabling the production of multiple ion species and ultra-high dose rates. However, we outline several features for which significant progress is required before reaching clinical applications.

1 Introduction

From the initial proposition of R. Wilson [1] in 1946 regarding the use of accelerated protons for radiotherapy, ion beams have proven to be an effective tool for cancer treatment. The key advantage of protons over X-rays is the precision with which the radiation dose can be delivered to the target tissue. In the context of a rising world population and an increase in the complexity of the disease, there is a prompt need for novel techniques to be developed towards treating patients on a large scale and with the high precision necessary for a better quality of life. By February 2020, around 220,000 patients [2] have been treated with particle radiotherapy at 102 therapy facilities in operation worldwide. Approximately 80% of these patients were treated with proton beams, while for the others, biologically more efficient light-ion beams were used - Figure 1.

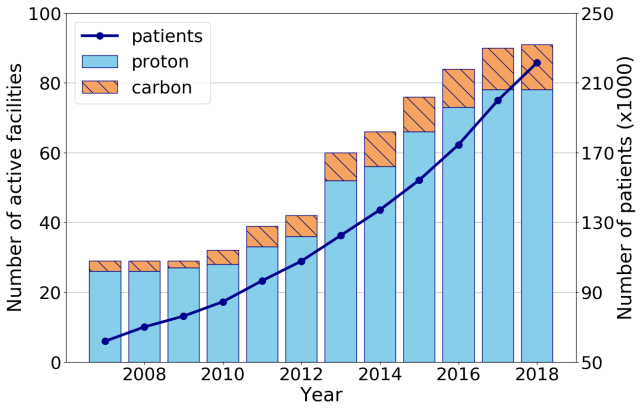

Figure 1: Statistics of patients treated in particle therapy facilities worldwide - data adapted from [2].

Hadrons are preferred since they have a significant increase in the dose at the end of their range [3]. These individual 'Bragg peaks' can be delivered sequentially in depth to obtain a spread out region of uniform energy deposition. To obtain the correct lateral dose profile, the monoenergetic beam is usually broadened by passive methods based on beam scattering and patient specific apertures. However, the state of the art technique is the so-called pencil beam scanning [4] – the beam is swept across the transverse plane delivering the dose in a grid of spots. This is considered the optimal method since it removes the need for patient-specific devices and minimises the radiation of healthy tissues. Also, the parallel advance of imaging techniques makes it suitable for future treatment of moving organs.

The main challenge in providing this treatment to a larger fraction of the population is to reduce the cost, size and the difficulty of the operation of the treatment facilities. The key element of such a facility is the accelerator. Most often, it dictates the specific requirements of the beam delivery system as well as the performance of the treatment facility. Further development is required to ensure that the treatment plan for patients will be determined by the clinical need and will not be limited by the accelerator technology.

In the current state of the field, protons are accelerated to therapeutic energies from 70 to 250 MeV mainly with cyclotrons, while only synchrotrons are used for carbon ions up to 400 MeV/u. Each has its advantages and disadvantages. State of the art intensity-modulated proton therapy may require up to 60 layers of energy for each beam delivery [5]. Both accelerator technologies above are able to vary the energy within an order of a couple of seconds which is inefficient and significantly increases the time that the patient needs to stay still. Furthermore, the use of heavier particles such as helium and carbon drastically increases the cost of such accelerators.

Laser-driven ion beams have been proposed as an alternative to conventional accelerator facilities for radiotherapy applications as they can provide relatively higher dose rates and can produce carbon ions in addition to protons. Recent studies [6] have shown radical improvement in normal tissue sparing during treatment with ultra-high dose rates for the same total amount of radiation delivered.

Other competing technologies are under study for cost and performance, such as FFAs (fixed-field accelerators) [7] and high-gradient linacs [8].

2 Cyclotrons

The cyclotron was invented in the early 1930s as the first cyclic accelerator. However, it is still one of the most used technologies for accelerator applications today, including proton therapy, due to its great reliability and relatively small footprint. Out of the current 102 operational hadron therapy facilities, 63 use a cyclotron.

Cyclotrons produce a continuous stream of protons accelerated to the maximum design energy. They are usually more compact and able to achieve high beam intensity. The protons follow a spiral orbit (Figure 2) in a plane between the poles of a

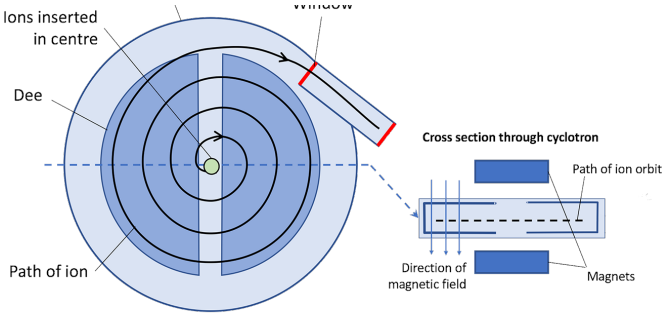

Figure 2: Principal components of a cyclotron and particle path.

single magnet. An oscillating RF electric field ensures the acceleration between the Dees for a few hundred turns.

Proton therapy requires acceleration up to 250 MeV. During acceleration, there is a significant change in the revolution frequency of protons

$$\omega = \frac{qB}{2\pi\gamma m_p} \tag{1}$$

due to the dependence on the Lorentz factor γ; q, m_p are the charge and mass of the proton; B is the applied magnetic field strength.

This frequency change is compensated by either increasing the B-field with radius (isochronous cyclotron) or by changing the frequency of the accelerating electric field (synchrocyclotron).

A typical normal conducting cyclotron has a mass around 200 tons and a diameter of about 5 m. A more recent synchrocyclotron from Mevion [9] uses superconducting magnets that reduce the total mass to only 20 tons [10]. Commercial companies are currently pushing the magnetic field up by factors of 2-4 by switching from normal-conduction to super-conducting magnets, which has led to a significant drop in price. Larger reduction in cost and size is believed to be possible in the future by studying the next step in the sequence resistive magnet accelerator – conventional superconducting cyclotron – iron-less facility [11]. Studies have started to design a cyclotron with no iron yoke, thus substantially reducing the weight and the time taken to change the magnetic field. Both roles of the yoke to shape the magnetic field in the accelerating gap and shield the rest of the cyclotron from the field would be taken over by a system of SC coils.

However, cyclotrons with strong magnetic fields can only operate in pulsed mode (synchrocyclotrons). Such a beam imposes minor limitations

to the spot-scanning technique, but it does not allow for the more advanced continuous line scanning.

The main disadvantage for proton therapy is that cyclotrons cannot provide fast beam energy modulation required for the novel beam-scanning technique. This is due to the use of energy degraders which are mechanically inserted in the path of the beam before the treatment room. This method further requires an energy selection system and increased radiation shielding. To compensate for the particle loss inside the energy degraders, a higher circulating current is combined with a good extraction efficiency. Particle loss of up to 99% is possible when degrading to the lowest energy transported and collimating the beam for proper beam-size and divergence. Thus, the cyclotron gets radioactive due to beam losses, especially for a low extraction efficiency.

A further major disadvantage of cyclotrons is that energies above 250 MeV, which are desirable for imaging the patient during the treatment, are not achievable while maintaining a compact size. Also, while significant effort has been done to design a cyclotron suitable for carbon therapy [12], there are no future plans for a facility based on it.

3 Synchrotrons

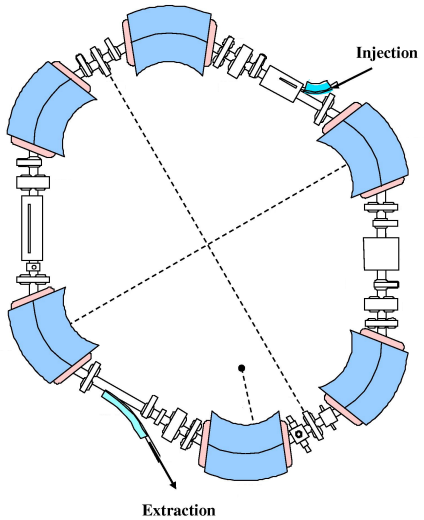

Figure 3: Synchrotron lattice used by Hitachi - adapted from [13].

Synchrotrons accelerate pulses of particles to the desired energy. The particle bunches are initially accelerated by a linac and then injected into the synchrotron. Typically, the ring is made of 4 to 8 dipoles with quadrupole and sextupole magnets in between them - Figure 3, as well as an RF cavity. The magnetic field and RF-frequency are synchronised with the revolution frequency of the particles such that the radius of the orbit remains constant during acceleration. Once the specified energy is achieved, a particle bunch is extracted from the synchrotron into a transport line towards the treatment rooms. The beam produced is characterised by a dead time of 1-2 s. This is required to ramp down the magnetic field and re-accelerate the next particle bunch. Thus, the energy can be adjusted cycle by cycle. In general, for the application of one treatment layer of radiation at the patient, one to three filling and acceleration sequences are required.

The main advantage of synchrotrons is the ability to provide active energy modulation and smaller energy spread with lower power consumption [5]. Since the path of the particles is fixed, synchrotrons are built with much smaller magnets than cyclotrons, even though additional quadrupoles are needed for the strong focusing. The extraction may occur on a relatively long period of time (up to 5 s) during which the magnetic field is kept constant (flat-top). This allows the beam to be scanned at the patient in a similar manner to a continuous beam. Energy changes reach a time scale of milliseconds as the energy of a slow extraction synchrotron can be varied during the extraction of a single pulse.

Another advantage is that because there is no need for an energy degrader, the average current required is greatly reduced. Furthermore, synchrotrons can accelerate particles with larger magnetic rigidities. Thus, they are the only technology used in present operational facilities for carbon therapy such as HIT, CNAO, MedAustron and NIRS [14].

The phase space area occupied by the beam is characterised by ϵ, the beam emittance [15]. While the emittance obtained with a synchrotron is well suited for treatment, space charge effects limit the maximum achievable beam current. Storing more charge is possible if the injection energy is increased. However, this drives the cost up since a longer pre-accelerator is needed. Another challenge for a facility which uses a synchrotron is the treatment of targets inside moving organs. The main strategy is based on the ability to start and stop the beam quickly enough to deposit the charge in

the right location. Some fast extraction schemes [16] have been proposed which can achieve repetition rates as high as 30 Hz with the beam fully extracted in one turn. However, to deliver the dose with 1% accuracy, the energy change and beam scanning needs to be done in about 20 ms [14], still faster than currently possible.

Multiple optimisation techniques have been developed to build smaller and cheaper synchrotrons. Better magnet designs with an increased ramping speed allow for the decrease in the dead time between spills. The power consumption has been reduced by improving the injection chain using a Radio Frequency Quadrupole (RFQ) directly injecting into the synchrotron. Modifications of the beam optics and field-regulation of the magnets [17] further improved the treatment time. Only recently, superconducting magnets have been investigated for use in medical synchrotrons at NIRS (Japan) where a reduction in diameter from 25 m to 7 m is possible for a carbon-ion accelerator. At HIT (Germany), the efforts have been focused on the stability of the extracted beam intensity which is crucial for continuous scanning.

However, no substantial size reduction is expected in the near future for proton therapy facilities driven by a synchrotron. The cost reduction is possible with further optimisation of magnets, RF cavities or injection schemes, but the process contains many small slow steps.

4 Laser-driven acceleration

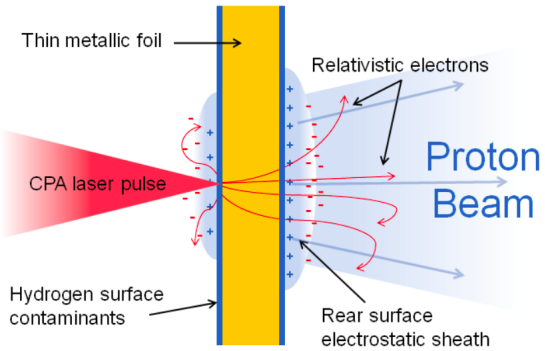

Figure 4: Main aspects of Target Normal Sheath Acceleration.

4.1 Beam generation

Strong laser pulses are considered to be a promising alternative to conventional accelerators since laser and optical components are typically smaller, lighter and easier to maintain compared with beam line magnets. The most attention has been devoted to TNSA (Target Normal Sheath Acceleration) [18]: a high intensity laser pulse is incident on a target doped with hydrogen atoms. The energy absorption in the foil creates a plasma and electrons are pushed out of the foil. The charge separation induces a strong electrostatic field which accelerates the protons out of the rear surface of the target - Figure 4.

The most studied target type is a thin foil (few μm to tens of μm), but other schemes have been proposed (e.g. liquid sheets [19] or cryogenic-hydrogen ribbons [20]). The laser regime of relevance for TNSA is characterised by an irradiance $I\lambda^2 > 10^{18}$ Wcm$^{-2}\mu$m^2, where I and λ are the laser intensity and wavelength. Above this threshold, the laser pulse can efficiently couple energy into relativistic electrons through the ponderomotive force. When the electrons interact with an inhomogeneous electromagnetic field, the ponderomotive force pushes the electrons out from the high intensity regions.

The space-charge field formed at the rear of the target holds the hot electrons within a sheath extending by approximately a Debye length λ_D from the surface of the target. This allows the initial accelerating field to be modelled by [21]

$$E(0) = \frac{k_B T_h}{e\lambda_D} = \sqrt{\frac{n_h k_B T_h}{e\lambda_D}} \qquad (2)$$

where n_h and T_h are the density and temperature of the hot electrons. For typical values $\lambda_D \sim 1\mu$m and $T_h \sim 1$MeV, the accelerating field is of order TV/m. Experimental results showed a preferential acceleration of light ions (protons, carbon and oxygen ions) from the surface layers of the target.

A large number of experiments have demonstrated the generation of multi-MeV proton and ion beams since the first report of laser acceleration of protons [22] in 2000 for several laser and target parameters. The energy spectra of the ion beams are broadband, typically with an exponential profile, up to a high energy cut-off [21]. The highest reported TNSA energies around 60 MeV were obtained using PW lasers.

4.2 Clinical feasibility

The ion beams obtained by TNSA are superior to those of conventional RF beams in two main

aspects: very low transverse emittance and high number of particles per shot. However, the beam has high divergence, high energy spread and low particle occupancy towards the high-energy end of the spectrum. These properties are listed in Table 1. Therefore, the design of an ion therapy facility based on TNSA has to solve the inherent challenges of beam capture and focusing.

When compared to conventional proton and ion sources, laser pulses can accelerate ions to much higher energies. Conventional sources produce low energy particles (tens of keV/u). In such a beam, the electrostatic repulsion limits the total charge that can be captured and accelerated. Laser-driven ions are generated at higher energies (10 MeV or more) where the effect of space-charge forces becomes negligible. Then, the beam-current is only limited by the capacity of the capture system.

Apart from the reduced size and cost of optical equipment, the laser-driven ion beams are a promising alternative in the view of new studies that support radiotherapy (RT) with ultra-high dose rates [6] (FLASH-RT). When compared to conventional radiotherapy, FLASH-RT was shown to reproducibly spare normal tissue for the same total amount of treatment dose [23]. Previous experiments using laser-driven proton beams [24] have reported on-cell dose rates of the order of 10^9 Gy/s. By contrast, the differential effect of FLASH between tumour and normal tissue was observed for a dose rate of around 200 Gy/s, well within the capabilities of laser-driven sources.

Extensive research is ongoing to optimise the interaction targets for stability and reproducibility [25] and to investigate other mechanisms such as radiation pressure acceleration [26] or breakout afterburner acceleration [27].

5 Conclusion

The above discussion shows that clinical treatment imposes several conditions on the design of an accelerator that also needs to satisfy size and cost constraints. Differences arise between the performance of cyclotrons and synchrotrons, the only technologies met in operational facilities today. When looking at particular requirements, both have disadvantages, mainly in providing the right beam properties required by the novel advances in treatment delivery: continuous beam-scanning, high dose rates or beam-imaging guidance. Extensive optimisation studies are slowly driving a reduction in size and cost for both accelerator types, but a step-change approach becomes increasingly more necessary. The unique properties of laser-driven ion bunches may open new opportunities for an improved treatment by enabling ultra-fast delivery of ultra-high dose and mixed-ion production from the same target.

Table 1: Properties of beams accelerated via TNSA

Characteristic	**Value**
ultra-low transverse emittance	> 0.004 mm-mrad
ultra-short bunch duration	≤ 1 ns
high brightness	$10^{11} - 10^{13}$ protons/shot
low number of protons at the high-energy end	$\sim 10^6 - 10^7$ particles/MeV
large divergence	up to 10s of degrees, energy dependent
high energy spread	up to 100%$\Delta E/E$

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