COMMERCIAL ACCELERATORS FOR PROTON THERAPY - AN OVERVIEW

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Abstract

There are different accelerator types used for proton therapy of diverse tumours. In use are mostly classical cyclotrons, synchrocyclotrons and synchrotrons. In addition, linear accelerators were or are under development. This paper will give an overview on commercially available systems. Not only technical aspects are discussed, but also new developments in treatment methods like ARC and FLASH therapy as well as irradiations in upright position and the backlash on the used accelerator types. Furthermore, practical issues like certification and embedding those systems in a hospital environment will be described and evaluated.

HISTORY

Two discoveries in physics laid the basis for radiotherapy: 1895 Wilhelm Conrad Roentgen found the X-Rays [1] and in 1904 William Henry Bragg published his measurements of energy loss of low-energetic α-particles in air, showing a maximum at end called "Bragg peak" [2], see Fig. 1 for high-energetic particles.

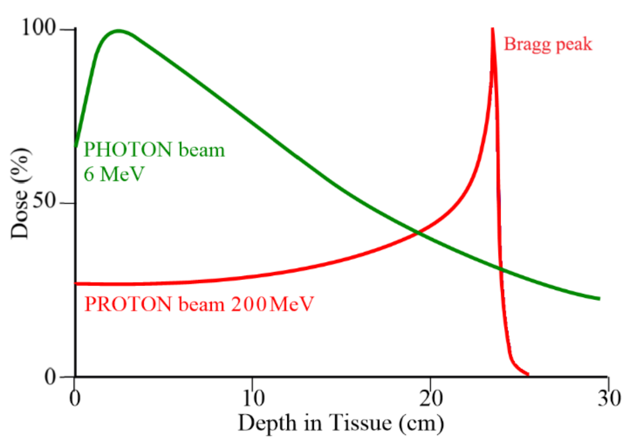

Figure 1: Dose-depth curves of high energetic X-Ray photons and protons in tissue [3].

Whereas X-Rays were used for diagnostics and radiation therapy very soon, becoming the main treatment option in oncology in the following decades, high energetic proton beams were not available before Ernest O. Lawrence and M. Stanley Livingston invented the cyclotron in 1930 [4] and further developments resulted in powerful systems around twenty years later. In 1946 R.R. Wilson first outlined the advantages of radiotherapy with protons [5], pointing to the finite range and Bragg peak for treating deep-seated tumours.

First biological studies started in the early 1950s at LBL, Berkeley and first proton treatments of patients followed in the next years. Later on, other institutes worldwide succeeded, still on an experimental basis at research laboratories and with relatively small patient groups in the beginning. First proton treatment installations at hospitals started in the 1990ies and commercially available systems were offered as from around 2000.

USED ACCELERATOR TYPES

Different accelerator types are used for proton therapy, mostly classical cyclotrons, synchrocyclotrons and synchrotrons [6]. In addition, linear accelerators were or are under development and are described here shortly. Exotic developments like FFAGs, Dielectric Wall or Laser-Driven Accelerators may be options for the future, but are not relevant nowadays and are not scope of this paper.

Cyclotrons

Isochronous cyclotrons used today for proton therapy consist of the following main components [7]:

1. Proton source: Usually Penning effect sources (H_2 gas ionization by energetic electrons in an electrical discharge) are positioned in the middle of the cyclotron.
2. Magnet, resistive or super-conducting: The isochronous cyclotron employs an azimuthally varying field (AVF) to enable isochronism and vertical focusing.
3. RF: The isochronous cyclotron is based on a fixed radio frequency (RF) during acceleration, usually with frequencies between 60 and 90 MHz and 100– 200 kW power is needed. Thus, a c.w. beam is the result.
4. Extraction system: A thin vertical blade acts as the septum and the electrical field of some ten kV deflects the beam out of the cyclotron.

Figure 2: IBA 230 MeV resistive isochronous cyclotron [7].

Following the cyclotron, see Fig. 2, a passive energy variation system is needed, a variable thick target wheel or a wedge-like overlapping slit system, both called degraders. From this point on all beam parameters for tumour

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irradiation are prepared. Different beam guidance can be arranged behind: fixed horizontal or vertical lines, but also gantries.

Synchrocyclotrons

Synchrocyclotrons are increasingly being used in modern proton therapy in place of conventional, isochronous cyclotrons, primarily to make the systems more compact, cost-effective and requiring less maintenance. A synchrocyclotron operates with a timing-varying RF frequency and a decreasing magnetic field, resulting in a pulsed beam (typically 1 kHz rep. rate and 1% duty cycle) with vertical focusing. Although both types of cyclotrons accelerate protons in a circular path, synchrocyclotrons offer decisive technical advantages for everyday clinical practice:

- Higher magnetic fields (compactness): Synchrocyclotrons can be operated at significantly higher magnetic fields (normally 3-5T, but up to 8-10T possible) than conventional cyclotrons. This allows the machines to be built much smaller and lighter. This is crucial for mounting the accelerator directly on a rotating gantry (e.g., the Mevion S250-System, see Fig. 3).
- Reduced space requirements & costs: Thanks to their compact design, the required bunker structures are smaller, which reduces capital expenditure and also radiation protection requirements.

Figure 3: Ken Gall and the Mevion S250 8.9T synchrocyclotron (within [8]).

Synchrotrons

Besides cyclotrons also synchrotrons can provide beam for proton therapy. The technique is however much more complex, see Fig. 4:

1. Proton source: For highly stable current operation mostly ECR ion sources are used.
2. Injector linac: As synchrotrons need a pre-accelerated beam of some MeV an injector linac is necessary. Mostly RFQ and DTL cavities (fixed frequency around 200 MHz) are used to reach this energy.
3. The synchrotron itself – with a diameter between 6m and 8m – consists mainly of 4-6 dipoles, quadrupole and sextupole magnets for focusing the beam as well as bumper magnets for the injection phase. The acceleration is realized by a frequency variable (mostly between 1-10 MHz) ferrite filled cavity. The ramped operation of all these components needs a special control system to produce a variable end energy.
4. In addition, a sophisticated extraction system to produce a smooth, stable beam is adapted [9] to extract the protons by an electrostatic and/or magnetic septum system.

The higher complexity of a synchrotron-based system brings some advantages:

- No component contamination by a degrader and therefore less (radioactive) waste.
- Less shielding is needed.
- An immediate maintenance entry is possible.

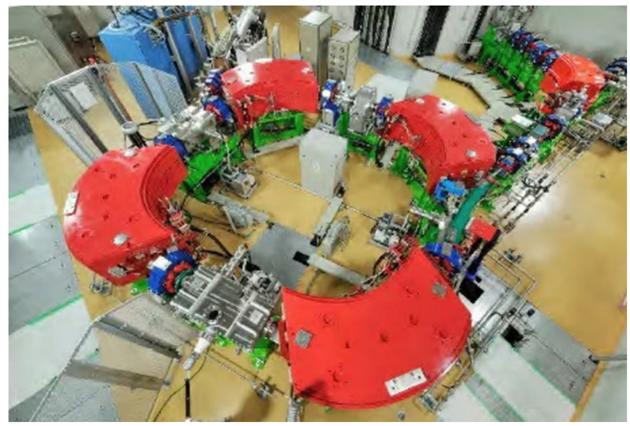

Figure 4: Hitachi`s solution consisting of an injector linac and an energy variable (70 -230 MeV) synchrotron [10].

Linacs

In contrast to the above-described circular machines in principle also linear accelerators can produce beams of up to 250 MeV (61% of the speed of light) for proton therapy.

Figure 5: AVO Linac test facility at Daresbury Lab during commissioning : ECR source (from DREEBIT; 2,45 GHz), RFQ (Design by CERN, end Energy 5 MeV), SCDTL cavities (Design ENEA, Italy; end energy 37,5 MeV) und CCL cavities (up to 230 MeV).

Such the increase of speed must be taken into account which demands different cavity types and frequencies, typically staged in the order from 750 MHz to 3 GHz with a beam pulse repetition rates of up to 200 Hz, see Fig. 5 for an example. The RF power is generated by a series of (different) klystrons, each driving a section of the linac.

Table 1: Overview on commercially available single-room proton systems

Company	IBA	Mevion	Hitachi	ProNova	P-Cure
Productname	ProteusOne	S250i	PROBEAT	SC360	
Characteristic					
Country	Belgium	USA	Japan	USA	Israel
Accelerator system	Synchro-Cyclotron	Synchro-Cyclotron	Synchrotron	Isochronous Cyclotron	Synchrotron
Beam delivery	220-degree rotating gantry	190-degree rotating gantry	360-degree rotating gantry	360-degree rotating gantry	horizontal beam
Patient positioning	6D robotic couch	6D robotic couch	6D robotic couch	6D robotic couch	robotic chair
Certification	MDR, FDA 510(k)	MDR, FDA 510(k)	MDR, FDA 510(k)	FDA 510(k)	FDA 510(k)

The most ambitious project to develop such a linac based proton therapy unit was carried out by Advanced Oncotherapy Plc (AVO). By end of September 2022 the test facility with the 20m long linac was ready and an end energy of 230 MeV was achieved; in addition, the treatment room was finished, too. But the development found no further investors, thus the AVO activities were stopped in 2023 and the company entered into administration in May 2024 [11].

A new attempt to realize a similar linac system is now the ERHA (Enhanced Radiotherapy with Hadrons) project by LinearBeam [12], but it is still under development.

SYSTEM CERTIFICATIONS

All components of a proton therapy facility including the above-described accelerators, the beam lines to the treatment rooms (fixed horizontal or vertical as well as gantries) together with the beam adaption (e.g., pencil beam scanning) and patient positioning systems, mainly robotic couches, form a medical product. For these there are very strict rules in the different economic regions in the world. In the EU the latest version is the Medical Device Regulation (EU) 2017/745. In the U.S. medical products need a FDA 510(k) approval, which differs to the EU regulation partly. Other countries may have their own certification systems or adapt more or less the EU or U.S. regulations. In addition to the enormous technical documentation and testing protocols for certification, any changes of a medical product trigger a new labour-intensive revision. Altogether these regulations set the bar high for new products on the market.

OVERVIEW ON COMMERCIALLY AVAILABLE SYSTEMS

There are a limited number of companies worldwide, which produce proton therapy systems or have done that in the past. The market, estimated at around USD 1.6 billion in 2023, is expected to grow to between USD 3 billion and nearly USD 6 billion by the early 2030s. And the market moves to standardized single-room systems in contrast to individually adapted multi-room facilities at large hospitals in the early stage of proton therapy.

Therefore Table 1 contains only the companies which actually distribute single-room proton therapy systems, which account for the majority of the market. (The list may not be exhaustive. E.g., Siemens/Varian is not included as they withdraw their product from the market end of 2022).

The global market leaders are IBA worldwide, Hitachi and Mevion Medical Systems. Further companies sell proton therapy facilities in different configurations: Mitsubishi, Sumitomo, Toshiba, ProTom Asia.

NEW TREATMENT METHODS

Further developments of proton therapy methods at public institutes and commercial companies are still ongoing. The aim is always to enhance the treatment capabilities (medical, technical) and precision, while minimizing the side effects. Some of these progresses are described here, especially in conjunction to the accelerator technology.

ARC Therapy

Arc Therapy offers dosing for a multiplicity of angles within in one go using a "step-and-shoot" mode or better with a continuous rotation, aiming to enhance treatment conformity and minimizing doses to the overlying tissue. First gantry-based systems offer this method as an option, the same procedure can be realized using a horizontal beam and a rotatable chair. A synchronisation between the rotation (either gantry or chair) and the adapted beam is necessary, which is easier with cyclotrons and synchrocyclotrons, but more difficult with synchrotrons.

FLASH Therapy

There is a big interest towards the use of ultra-high dose rate (UHDR) irradiation with >40 Gy/s. This so-called FLASH therapy showed additional treatment efficacy on tumours while reducing side effects on organs at risk with high-energetic electron beams. If this impact can also be proven with protons is still under investigation. Nevertheless, cyclotrons and synchrocyclotrons could provide these UHDR beams, while synchrotrons are not able to provide such high proton currents. UHDR treatments would significantly reduce the irradiation time (also besides the FLASH effect), which is an overall aim in radio-oncological therapy due to higher precision and more patient comfort.

Irradiations in Upright Position

The idea to irradiate patients in upright position is not new, but compact, reliable systems with an integrated, vertical CT have entered the market yet in the last years as alternatives to gantries (partly). The CT is absolutely necessary as a human body is not rigid, especially the abdomen area is very soft. Therefore, the tumour of a patient positioned on a chair-like system needs to be scanned to localize it correctly before the irradiation can start. In Fig. 6

such a system is shown, where the patient can also be rotated in any angle. More or less all companies in proton therapy are under way to adapt such systems, as any accelerator system with horizontal beam line can be connected.

Figure 6: Leo Cancer Care's Upright CT scanner with patient positioning system MARIE [13].

EMBEDDING ACCELERATOR SYSTEMS IN A HOSPITAL ENVIRONMENT

The building around a proton therapy system accounts for a significant proportion of the whole project costs. And the planning process for embedding such a facility in an existing radio-oncological section of a hospital – as well as a new stand-alone facility – may take a sufficient amount of time of planning activities including obtaining the necessary construction permits and radiation protection licences.

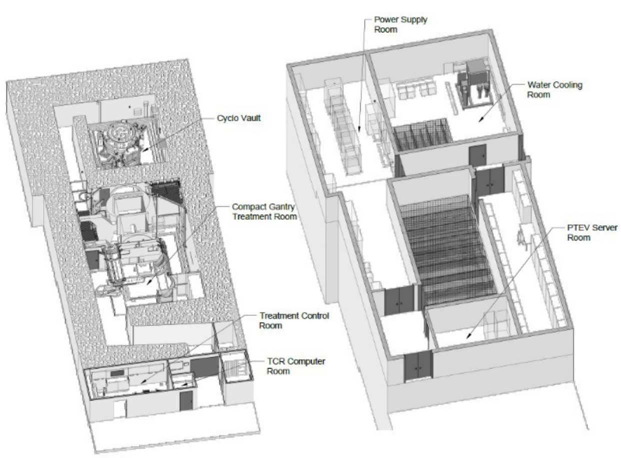

Figure 7: An example for a very compact proton therapy facility, based on a superconducting synchrocyclotron and a gantry (left). The related technical rooms are shown on the right side (IBA ProteusOne [14]).

As building costs are proportional to the enclosed volume investors demand the most compact proton therapy system with low operational costs. Criteria are the space for the accelerator and the treatment room plus the space for infrastructure and technical equipment and how many levels in a building have to be available. Systems with gantries always need two levels for installation, arrangements with a chair only one, but these have less flexible treatment options. Synchrotrons including the injectors need more space than superconducting cyclotrons, see Fig. 7 for an example. Linac-based installations need small, but around 20m long tunnels only for the accelerator, which are more difficult to embed in a compact building. All these questions – and even much more – have to be discussed in the selection process where the radio-oncologists give the main input, which treatment possibilities must be covered by the proton beam facility.

CONCLUSION

According to the latest statistics from the Particle Therapy Cooperative Group (PTCOG), by the end of 2025, there were over 125 operational proton therapy centres worldwide, primarily distributed across North America, Europe and East Asia, with the total number of treated patients exceeding 450,000 [15]. And further developments at public institutes as well as at commercial companies are still ongoing, as proton therapy is a growing market. The near future will see more centres worldwide with further optimized treatment methods.

ACKNOWLEDGEMENTS

The paper is based on knowledges and experiences obtained in the last six years during the selection process for an extension of HIT with an additional single-room proton facility. In particular, the author would like to thank Prof. Dr. J. Debus for fruitful discussions during this time. Furthermore, additional thanks go to the selection team at the University Hospital Heidelberg, especially Gabriele Sroka-Pérez, Frank Rothe and Dominik Pieper for additional information. Many thanks go to all my HIT co-workers as well as colleagues from other facilities for debating pros and cons of different proton therapy methods.

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