Innovations in the Next Generation Medical Accelerators for Therapy with Ion Beams

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Abstract. Modern hadron-therapy accelerators have to provide high intensity beams, for innovative dose-delivery modalities such as FLASH, pencil beams for 3D scanning, as well as multiple ions with radio-biological complementarity. They need to be compact, cheap and have a reduced energy footprint. At the same time, they need to be reliable, safe and simple to operate. Cyclotrons and compact synchrotrons are nowadays the standard for proton therapy. For heavier ions such as carbon, synchrotrons remain the most viable option, while alternative solutions based on linacs, FFAs or cyclotrons are being proposed. In this context, the European project HITRIplus studies the feasibility of an innovative super-conducting (SC) magnet synchrotron for carbon ions, with state-of-the-art multi-turn injection from a specially designed linac and advanced extraction modalities. A compact synchrotron optimized for helium ions, making use of proven normal-conducting technology, is also being designed.

1. Introduction

Radiation therapy with protons and other ions has the advantage, over conventional treatment with photons, of better sparing the healthy tissues, because of two major reasons: the dose is deposited at a specific depth depending on the energy of the incoming beam (Bragg peak) and ions can be steered with magnetic fields, thus allowing for fast pencil beam (3D) scanning.

Proton therapy still occupies a niche, there are about 100 proton therapy facilities in the world [1], compared to the over 14’000 X-ray machines, but it is rapidly expanding. A few major vendors of cyclotrons and compact synchrotrons (e.g. IBA and Hitachi) provide turn-key facilities of 500-800 m^2 (single room, equipped with a gantry).

Carbon ions (C-ions) are also used in radiation therapy, because of their higher Relative Biological Effectiveness (RBE), a factor 3 compared to protons and X-rays, and the possibility to also treat oxygen-depleted tumours, the so called “radio-resistant” tumours. The energy needed to penetrate up to 33 cm is 430 MeV/u for C-ions (250 MeV for protons), corresponding to a beam rigidity of 6.6 T m, compared to 2.42 Tm for protons. C-ions are therefore a factor 2.7 more “rigid” than protons, thus requiring larger accelerators, or a different technology. The 13 facilities in the world [1] providing C-ions to 400-430 MeV/u are based on a 20-25 m diameter synchrotron (only one project under construction is based on a cyclotron) and have several treatment rooms. Their cost is proportionally larger.

Helium ions are in-between [2]. They have a sufficient RBE to treat most of the tumours, suffer less scattering than protons and do not present the fragmentation tail of C-ions. They require a maximum energy of 220 MeV/u, for a range of 30 cm and a beam rigidity of 4.5 Tm. Other species are being considered in addition to protons, helium and carbon ions, such as oxygen, and extensive radio-biology research is still needed to characterize them.

To promote innovation in the field of ion therapy accelerators and propose a new generation of ion therapy facilities in Europe, some collaborative initiatives have been recently launched. The first is the CERN-based international collaboration NIMMS (Next Ion Medical Machine Study) [3]. NIMMS has then joined the EU Integrating Activity HITRIplus [5], together with other laboratories and partners, among which the South East Europe International Institute for Sustainable Technologies (SEEIIST) which federates the countries in the SEE [4], for a common facility in the region.

2. SC magnet synchrotron

The first innovation considered for the next generation of facilities is the SC technology, which allows to significantly reduce the dimensions of the facility (and its cost by at least 20% [3]) and goes toward the implementation of single-rooms facilities for C-ion therapy. The SC technology, however, introduces new challenges and considerations, related e.g. to the slower ramp-rate and to the powering and cooling strategy for energy efficiency [6].

In Japan, the effort is focused towards the development of the Quantum Scalpel (QST-NIRS), based on a compact synchrotron with SC magnet, of a similar size of a proton accelerator, eventually fed by a laser accelerator.

In Europe, within HITRIplus, a compact synchrotron with SC magnets is also being developed, based on the work [7] initiated by the TERA Foundation. Figure 1 [3] shows its potential implementation as a single-room facility of 21m x 56 m, with its gantry.

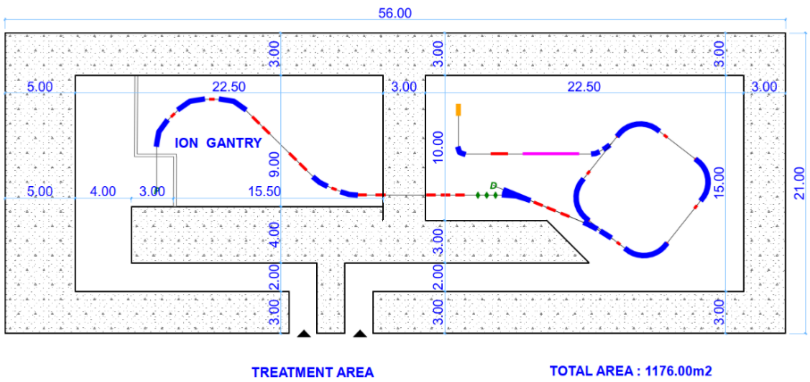

Figure 1: Layout of a compact single-room SC ion therapy facility [3].

After a first design [7] based on four 90^0 Canted Cosine Theta (CCT) magnets, the layout has evolved into a triangular shape. Figure 2 shows a sketch of the new triangular baseline and its optics. The lattice has three straight sections with zero dispersion, to accommodate injection and extraction septa and RF.

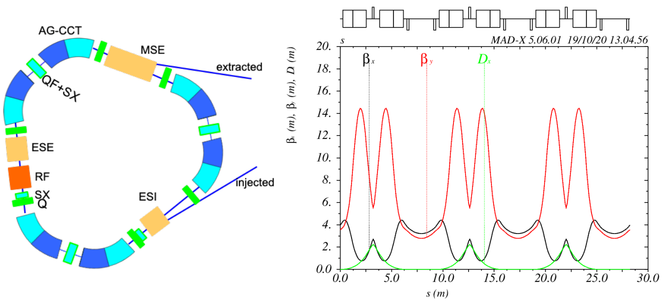

Figure 2: Sketch and optics of the SC synchrotron, triangular layout (new baseline in HITRIplus) [8]

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The main bending units, which are "cold", comprise two 60^0 CCT magnets, with nested alternating-gradient (AG) layers [9] and a SC quadrupole in between, which carries also sextupole coils for chromaticity control. The presence of the AG layers, although it makes the magnet design more complicated, provides periodic focusing while bending, reducing the beta-function and the beam size. The optics is flexible thanks to external "warm" quadrupoles (also equipped with additional coils to provide orbit correction and sextupole excitation) to move the working-point from the injection tune to the extraction on a third order resonance (Q_x=2.66).

A strong program for the SC magnet development is ongoing within HITRIplus, with contributions from another European Program I.FAST and several additional collaborations and national programs [10]. The magnet parameters are listed in Table 1.

Five demonstrator magnets of about 1 m length with different conductors and configurations are going to be built within the next two years, to test key aspects of these magnets: manufacture of strongly curved magnets, thermal behaviour, CCT technology, and the possibility to use High Temperature Superconductivity (HTS).

From the beam optics point of view, these magnets also represent a challenge, because of the strong curvature with respect to their length that requires a new definition and correct modelling of higher order field components [11].

Table 1: SC Magnet parameters

Parameters	**Gantry**	**Synchrotron**
B field	4 T	3 T
Aperture (D)	80 mm	80 mm
Angle	45^0	60^0
Ramp rate	0.4 T/s	0.8 - 1 T/s
Coils	Combined function	AG-CCT

3. Lightweight gantry

The first ever built gantry for C-ion (at HIT, Heidelberg) weighs 600 tons. The use of SC technology allowed to decrease the weight of the second C-ion gantry (at HIMAC, Chiba) to 300 tons. After its successful commissioning, a third one has been installed in Yamagata.

With SC magnets weighting maximum 5 tons each, a total radius of 5 to 6 m and scanning magnets downstream of the last bend, the TERA foundation proposed the concept of a light-weight gantry attached to the wall and rotating by 220^0 [7] [12], Figure 3. The major advantage in this design is that the rotating part is less than 40 tons (there is no counterweight) and therefore it can be supported by the shielding wall and its rotation can be driven by an electric motor with high-torque planetary gears. The concept has been further studied within HITRIplus [13] but the decision was to adopt for a future European SC gantry a more conservative design, with counterweight, a cradle and a 360^0 rotation.

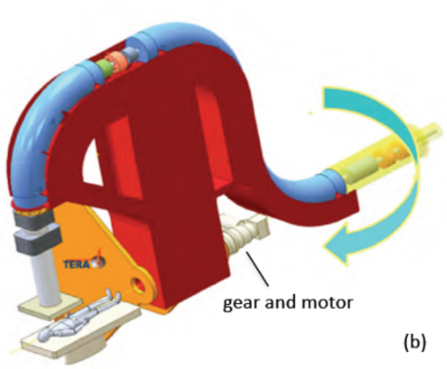

Figure 3: Concept of gantry attached to the wall [7]

Other solutions to deliver beam from different angles with a static device and a toroidal configuration have been proposed, such as Gatoroid, developed at CERN [14], but also considered too complex for a C-ion gantry.

Within the community, there is also the discussion on whether the gantry is needed at all, and whether is not enough to rotate the patients, once it is accepted that they can be treated in vertical position [15]. The idea of a chair is indeed very old, but it had been abandoned because of the necessity of imaging the patient in the treatment position. Because only recently vertical CT scans or open-filed MRI became available, the chair is now back into consideration, also for treatments other than eye melanoma, like in the head-and-neck, torax, abdomen and pelvis. This solution would drastically reduce the size and cost of a C-ions facility.

4. Flexible beam delivery and Multi-Turn injection

Today, in the European synchrotron centers, the beam is accelerated at a different energy for each cycle, delivered to the corresponding layer on a timescale of several tens of seconds and then dumped. Development is ongoing to have a cycle in which the beam is accelerated (or decelerated) at different steps in energy to allow for multi-energy beam delivery, as it is successfully done at HIMAC (Chiba) [16].

Moreover, new irradiation techniques (FLASH) of delivering high dose within a few hundreds of milliseconds seem promising for sparing normal tissues [17, 18, 19]. The next generation synchrotron needs to be able to deliver the entire stored beam with this modality.

These two techniques, and in general a flexible beam delivery, requires a factor 10 to 20 higher intensity stored in the ring. New C-ion sources under development promise a factor 3 higher beam current [20], still a much longer and efficient multi-turn injection need to be designed, for an injection energy of 5 MeV/u. The injector linac as well need to be optimized for maximum transmission.

5. New linac designs

The linac injector to an ion therapy synchrotron is a critical element, with a strong impact on the cost and performance of the facility. Within HITRIplus, new designs are being explored in two directions. The first consists in improving the standard 217 MHz IH-based design presently used in all the European ion therapy centres [21]. The second option is to adopt the higher 352 MHz frequency that allows using compact RF structures powered by low-cost klystrons [22]. Both designs are optimised for acceleration of C^{4+} up to the synchrotron injection energy of 5 MeV/u. Since the linac is used for synchrotron injection only for a very small fraction of time, an interesting option consists in adding two more sections, the first optimised for He^{2+} going to 7 MeV/u, and the second for protons up to 10 MeV. Such a linac could be operated at higher duty cycle and be used to produce radioisotopes for theragnostics, like ^{211}At for targeted alpha therapy [23].

An even more attractive option, though, consists in covering the full energy range required for C-ion treatment with a compact High-Frequency (HF) linac. In this case, fully stripped C^{6+} produced by a low-emittance EBIS source are accelerated. After the initial exploration by TERA of a 3 GHz linac design [24], the layout has been further refined with the addition of a 750 MHz compact RFQ injector and with the design of a medium-energy section with an active 180^0 bend, to reduce the footprint of the facility [25]. A low-energy test stand with a He^{2+} ion source (easier to produce than C^{6+}) and an RFQ is in preparation at CERN.

6. Single ion (helium) optimization

Treatment plans with multi-ions (like carbon or oxygen and helium) to cover different regions of the tumour are under discussion and attract great interest [26, 27]. This requires fast switching from one cycle to the next between ions species and multiple ion sources. The opposite approach, instead, consists of having a synchrotron optimized for one ion species only, namely He-ions.

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To exploit the potential of He-ion therapy, the NIMMS collaboration with the contribution of HITRIplus has recently developed the concept of a compact facility based on a synchrotron optimised for helium beams [28, 29].

The accelerator has a triangular layout, similar to the one of the SC synchrotron but with warm magnets, which implies that the beam size in the vertical plane needs to be smaller than in the horizontal (for the SC-magnet version, the aperture was round). Figure 4 shows a sketch of the layout and the optics, for a tune close to Q_x =2.67. The extraction septa (electrostatic and magnetic) are located respectively in the first and the third straight section and have a relative phase advance of about 270^0, thus the first one is placed on the inside of the ring and the other on the outside. The overall circumference is 33 m.

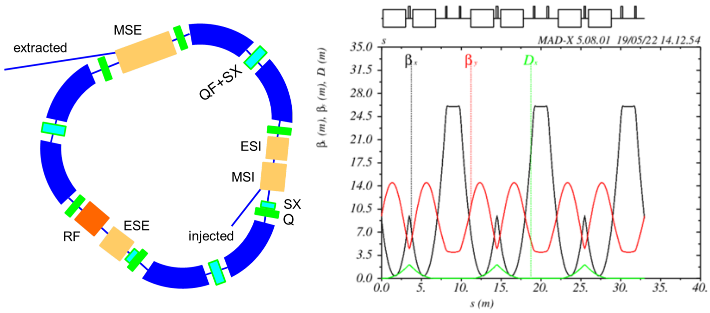

Figure 4: Sketch and optics of the He-ions synchrotron.

7. Final considerations

Innovations in ion therapy accelerators can be as usual grouped in three categories: development, disruption and low-tech.

Developments are gradual and reside in improvement of existing solutions. An example is the baseline for the SEEIIST facility [5] that includes a “conventional” warm synchrotron with a factor 20 higher intensity, improved injection and extraction, possibility to treat with multiple ions within a single treatment, optimization of the workflow and a fast and safe switch between treatment and research rooms. The second example of this type of innovation is the Helium synchrotron, which is based on known technology and the advanced features previously described, and which answers, in a short timescale, the needs of the medical community to treat patients with Helium.

Disruption implies a change of technology, therefore higher risks which need to be mitigated with extensive R&D. In this category we find the SC magnet compact synchrotrons and the full-energy HF linac (as well as FLASH dose delivery, laser acceleration, addictive manufacturing, AI/ML techniques). The power of disruptive technology implies rethinking completely the way the machine is designed, to fully exploit its potential, and not simply adding it as a “cool feature” in a conventional design. In this respect, the adoption of SC magnets and the challenge of slow ramp-rate makes it mandatory to accumulate the full beam intensity to irradiate in one cycle or perhaps to rethink the optics and adopt an FFA approach [30, 31]. Viceversa, for the HF linac varying rapidly (100 Hz) the beam parameters, a low beam current is the preferred strategy.

Finally, “**low tech**” innovation is the less glamourous, but it is key to democratize access to ion therapy. It focuses on providing solutions which are easy to operate, maintain and industrialize and which reduces the price of the facility. A very good example is the developments of alternatives to gantries (such as rotating chair), leveraging advancement in other fields, such as imaging, robotic positioning and new treatment modalities.

References

[1] PTCOG: Particle Therapy Co-Operative Group, website, accessed March’23 https://www.ptcog.site/index.php/facilities-in-operation.

[2] Mairani A et al 2022 *Roadmap: helium ion therapy* Phys. Med. Biol. **67** doi: 10.1088/1361-6560/ac65d3.
[3] Vretenar M et al 2021 *The Next Ion Medical Machine Study at CERN: towards a next generation cancer research and therapy facility with ion beams*, in Proc. IPAC21.
[4] Heavy Ion Therapy Research Integration (HITRIPlus) project website. https://www.hitriplus.eu/.
[5] Damjanovic S *et al.* 2021 *A novel facility for cancer therapy and biomedical research with heavy ions for the South East European International Institute for Sustainable Technologies* in Proc. IPAC21, MOPAB414.
[6] Bisoffi G et al 2022 *Energy Comparison of Room Temperature and Superconducting Synchrotrons for Hadron Therapy* Proc. IPAC22, Bankgok, Thailand, doi:10.18429/JACoW-IPAC2022-THPOMS049.
[7] Benedetto E et al. 2020 *A carbon ion superconducting gantry and a synchrotron based on Canted Cosine Theta magnets* arXiv:2105.04205.
[8] Benedetto E 2022 *Carbon ion compact medical synchrotron: key parameters.* CERN-NIMMS-Note 09.
[9] Brouwer L et al 2016 *Design of an Achromatic Superconducting Magnet for a Proton Therapy Gantry* IEEE Trans. Appl. Supercond. 27, 44001006.
[10] Rossi L et al 2021 *A European Collaboration to Investigate Superconducting Magnets for Next Generation Heavy Ion Therapy IEEE Transactions on Applied Superconductivity*, vol. 32, 4400207.
[11] Benedetto E et al 2023 *Strongly Curved Super-Conducting Magnets: Beam Optics Modeling and Field Quality Proc. IPAC'23*, Venice, Italy.
[12] Amaldi U et al 2021 *SIGRUM – A superconducting ion gantry with Riboni's unconventional mechanics* CERN-ACC-NOTE-2021-0014;CERN-NIMMS-Note-002, https://cds.cern.ch/record/2766876.
[13] Pullia M et al 2022 *Explorative Studies of an Innovative Superconducting Gantry Proc. IPAC'22*, Bangkok, Thailand.
[14] Bottura L, Felcini E and De Rijk G 2020 *GaToroid: A novel toroidal gantry for hadron therapy* Nuclear Instruments and Methods in Physics Research, Section A. 983, 164588.
[15] Volz L, Sheng Y, Durante M, Graeff C 2022 *Considerations for Upright Particle Therapy Patient Positioning and Associated Image Guidance* Front Oncol 12:930850. doi: 10.3389/fonc.2022.930850.
[16] Iwata Y et al. 2010 *Multiple-energy operation with quasi-DC extension of flattops at HIMAC* Proc. IPAC10, Kyoto, Japan, pp. 79-81, MOPEA008.
[17] Bourhis J, Sozzi W J, Jorge P G, et al. 2019 *Treatment of a first patient with FLASH-radiotherapy* Radiother Oncol, 139, pp. 18-22.
[18] Buonanno M, Grilj V, Brenner D J 2019 *Biological effects in normal cells exposed to FLASH dose rate protons* Radiother Oncol, 139, pp. 51-55.
[19] Mascia A E, Daugherty E C, Zhang Y, et al. 2023 *Proton FLASH Radiotherapy for the Treatment of Symptomatic Bone Metastases: The FAST-01 Nonrandomized Trial* JAMA Oncol. 2023;9(1):62–69. doi:10.1001/jamaoncol.2022.5843
[20] Castro G et al. 2022 *The AISHa ion source at INFN-LNS* J. Phys.: Conf. Ser. 2244 012025
[21] Ratzinger U et al. 2022 *Linac Design within HITRIplus for Particle Therapy* Proc. LINAC22, UK, 2022. https://doi.org/10.18429/JACOW-LINAC2022-MOPOGE01.
[22] Nikitovic L, Torims T, Vretenar M 2023 *Comparison of 352 MHz Linac Structures for Injection into an Ion Therapy Accelerator* Proc. IPAC'23, Venice, Italy.
[23] Vretenar M, Mamaras A, Bisoffi G, Foka Y 2022 *Production of Radioisotopes for Cancer Imaging and Treatment With Compact Linear Accelerators* Proc. IPAC'22, Bangkok, Thailand.
[24] Andrés S, Amaldi U and Faus-Golfe A 2013 *CABOTO, a high-gradient linac for hadrontherapy* J Rad Res, vol. 54, pp. i155-i161.

[25] Bencini V 2019 *Design of a novel linear accelerator for carbon ion therapy* Geneva: CERN-THESIS.
[26] Inaniwa T et al 2017 *Treatment planning of intensity modulated composite particle therapy with dose and linear energy transfer optimization* Phys Med Biol 62:5180-5197.
[27] Kopp B et al 2020 *Development and validation of single field multi-ion particle therapy treatments* Int J Radiat Oncol Biol Phys 106:194-205.
[28] Vretenar M et al. 2022 *A Compact Synchrotron for Advanced Cancer Therapy with Helium and Proton Beams* Proc. IPAC'22, Bangkok, Thailand , paper THPOMS021.
[29] Vretenar M et al 2023 *Conceptual design of a synchrotron-based facility for cancer therapy and biomedical research with helium and proton beams* Proc. IPAC'23, Venice, Italy, 2023, this conference.
[30] Peach K et al. 2013 *Conceptual design of a nonscaling fixed field alternating gradient accelerator for protons and carbon ions for charged particle therapy* Phys. Rev. ST Accel. Beams, vol. 16, no. 3, p. 030101.
[31] Taylor R, Steinberg A et al. 2023 Slow Extraction Techniques from Fixed Field Accelerators” Proc. IPAC'23, Venice, Italy, this conference.