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THE NEXT ION MEDICAL MACHINE STUDY AT CERN: TOWARDS A NEXT GENERATION CANCER RESEARCH AND THERAPY FACILITY WITH ION BEAMS

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Abstract

Cancer therapy with ions has several advantages over X-ray and proton therapy, but its diffusion remains limited primarily because of the size and cost of the accelerator. To develop technologies that might improve performance and reduce accelerator cost with respect to present facilities, CERN has recently launched the Next Ion Medical Machine Study (NIMMS), leveraging CERN expertise in accelerator fields to disseminate technologies developed for basic science. A perspective user and key partner of NIMMS is the SEEIIST (South East European International Institute for Sustainable Technologies), established to build in the region an innovative facility for combined cancer therapy and biomedical research with ion beams.

THE NEXT ION MEDICAL MACHINE STUDY AT CERN: TOWARDS A NEXT GENERATION CANCER RESEARCH AND THERAPY FACILITY WITH ION BEAMS

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Abstract

Cancer therapy with ions has several advantages over X-ray and proton therapy, but its diffusion remains limited primarily because of the size and cost of the accelerator. To develop technologies that might improve performance and reduce accelerator cost with respect to present facilities, CERN has recently launched the Next Ion Medical Machine Study (NIMMS), leveraging CERN expertise in accelerator fields to disseminate technologies developed for basic science. A perspective user and key partner of NIMMS is the SEEIIST (South East European International Institute for Sustainable Technologies), established to build in the region an innovative facility for combined cancer therapy and biomedical research with ion beams.

For SEEIIST and other potential users, three options were considered. Conceptual designs of a warm-magnet synchrotron at high beam intensity, of a compact superconducting magnet synchrotron, and of a high-frequency linear accelerator have been compared in terms of cost, risk and development time. The development of curved superconducting magnets, of compact synchrotrons and ion gantries, and of linacs is being pursued within EU-funded projects or specific collaborations.

INTRODUCTION

Cancer treatment with beams of protons or heavier ions, usually called hadrontherapy, is increasingly employed in the treatment of large deep-seated tumours, particularly of the radio resistant type. It constitutes an accurate alternative to conventional X-ray therapy ensuring a reduced dose to organs surrounding the tumour, thanks to the characteristic dose distribution provided by the “Bragg peak” energy loss of hadrons. Therapy using protons is rapidly growing, supported by four commercial vendors that offer turnkey facilities providing standard treatment procedures, while therapy with ions has a more limited diffusion. Only 13 facilities worldwide offer treatment with Carbon ions, 9 in Asia and 4 in Europe, despite its advantages with respect to proton therapy. Thanks to their higher ionisation per length, ions can destroy hypoxic radio-resistant tumour cells providing at the same time increased dose conformity and reduced integral dose. Recent tests of combining ion therapy with immunotherapy have shown encouraging results in reducing diffused cancers, via the immune response triggered by DNA fragments released during ion treatment. While the present experience is limited to Carbon treatment, there is an increasing interest in other ions (He, Li, O…) as well as a strong demand for clinical and pre-clinical research with ions, to optimise treatment procedures.

The main factor limiting the diffusion of ion therapy is the size and the related cost of the accelerator. The energy required for full body penetration is considerably higher, 430 MeV/u for Carbon compared to 250 MeV for protons. This corresponds to a factor 2.7 in the radius of the accelerator, assuming the same maximum field in the accelerator magnets for both particles.

So far, therapy with ions is provided by large synchrotrons designed for operation with both protons and ions. This is the case of the four European facilities that were designed in the 1990’s for dual proton-carbon use, two based on the developments made at GSI and two on the outcomes of the PIMMS (Proton-Ion Medical Machine Study) collaboration based at CERN in the period 1996-2000 [1].

In a similar way as proton therapy has been boosted by the development of compact cyclotron-based accelerator designs, there is a clear demand from the scientific and medical communities for the development of more compact and economical ion therapy accelerator designs, to make this cutting-edge treatment accessible to a larger fraction of cancer patients. Following the same scheme of the PIMMS study, this demand has been initially addressed by the TERA Foundation that in collaboration with CERN developed a preliminary conceptual design of superconducting ion therapy synchrotron and gantry [2]. As a follow-up of this collaboration, CERN has taken the initiative to initiate and coordinate a wider European effort to develop new advanced accelerator designs for ion therapy launching in 2019 the Next Ion Medical Machine Study (NIMMS). This collaborative study is intended to demonstrate the societal impact of technologies developed for particle physics, leveraging on the wide range of CERN’s technologies and expertise in the fields of advanced magnet design, superconducting materials, and beam optics.

To define a programme for NIMMS and to pave the way to a larger collaboration, a Workshop at ESI Archamps in June 2018 gathered major worldwide experts from both the medical and the accelerator communities, to understand the potential of ion therapy and to highlight directions to improve its diffusion [3]. On top of agreeing on the major limitations related to the cost and size of both accelerator and gantry, the participants concluded that a next generation facility should reduce treatment time thanks to higher beam intensities, should be able to profit of improved delivery schemes including of the FLASH type, and should operate with different ions for experiments and possibly treatment.

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To reach these goals, the Workshop highlighted two innovative accelerator designs: a) a superconducting synchrotron operating at a field of 3 - 5 T, with >10^{10} ions/cycle, and b) a high-frequency linac accelerating fully stripped Carbon ions, operating at 200 Hz with 10^8 ions/pulse. In parallel, a superconducting gantry was considered as an essential tool for any new ion therapy facility.

Another crucial outcome of the Workshop was the establishment of a collaborative network linking key European research institutions with the four European ion therapy centres, and with the new SEEIIST (South East Europe International Institute for Sustainable Technologies) initiative, which aims at the construction of a new Research Infrastructure for cancer research and therapy in South East Europe over the next decade. Promoted by eight member countries and two observers in the region, the SEEIIST international facility will devote 50% of its operation time to experiments in pre-clinical radiobiology and medical physics with ions, filling gaps in the European cancer research programme and in the geographical distribution of research and therapy infrastructures in Europe, involving countries formerly at war in the tradition of science for peace [4].

Within this collaboration, the NIMMS project has been structured as a toolbox concentrating on the development of key technologies corresponding to CERN core competences, to be assembled and used for future project like the SEEIIST. As an initial step for the benefit of SEEIIST and other potential users, three accelerator options were analysed and compared. Conceptual designs of a warm-magnet synchrotron at high beam intensity, of a compact superconducting synchrotron, and of a high-frequency linear accelerator have been compared in terms of performance, cost, risk, and development time.

ADVANCED WARM SYNCHROTRON

The reference for the comparison is a PIMMS-type synchrotron as proposed in the early SEEIIST proposal [5], integrated with new features to optimize the dose delivery. In particular, the possibility to deliver the entire dose of 2 Gy for a 1-liter tumour in one or few synchrotron cycles is taken as baseline for both the superconducting and the warm-magnet synchrotron. This corresponds to achieving a challenging beam intensity of $2 \cdot 10^{10}$ Carbon ions /cycle (and corresponding higher intensity for the other species [6]), which requires the increase of the ion source current, a better transmission through the linac, and the optimization of the multi-turn injection process. The full beam will be either slow-extracted at multiple energies or fast extracted for FLASH schemes [7]. Moreover, a new injector linac design for higher current and lower cost is also considered, with energy in the range between 5-10 MeV/u and the option of producing radioisotopes for therapy and imaging between synchrotron injections. The accelerator feeds three treatment rooms, equipped respectively with an horizontal beamline, an horizontal and a vertical beamlines, and a rotating superconducting gantry, as well as two beamlines for experiments. The layout of the warm synchrotron facility is presented in Fig. 1.

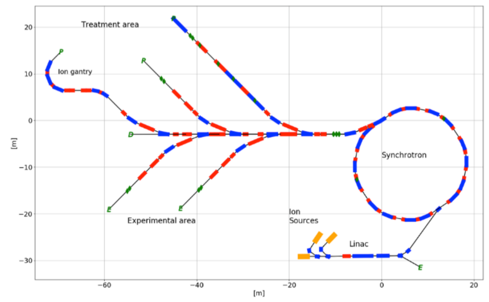

Figure 1: Layout of the synchrotron-based facility.

SUPERCONDUCTING SYNCHROTRON

Inspired by similar ongoing developments in Japan [8], the TERA Foundation developed a compact superconducting synchrotron design, characterized by the fact that the same 90° magnet unit is used for both the synchrotron and the gantry [2]. As an additional novelty, the design is based on Canted-Cosine-Theta magnets with Alternating Gradient (AG-CCT) as developed for proton gantries [9]. This design has been refined and developed, and is considered as an alternative for the SEEIIST.

The ring (Fig. 2) consists of four 90^0 CCT magnets which carry along the curvature an alternating gradient (AG) either focusing or defocusing of the same absolute amplitude. It has a two-fold symmetry where the straight sections for the injection, extraction, and RF systems are kept as short as possible.

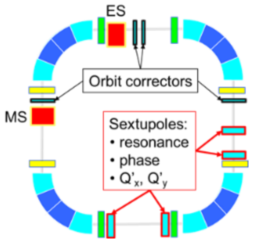

Fig.2: Layout of the superconducting synchrotron

The four main magnets are powered in series, as well as their AG coils. To add tunability, two extra families of small quadrupoles are added in the four straight sections. The resulting ring has a 27 m circumference, for a maximum bending field of 3.5 T.

HIGH-FREQUENCY LINAC

Linear accelerators for proton therapy are in advanced development phase, expected to present advantages in terms of costs and therapeutic beam quality [10, 11, 12]. A linac-based accelerator for therapy can be pulsed at repetition frequency ≥100 Hz, keeping a different number of accelerating cavities active for each pulse. This provides a simple, efficient, and rapid way to change the beam energy for longitudinal “painting” of the tumour. A Carbon version of the linac requires a significant length of about 50 m, but the footprint can be reduced folding the linac into two straight sections with a curved 180^0 section in between, the so-called “bent linac” (Fig. 3). The purpose is to optimize the footprint to fit in a rectangular room, while preserving the high beam quality that characterizes linacs [13].

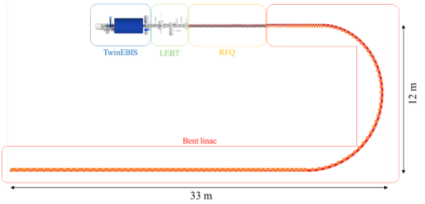

Figure 3: Layout of the bent linac

Because of the high operating frequencies, 750 MHz in the injector and 3 GHz in the main section, the linac can accelerate only particles with minimum q/m=0.5, requiring a special ion source development. In the present design, the fully stripped Carbon ions are produced in a TwinEBIS source presently under commissioning at CERN, designed to generate 10^9 ions in a 5 µs pulse at 200 Hz repetition rate [14]. The 5 MeV/u 750 MHz RFQ is followed by a fixed energy section to 30 MeV/u, by the bent section alternating accelerating cavities and short permanent dipoles operating at 1 T up to 100 MeV/u, and by the energy modulated section to 430 MeV/u. For the fixed energy section, three types of accelerating cavities are being considered, a 750 MHz Drift Tube Linac (DTL) operating in standard or in Quasi-Alvarez configuration, and a 3 GHz Side Coupled DTL [6]. Cell Coupled Linac structures at 3 GHz cover both the bent and the energy modulated section.

COMPARISON OF OPTIONS

Figure 4 shows the layout of a research and therapy facility based on each of the three accelerator options above. Even if the accelerator area is 50% smaller for both superconducting (SC) synchrotron and linac as compared to the conventional synchrotron, when the overall facility surface is considered, the reduction in size amounts to less than 20%. The estimated cost of SC-magnet synchrotron and linac are very similar, both about 20% lower than the conventional synchrotron, without considering additional savings related to the smaller area. The two synchrotron designs have similar performance, while the linac has the advantage of the easier energy modulation that requires, however, a fast control of the extracted beam intensity. The R&D time is considered as slightly longer for the linac. Following this study, SEEIIST has adopted as baseline configuration for fast construction a warm-magnet synchrotron with improved performance, promoting the development of superconducting magnets for the SC synchrotron to be considered as a longer-term alternative option [7].

SUPERCONDUCTING GANTRY

All the accelerator options above make use of a new lightweight superconducting gantry concept originally developed in collaboration between TERA Foundation and CERN [15], which is now going to be designed and prototyped within a collaboration of CERN, INFN, CNAO, and MedAustron with the support of the EU Horizon 2020 Project HITRIplus [15]. The gantry is attached to a wall or pillar and rotates by less than 360^0 without counterweight, moved by a gear-motor system. The SC magnets are grouped in two cryostats, with the scanning magnets placed at the exit of the bending section. Two versions of the magnets are under development, the first of the cos-theta type with 3-3.5 T field, leading to ~6 m external radius, and the second of a more ambitious Canted-Cosine Theta (CCT) type reaching up to 5 T and an external radius < 5 m.

CONCLUSIONS AND FUTURE PLANS

The preliminary analysis indicates that both SC synchrotron and the linac are viable options for a next generation ion therapy facility, requiring R&D in the fields of SC magnets the first, and of low-energy injector and RF structures the second. Development of bent CCT magnets at field between 3 and 5 T is going to take place within two recently approved European Projects, HITRIplus [16] supporting ion therapy, and I.FAST [17] developing advanced accelerator technologies, both with 4 year duration. HITRIplus will also coordinate the design of a new injector linac for ion therapy facilities, and the design of a compact SC synchrotron to be used in a SEEIIST-type facility or in a small single-room version of about 1'000 m^2 surface (Fig. 5).

On top of participating in these collaborations, NIMMS is going to contribute to the construction and testing of the low-energy section of the high-frequency linac and will launch a new initiative on applying modern Machine Learning to optimise design and operation of ion therapy accelerators.

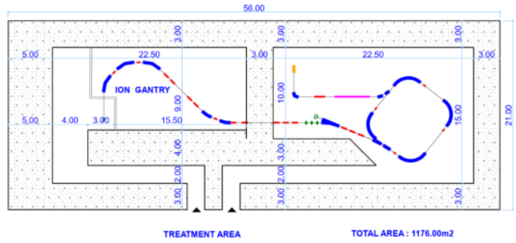

Figure 5: A compact single-room SC ion therapy facility.

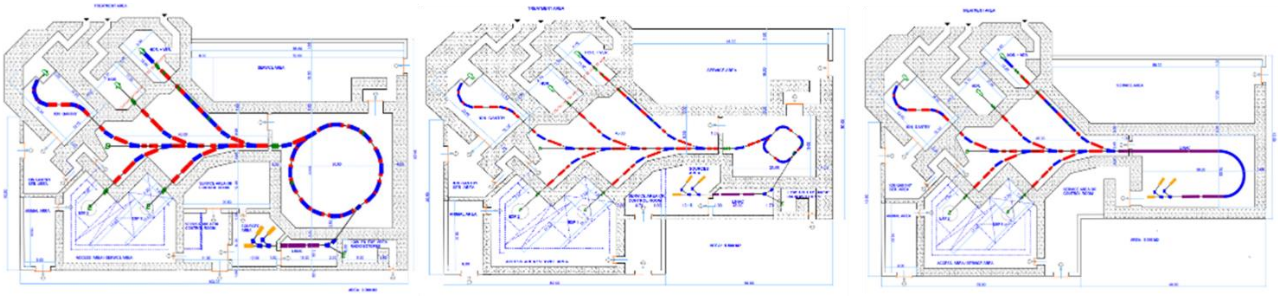

Figure 4: Layout of an ion research and therapy facility, based on warm-magnet synchrotron, SC synchrotron, and linac.

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