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CONCEPTUAL DESIGN OF A COMPACT SYNCHROTRON-BASED FACILITY FOR CANCER THERAPY AND BIOMEDICAL RESEARCH WITH HELIUM AND PROTON BEAMS*

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Abstract

Thanks to their superior dose conformality and higher radiobiological effectiveness with respect to protons, helium ions are considered as the new tool of choice in the fight against cancer using particle beams. A facility to produce helium beams at therapeutical energy can also accelerate protons, at energies permitting both standardised treatment and full body radiography, and heavier ions for treatment of shallow tumours and for research. Equipped with FLASH beam extraction, it will be able to couple the protection to healthy tissues provided by Bragg peak and FLASH effect.

This paper presents the basic layout of a facility based on a compact synchrotron of new design that can accommodate a wide research programme with patient treatment, sharing the beam between two treatment rooms and an experimental room. The linac accelerator may be designed to allow a programme for production of new radioisotopes for therapy, diagnostics and theragnostics using helium ions, in parallel with the operation as synchrotron injector.

Overall cancer and conventional radiotherapy statistics, along with an estimate on the number of patients that can benefit from this facility is presented for the case of the Baltic States, as a candidate for hosting the facility.

HELIUM IONS FOR CANCER THERAPY

First developments of therapeutical use of helium ion beams for cancer therapy were done by the pioneering work at Lawrence Berkeley National Laboratory (LBL) in 1952. Studies of helium ion radiotherapy at LBL continued further from 1975 with a 10-year long clinical trials with more than 500 patients [1], as well as using helium ions as a reference in comparative studies with heavier ions [2]. Although promising results were achieved in treatment of small tumours close to critical organs [1], a period of silence in helium ion radiotherapy followed with technological developments focused mainly on proton and carbon ion therapy. Despite that, interest in scientific research and clinical use of helium ion radiotherapy has resurfaced in recent years.

Rationale of clinical use of helium ion beams can be attributed to the intermediate physical and biological characteristics compared to proton and carbon ion beams. Due to increased mass of helium ions, multiple Coulomb scattering and range straggling is reduced, resulting in a decreased lateral penumbra, sharper Bragg peak and distal fall-off (see Fig. 1). On the other hand, compared to carbon ions helium ions undergo less nuclear fragmentation processes, resulting in better distal dose conformality due to reduced “fragmentation tail”. The less complex secondary fragment spectrum also decreases uncertainties in biological effect estimations compared to carbon ions [3]. With decreased neutron production compared to carbon ions and possibly even lower neutron biological dose than with proton beams [3], neutron dose associated risks in paediatric patients could be greatly reduced. With linear energy transfer (LET) values for helium ions in the range of 4 to 40 keV/µm, an increased relative biological effectiveness (RBE) and reduced oxygen enhancement ratio (OER) is achieved compared to protons, indicating a treatment possibility of certain radioresistant tumours using helium ions.

Due to these characteristics, helium ion radiotherapy could provide a compromise between dose conformality and biological effectiveness among the various ions considered for clinical use. Helium ion beams have been already commissioned for clinical use at Heidelberg Ion-Beam Therapy Center (HIT) [4]. Plans of helium ion beam integration are foreseen at other ion therapy facilities in Europe and Japan [5].

With the first clinical patient treated at HIT in 2021 [4], more and more active work of helium ion therapy clinical research and integration is foreseen. Since potential use of helium ion beams for FLASH therapy has also been shown experimentally [6] and better performance for ion radiography and possibilities of other novel treatment modalities are expected, helium ion beam therapy has to be considered as a developing and promising innovation for future cancer treatment.

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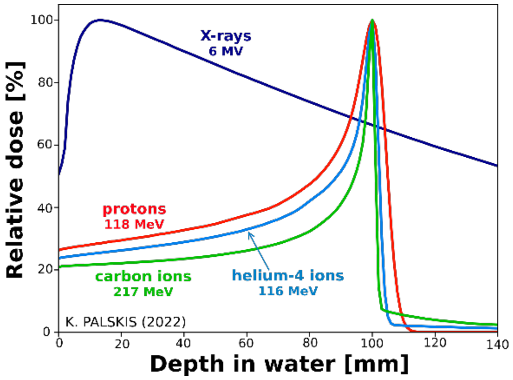

Figure 1: Bragg peak for proton, helium and carbon ions compared to X-rays.

A MULTI-PURPOSE FACILITY

A compact accelerator designed for acceleration of helium ions at the maximum energy of 220 MeV/u, corresponding to a penetration of 30 cm in water, can be the core of a multi-purpose facility devoted to different experimental programmes in the field of nuclear medicine [7, 8].

The proposed layout of the facility is presented in Fig. 2. Two ion sources deliver beams of protons or fully stripped helium ions, while provision is made for a third ion source delivering fully stripped carbon ions. The beams are then accelerated in a linac designed for particles with charge to mass ratio 1/2, up to an energy of 7 MeV/u. The linac is designed for 10% duty cycle, much higher than what required for injection into the synchrotron, to allow production of radioisotopes for therapy and imaging (and for the combination of two, theragnostics) using the beam pulses that are not injected into the synchrotron. A straight beam line at linac exit brings the beams to the radioisotope production target and room.

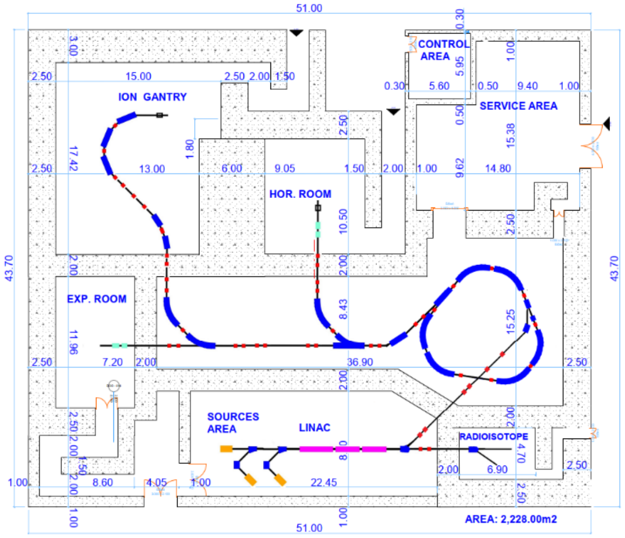

Figure 2: Layout of the facility.

Protons and helium beams can be injected and accelerated in the synchrotron. Helium beams accelerated up to 220 MeV/u can be sent to a research beamline, or to two treatment rooms, one equipped with a fixed beam line and the other with a gantry. Protons can also be used for research and for treatment. In addition, the higher proton energy achievable thanks to the synchrotron magnetic rigidity of 4.5 Tm makes full body scans for online proton radiography possible using low intensity proton beams. It is foreseen that the facility will use the new superconducting ion gantry being developed by a wide European collaboration [9]. Additional experimental programmes with carbon ions will be also possible, by retuning the helium ion source or, preferably, by adding a third source dedicated to production of heavier ions at lower intensity.

FLASH beam extraction from the synchrotron will be possible, allowing for an experimental programme on FLASH with ions and eventually FLASH treatment with helium or proton beams.

The total surface for the facility including treatment rooms and shielding is expected to be about 2,200 m^2.

ACCELERATOR DESIGN

The helium source will provide a $^4He^{2+}$ current of at least 2 mA to deliver 8 x 10^{10} ions at synchrotron via multi-turn injection, required to irradiate a 1 litre tumour volume with 2 Gy with a margin of a factor 2 to account for inefficiencies in the extraction process. A source of the AiSHA type is foreseen to achieve these operational values [10]. This ion source has been able to accelerate up to 5 mA of helium in CW operation, although with a larger emittance than what required for injection into the linac. It is expected that it can easily provide 2 mA for the synchrotron injection as well as for production of radioisotopes at higher duty cycle. The main accelerator components are described below.

Linac Injector

The ion sources are followed by a Radio Frequency Quadrupole (RFQ) and by three Drift Tube Linac (DTL) tanks, all operating at 352 MHz frequency. Their mechanical design can be the same used for the recent CERN Linac4 accelerator [11]. The RFQ will be about 3 m long, accelerating the beam to 2 MeV/u.

The first DTL tank will be 2.7 m long and will accelerates the He beam to 5 MeV/u, which corresponds to the injection energy into the synchrotron. During injection cycles, the other tanks are unpowered and detuned to transport the beam without perturbations. The second tank will be also designed for helium ions, accelerating in 1.5 m the beam to an energy of 7 MeV/u, required for safe production of ^{211}At for targeted alpha therapy [12]. The third tank of 1.1 m will accelerate only protons to 10 MeV, for proton injection in the synchrotron and for production of conventional radioisotopes in the target area. The RF power required to feed the three tanks is 400 kW, 200 kW, and 150 kW, respectively [13]. A scheme of the injector linac is presented in Fig. 3.

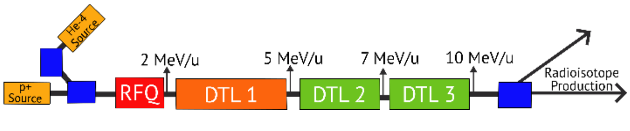

Figure 3: Scheme of the injector linac.

Synchrotron Design

The synchrotron will have a triangular layout and an overall circumference of 33 m [7, 8]. The bending sections will be made of two 60° dipoles reaching the maximum magnetic field of 1.65 T, and a strong quadrupole in between The zero-dispersion straight sections will host the injection and extraction equipment and the RF cavities, as shown in the layout of Fig. 4. The main design challenge being compactness, the correctors will be combined as much as possible in a single magnet, carrying multipole components. In the design, the horizontal tune is moved from Qx=2.73 for optimal multi-turn injection down to Qx=2.67 for slow extraction on the 3rd order resonance.

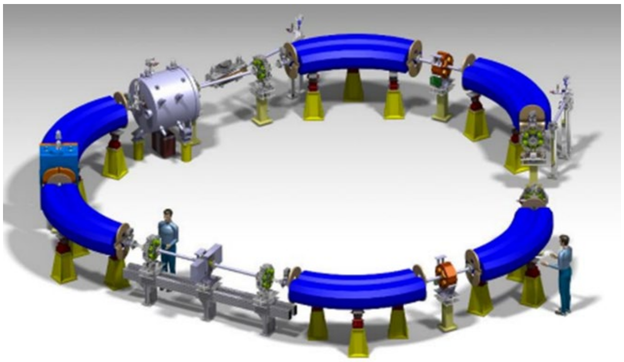

Figure 4: 3D schematic view of the synchrotron.

Extraction

Two extraction modalities are under consideration: conventional slow extraction, producing beam uniformly over a second-long timescale, and FLASH extraction, producing a more intense beam under 100 ms timescale [14]. Slow extraction will be available via both single-energy and multi-energy extraction [15] and will be driven via radiofrequency knock-out (RF-KO). The transverse exciter will require higher voltages than conventional designs [16], to handle higher emittance beams and faster extraction timescales [17]. For smaller, millisecond time structures, the accelerating RF cavity will require a digital system to control the phase, voltage, and frequency to incorporate burst extraction with RF phase-displacement [18, 19].

The compactness of the synchrotron constrains the design of the extraction optics. High amplitude particles are selected with the aperture of the electrostatic septum (ES), where they receive a small deflection that translates into a separation from the circulating beam at a phase advance of 280° at the magnetic septum (MS). The phase space between the drift sections requires the ES to be on the inside of the ring and the MS on the outside. Detailed studies of the beam at injection, including orbit distortion, are needed to assess that the horizontal position of the septa guarantees a large enough aperture. The position of the virtual resonant sextupole is chosen to provide a 45° phase advance with respect to the ES. The gaps of the ES and MS are 20 mm and 85 mm respectively, to contain an extracted beam with a spiral step of 10 mm.

IMPLEMENTATION IN THE BALTIC STATES

According to the data of the European Network for Light Ion Hadron Therapy (ENLIGHT) [20], the South-East Europe and the Baltic States (Estonia, Latvia, and Lithuania) remain the only regions in Europe without national or regional particle therapy centres. To overcome this gap, the idea and design of a novel multi-purpose facility has been embraced by the CERN Baltic Group [21] for development of an innovative particle therapy centre in the Baltic region.

According to data collected in the Baltic States in 2022 [22], 38,031 new cancer cases have been registered in the 3 countries with a total population of about 6 million, yielding average incidence rate of 630 cases per 100,000 inhabitants. In 2021, around 34 % (13,045) of the patients have received conventional radiotherapy treatment. Having 28 conventional external beam radiation therapy LINACs and 7 brachytherapy units, the Baltic States are well equipped technologically. Advanced techniques as intensity modulated and volumetrically modulated radiation therapy, and stereotactic radiosurgery are commonly used. As for the diagnostics, the region has on average about 65 medical imaging units for cancer diagnostics per 1 million inhabitants.

With this expertise and statistical data, the Baltic region is developed enough for moving to cancer treatment with particle beams. According to guidelines and consensus statements [23, 24], clinical indications that mostly benefit from particle therapy are ocular, skull base and head and neck tumours, various sarcomas and other tumours in complex localizations, as well as paediatric cancers. Collection of further data for stratification of incidence for the different cancer types in the region is ongoing, though the overall estimates indicate a minimum of 400 to 500 patients per year that would benefit from such a facility.

It is important to note that the overall concept is broader than the establishment of a clinical facility, encompassing creation of a hi-tech research and scientific institution as well as using the infrastructure for involvement of industrial partners in the region. The facility would provide opportunities for research in medical physics, material science, accelerator technology, radiobiology as well as preclinical and clinical research in helium ion therapy, novel radiotherapy delivery techniques and nuclear medicine.

Presently, the CERN Baltic Group is actively engaged with relevant stakeholders and regional medical communities representing radiation oncology, radiology, and nuclear medicine to build consensus on future developments. As the facility would be jointly established by at least 3 countries, criteria for site selection have been developed – integration into a recognised clinical centre, proximity to transport infrastructure, interest of stakeholders as well as medical and scientific communities at large.

Implementing this ground-breaking technology for health promotion will require, along with sustainable technological solutions, active stakeholder engagement, policy makers support and appropriate financing schemes. Work shall continue on the technological aspects as well as in communicating its mission, services, and benefits.

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