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PERFORMANCE OPTIMIZATION OF ION BEAM THERAPY*

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on behalf of the OMA Consortium

Abstract

Proton beam therapy promises significant advantages over other forms of radiation therapy. However, to assure the best possible cancer care for patients further R&D into novel beam imaging and patient diagnostics, enhanced biological and physical models in Monte Carlo codes, as well as clinical facility design and optimization is required. Within the pan-European Optimization of Medical Accelerators (OMA) project collaborative research is being carried out between universities, research and clinical facilities, and industry in all of these areas. This paper presents results from studies into low-intensity proton beam diagnostics, prompt gamma-based range verification in proton therapy, as well as prospects for a new proton irradiation facility for radiobiological measurements at an 18 MeV cyclotron. A brief summary of past and future events organized the network is also given.

INTRODUCTION

The Optimization of Medical Accelerators (OMA) project [1] trains the next generation of radiotherapy specialists and optimizes cancer treatment using ion beams. The project has received four million Euro of funding to employ fifteen Fellows who undertake research projects at leading research centers, universities and industry. The project's R&D program ranges from life sciences (oncology, cell and micro biology and medical imaging) to physics and accelerator sciences, mathematics IT and engineering. Therefore, it is ideally suited for an innovative training of early stage researchers. By closely linking all the above research areas, OMA provides an interdisciplinary education to its Fellows and equips them with solid knowledge in research areas adjacent to their core research field, as well as with business competences and give them a great basis for a career in research.

RESEARCH

Research within OMA is carried out by the Fellows across three closely interlinked work packages. These are Beam Imaging and Diagnostics, Treatment Optimization, and Facility Design and Optimization. A roughly equal number of Fellows has their main research focus on each work package, but there are also many collaborative links between the individual projects and work packages so that an overall optimization of ion beam therapy can be achieved. The following examples highlight selected research results obtained across OMA.

Proton Beam Characterization

For any ion beam facility, a comprehensive set of beam diagnostics is required to measure all relevant beam parameters such as beam current, position, profile and emittance. Within OMA, there is a focus on the development of non-interceptive monitors that allow measuring key beam parameters without affecting the primary beam much.

At the Paul Scherrer Institut (PSI), OMA Fellow Sudharsan Srinivasan has been developing a non-interceptive beam current and position monitor to characterize beams with currents down to 0.1 nA. Cavity resonators are ideally suited for this task due to their ability to measure low currents and their superior sensitivity compared to other diagnostics such as wall current monitors [2]. ANSYS HFSS was used as simulation tool for the design and optimization of the resonator. The dielectric filled re-entrant cavity forming a coaxial line with the beam pipe has three main mechanical parts, as shown in Fig. 1: The beam tube; dielectric gap filled with Macor; and coaxial extension which is short-circuited downstream. This design combines mechanical simplicity with ease of manufacture due to its cylinder symmetry. The cavity is made of aluminium; the dielectric shifts the resonance frequency from 225.0 to 145.7 MHz; four magnetic pickup loops are mounted inside the resonator, see Fig. 1.

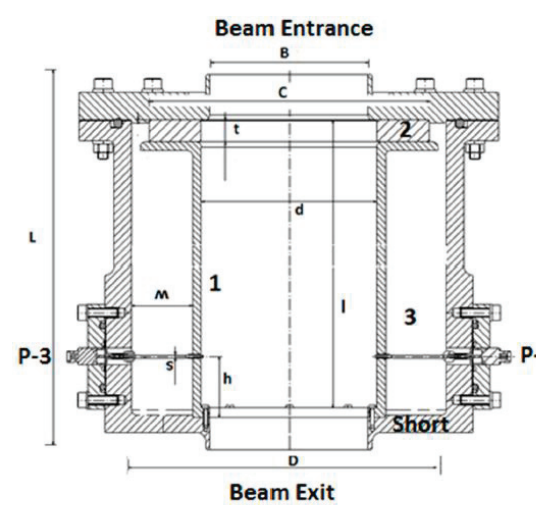

Figure 1: Dielectric-filled re-entrant cavity resonator as beam current monitor. The pickups in the figure represent the large magnetic loops in one plane (as port 3 and 5). Two small magnetic loops are in the other plane (as port 4 and 6). Port 1 is the beam entrance and Port 2 is the exit [3].

The monitor was characterized on a test bench at PSI and a very good agreement between these measurements and

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results from simulations was found [4]. Measurements with beam are now planned in summer 2019.

Complementary to this development, R. Schnuerer and OMA Fellow Jacinta Yap based at the University of Liverpool/Cockcroft Institute have been investigating the use of the Vertex Locator (VELO) detector technology, originally developed for the Large Hadron Collider beauty experiment (LHCb) as a non-interceptive online beam monitor. Due to the semi-circular cut-out in the sensor, a precise measurement of the beam halo without interfering with the beam core is made possible. By correlating the beam halo reading with data from an ionization chamber or Faraday Cup, a halo-dose correlation data base for different settings can be established and used for quality assurance purposes. A prototype of this monitor was successfully adapted to the specific requirements of proton beam facilities [5]. Proof-of-principle measurements using this monitor at the 40 MeV proton line at the University of Birmingham were completed earlier in 2019 [6]. They demonstrated VELO's unique proton counting capability.

Range Verification

To fully exploit the treatment potential of protons, in-vivo range verification is highly desirable. Prompt gamma rays, emitted in nuclear reactions between the primary proton beam used for treatment and tissue, are an ideal probe for range verification. They show a strong correlation with the proton dose and are emitted in real-time [7, 8]. Their detection requires specific detectors, so-called *prompt-gamma cameras*, due to the high energies of the gamma rays between 1–8 MeV [9] and the high background coming from neutron-induced events.

For achieving absolute range verification, measured profiles were compared to reference profiles, obtained from simulations. By shifting the profiles against each other and minimizing the deviation between both, a relative range shift was obtained. With information about treatment planning, this relative shift can then be attributed to an absolute proton range.

OMA Fellow Johannes Petzoldt who is based at IBA in Belgium, has developed an analytical model which computes the spectral and spatial prompt gamma emission based on the traversed target composition using pre-calculated tables [10]. The detected signal in the camera is calculated by a convolution of the emission and a transfer function that takes the geometry and the setup of the camera relative to the beam into account. This transfer function is derived from a fit to a Monte Carlo simulation and therefore an approximation. To improve the range retrieval, a correction function was developed to give a better agreement between simulation and experiment. This required studies into the parameters that have an influence on the geometry and the shape of the profiles, as well as the development of a method to calculate the correction functions within the required parameter space. In a last step, the so-called geometrical correction was then validated in benchmark experiments [11].

These studies showed a clear indication that at least four different parameters influence the geometrical response of the camera: These are beam energy, distance between collimator to beam axis and distance between camera to collimator, as well as offset from the isocenter. As one example, Fig. 2 shows the range shift after application of the geometrical correction.

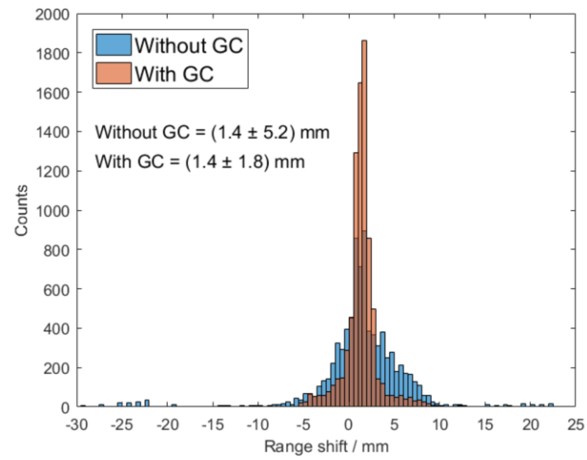

Figure 2: Histogram displaying the range shift between simulation and measurement for all delivered spots for a 25:20 geometry. Blue shows the results without applied geometrical correction while the orange bars include the geometrical correction.

This method for correcting the geometrical deviations between fast simulation and measurement improves the overall accuracy of the prompt gamma camera. It has been implemented within Reggui and already applied on patient data. This helps improve the accuracy of the obtained results.

18 MeV Proton Irradiation Facility

A feasibility study into a dedicated experimental setup for the irradiation of biological samples in a dedicated beam line, illustrated in Fig. 3, at the cyclotron facility at the National Centre of Accelerators in Seville, Spain was carried out by OMA Fellow Anna Baratto-Roldan. Using the facility's 18 MeV proton beam, opportunities for the irradiation of mono-layer cultures for the measurement of proton cell damages and Relative Biological Effectiveness (RBE) at energies below the beam nominal value were investigated.

Measurements at 18 MeV allow studying the impact of protons on cells at energies which correspond to the sharp end of the Bragg peak region of a clinical proton beam at much lower energy spread. Studies into the effect of such a beam on cells are limited to experiments with mono-layer cell cultures, for which the energy and the stopping power of protons reaching the cells can be calculated accurately. For floating cell cultures, one would have to take into account the beam energy degradation along the cell culture itself, introducing uncertainties due to the high variability of the stopping power in depth within the sample. Moreover, an additional source of uncertainty would arise from the imprecise knowledge of the position of the

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floating cells in the aqueous medium, which is important for an accurate calculation of the beam energy degradation.

The characteristics of the beam profile have been studied with Gafchromic EBT3 films under different irradiation conditions [12].

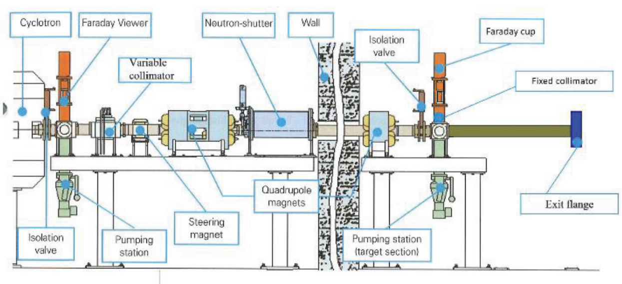

Figure 3: Layout of the external beam line.

The properties of the proton beam have been analyzed and compared with Monte Carlo simulations. A good agreement between the two was found. Meaningful dose rates of about 2–3 Gy/min have also been obtained and homogeneous lateral dose profiles with maximum deviations of 5% have been measured at a distance of approximately 50 cm in air from the exit window, placing a tungsten scattering foil of 200 µm in the beam path. These results are comparable to the ones obtained at similar facilities and now provide the basis for future studies [13].

TRAINING EVENTS

The OMA Fellows receive extensive research-based training within a unique international partnership. Since project start they have gained a broad insight into both, academic and industrial aspects associated with medical accelerators, with opportunities to undertake specific training and secondments within the network. The fundamental core of the training consists of dedicated cutting-edge research projects for each Fellow at their host institution. To complement this, the network provides opportunities for cross-sector secondments for all Fellows. An intra-network secondment scheme enables them to spend time working at other institutions within the network, receiving hands-on training in specific techniques and a broader experience in different sectors.

Another important aspect of the training is a series of network-wide events comprising several schools, topical workshops and an international conference, which are all open to the wider scientific community.

This interdisciplinary training concept is directly based on the successful programs developed within the DITANET, oPAC and LA^{3}NET projects [14-16]. To date, OMA has organized one Researcher Skills School, three international Schools on Medical Accelerators (4-9 June 2017 at CNAO, Italy) [17], Monte Carlo Simulations (6-10 November 2017 at LMU Munich, Germany) [18], and on Particle Therapy (1-5 April 2019 at TU Vienna with Medaustron as local host [19]. The network has also organized three Topical Workshops on Facility Design and Optimization at PSI in Switzerland [20], Diagnostics for Beam and Patient Monitoring [21], and Accelerator Design and Diagnostics [22]. Presentations from all training events are available via the respective event indico page. On 28 June 2019 an outreach Symposium will be held at the Arena and Convention Centre in Liverpool with talks live-streamed on the day [23]. The network will also organize an international Conference on Medical Accelerators and Particle Therapy in Seville, Spain in September 2019. This major event will summarize and promote the scientific results of the project and discuss remaining challenges and future collaboration [24].

The research results of the OMA project have been disseminated via scientific journals, international events, and via the project website www.oma-project.eu. This is complemented by targeted social media campaigns about cancer therapy and a quarterly newsletter, the *OMA Express*, which can be accessed via the project website.

The consortium as a whole and the Fellows individually have actively communicated the project to the general public. The Fellows have participated in a number of primary and secondary school visits, open days and science festivals to share their passion for science. Each OMA event featured a public lecture by a renowned scientist in the local language where the event was held. Finally, the network has successfully held pan-European outreach events with a global reach, such as Marie Curie Day 2017 [25], which has further boosted the impact of the project.

SUMMARY AND OUTLOOK

Cancer is a major social problem and it is the main cause of death between the ages 45-65 years. In the treatment of cancer, radio therapy (RT) plays an essential role. RT with hadrons (protons and light ions), due to their unique physical and radiobiological properties, offers several advantages over photons for specific cancer types. In particular, they penetrate the patient with minimal diffusion, they deposit maximum energy at the end of their range, and they can be shaped as narrow focused and scanned pencil beams of variable penetration depth. Although significant progress has been made in the use of particle beams for cancer treatment, an extensive research and development program is still needed to maximize the healthcare benefits from these therapies.

The 15 Fellows that are employed within the OMA project all carry out research that helps optimize the performance of ion beam therapy. This paper has given four examples of novel diagnostic techniques, enhanced computational tools and new research infrastructures that have been developed since project start.

The network brings together its partner organizations with the wider accelerator and medical community to stimulate discussions about research progress made and open challenges. A large number of international training events have also been offered. The final phase of the project will now focus on communicating all project results internationally and starting collaborative projects that emerge on the basis of ongoing R&D.

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