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OPTIMIZATION OF MEDICAL ACCELERATORS*

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Abstract

Between 2016 and 2020, 15 Fellows have carried out collaborative research within the 4 M€ Optimization of Medical Accelerators (OMA) EU-funded innovative training network. Based at universities, research and clinical facilities, as well as industry partners in several European countries, the Fellows have successfully developed a range of beam and patient imaging techniques, improved biological and physical models in Monte Carlo codes, and also helped improve the design of existing and future clinical facilities. This paper summarizes some of the research outcomes of this network. It presents results from tracking and LET measurements with the MiniPIX-TimePIX detector for 60 MeV clinical protons, a new treatment planning approach accounting for prompt gamma range verification and interfractional anatomical changes, and summarizes findings from high-gradient testing of an S-band, normal-conducting low phase velocity accelerating structure. Finally, it gives a brief overview of the scientific and training events organized by the OMA consortium.

INTRODUCTION

The OMA network has been built around 15 early stage researchers (ESRs) working on dedicated projects to maximize the benefits of the use of particle beams for cancer treatment [1]. The network consists of an international consortium of 38 partner organizations working in this field. It has provided a cross-sector interdisciplinary environment for beyond state-of-the-art research, researcher training, and new collaborations. The network has pushed technologies and simulation techniques significantly beyond the state-of-the-art and developed solutions that are now applied in clinical practice. The project has also established a comprehensive and unique postgraduate training concept that can also be applied to other research areas and that was presented to educators at national and international learning and teaching events. The Fellows have benefited from a well-rounded training and successfully completed their projects within the network. This paper illustrates some of the research outcomes in the network.

SELECTED RESEARCH RESULTS

OMA has significantly advanced knowledge in proton/ion beam therapy and related key technologies. Research within the network was 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 was achieved. One very successful example of a collaboration that OMA has enabled and which involved several project partners is recent work into the technical challenges in FLASH proton therapy, highlighted as EJMP's best paper in 2020 and winner of the Galileo Galilei award [2]. The following sections present selected research highlights obtained across OMA.

Studies with MiniPIX-TimePIX Detectors

Recent advancements in accelerator technology have led to a rapid emergence of particle therapy facilities worldwide, affirming the need for enhanced characterization methods of radiation fields and radiobiological effects. The Clatterbridge Cancer Centre, UK operates a 60 MeV proton beam to treat ocular cancers and facilitates studies into proton induced radiobiological responses [3]. As part of efforts to completely characterize the beamline and exploit characteristics of the beam, computational approaches to model the facility in several simulation codes have been developed. In particular, detailed models of the CCC treatment line was created for additional modelling capabilities for beam transport and radiobiological applications [4]. One significant parameter which relates a physical quantity of energy deposition to radiobiological effects was studied in great detail: the linear energy transfer (LET), a challenging physical quantity to measure [5].

MiniPIX-Timepix is a miniaturized, hybrid semiconductor pixel detector with a Timepix ASIC, enabling wide-range measurements of the deposited energy, position and direction of individual charged particles [6]. High resolution spectrometric tracking and simultaneous energy measurements of single particles enable the beam profile, time, spatial dose mapping and LET (0.1 to >100 keV/μm) to be resolved. As part of the Beam Imaging and Diagnostics work package, measurements were performed by OMA Fellow Jacinta Yap to determine the LET spectra in silicon, at different positions along the Bragg Peak (BP) [7].

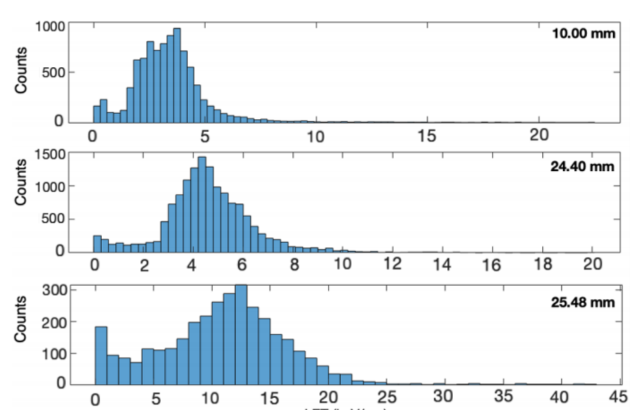

Figure 1: LET spectra with the sensor at 60º [7].

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Experiments were performed using the MiniPIX-Timepix detector system at the CCC 60 MeV proton therapy beamline to measure relevant quantities in order to resolve the LET at different positions along the Bragg peak. Two tilt angles were used and the results for an angle of 60º are shown in Fig. 1. Different PMMA blocks provided a range of water equivalent thicknesses to vary the penetration depth. Measurements of deposited energy and track lengths were obtained and allowed determining the LET spectra along the Bragg peak. Several uncertainties were noted with the experimental setup, resulting in wide distributions of cluster properties that will be subject to further studies. The measurements demonstrated the capability of the MiniPIX-Timepix detector to determine the LET and establish its applicability for clinical environments.

Advances in Treatment Planning

Prompt gamma (PG) imaging is widely investigated for spot-by-spot in vivo range verification for proton therapy. Previous studies pointed out that the accuracy of prompt gamma imaging is affected by the statistics (number of protons delivered per pencil beam) of the proton beams and the conformity between prompt gamma and dose distribution (PG-dose correlation) [8, 9]. Recently a novel approach to re-optimize conventional treatment plans by boosting a few pencil beams with good PG-dose correlation above the statistics limit for reliable PG detectability was proposed [10]. However, up to now, only PG-dose correlation on the planning computed tomography (CT) was considered, not accounting for the fact that the robustness of the PG-dose correlation is not guaranteed in the cases of interfractional anatomical changes.

OMA Fellow Liheng Tian used a research computational platform, combining Monte Carlo pre-calculated pencil beams with the analytical Matlab-based treatment planning system CERR, for treatment planning (TP) purposes. He applied Geant4 [11] for a realistic simulation of dose delivery and PG generation for pencil beams in heterogeneous patient anatomy using multiple CT images [12].

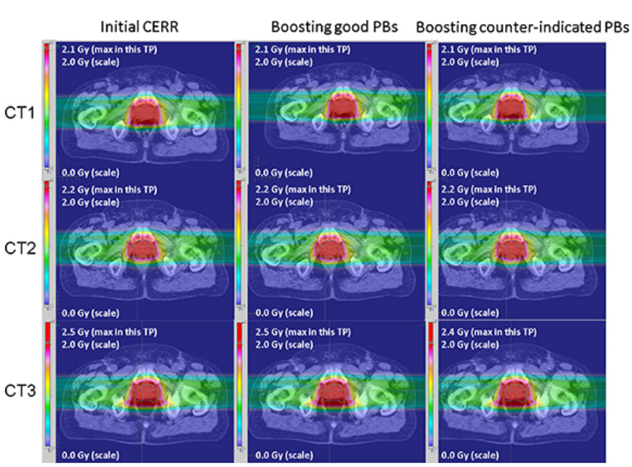

Figure 2: Dose distribution of initial TP (left), TP boosting good PBs (middle) and TP boosting counter-indicated PBs (right) on CTs at different time points for a prostate cancer patient [12].

A Monte Carlo treatment plan was created using CERR. Thereby, PG emission and dose distribution for each individual spot was obtained. Second, PG-dose correlation was quantified using the originally proposed approach by him, as well as a new indicator, which accounts for the sensitivity of individual spots to heterogeneities in the 3D dose distribution. This was accomplished by using a 2D distal surface (dose surface) derived from the 3D dose distribution for each spot. A few pencil beams were selected for each treatment field, based on their PG-dose correlation and dose surface, and then boosted in the new re-optimized treatment plan. All treatment plans were then fully re-calculated with Monte Carlo on the CT scans of the corresponding patient at three different time points.

Figure 2 shows changes to the TP using the improved modelling toolkit. The spots recommended by the indicators maintain a good PG-dose correlation in the cases of interfractional anatomical changes, thus ensuring that the proton range shift due to anatomical changes can be monitored. Compared to another proposed spots aggregation approach, the approach shows advantages in terms of the detectability and reliability of PG, especially in presence of heterogeneities.

High Gradient Testing of a Compact S-Band Structure

A novel high-gradient accelerating structure with low phase velocity, v/c = 0.38, has been designed, manufactured and high-power tested by OMA Fellow Anna Vnuchenko [13]. The structure was designed and built using the methodology and technology developed for CLIC 100 MV/m high-gradient accelerating structures, which have speed of light phase velocity, but adapts them to a structure for nonrelativistic particles.

The parameters of the structure were optimized for a compact proton therapy linac, and specifically for 76 MeV protons, but the type of structure opens more generally the possibility of compact low phase velocity linacs. The structure operates in S-band, is backward traveling wave (BTW) with a phase advance of 150 degrees and has an active length of 19 cm. The main objective for designing and testing this structure was to demonstrate that low velocity particles, in particular protons, can be accelerated with high gradients. In addition, the performance of this structure compared to other type of structures provides insights into the factors that limit high gradient operation.

The structure was conditioned successfully to high gradient using the same protocol as for CLIC X-band structures. A local accelerating gradient of 81 MV/m near the input end was achieved at a pulse length of 1.2 μs and with a breakdown rate (BDR) of 7.2×10^{-7} 1/pulse/m. Although problems were encountere during the initial tests, they provided important insight into high-gradient behavior and a comprehensive analysis has been carried out. Particular attention was paid to a detailed characterization of the distribution of BD positions along the structure and within a cell. Figure 3 shows the measured breakdowns (BDs) during structure conditioning.

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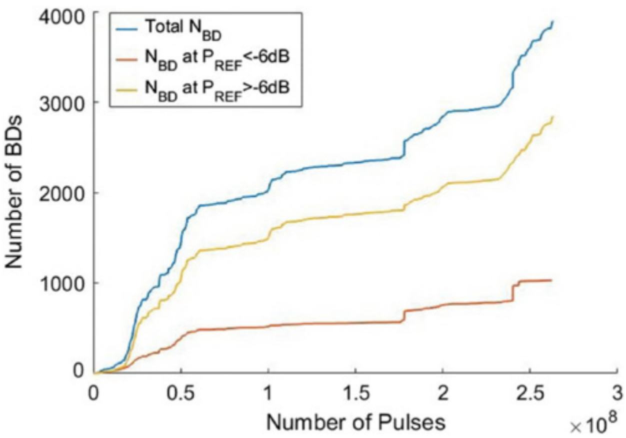

Figure 3: Number of breakdowns with reflection coefficient P_{REF} during the conditioning of the structure [13].

Future work will focus on testing the structure with the power flow in the correct direction. This is important to establish the achievable gradient over an entire structure. The existing structure, and an identical structure fabricated at the same time, will both be tested. This study gave an excellent example of how R&D into technology for fundamental research can make an impact also in other fields, in this case radiation therapy.

RESEARCHER TRAINING

The OMA Fellows received a comprehensive training within a unique international network. 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 consisted of dedicated cutting-edge research projects for each Fellow at their host institution. To complement this, the network provided opportunities for cross-sector secondments for all Fellows. An intra-network secondment scheme enabled 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 were all open to the wider scientific community.

This interdisciplinary training concept was directly based on the successful programs developed within the DITANET, oPAC and LA^{3}NET projects [14-16]. OMA has organized two Researcher Skills Schools, 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 on Accelerators for Science and Society was held at the Arena and Convention Centre in Liverpool with talks live-streamed on the day and now available on-demand via the event website [23]. The network also organized an international Conference on Medical Accelerators and Particle Therapy in Seville, Spain in September 2019. This event summarized and promoted the scientific results of the project and discussed remaining challenges and established a basis for future collaboration [24].

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

SUMMARY AND OUTLOOK

The OMA project has delivered excellent results with significant impact in the field of medical and particle and radiation physics. The network has achieved all of its ambitious targets with only minor deviations over the four year project duration. Research has advanced knowledge in proton and ion beam therapy and several examples were given in this paper. The results are expected to contribute important knowledge to the development of the next generation of medical accelerators. A comprehensive training program and interdisciplinary outreach and communication which has reached millions around the world were additional successes. The OMA partners will continue their collaboration and core activities such as regular newsletters and also workshops through the coordinator University of Liverpool. Joint research projects on the basis of the network are already emerging and are expected to make important contributions to an international effort to optimize medical accelerators.

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