LaGEMPix: a large area GEMPix detector with optical readout for hadron therapy

Hylke B. Akkerman[1], Albert J.J.M. van Breemen[1], Lucia Gallego Manzano[2,3], Natalie Heracleous[2], Ilias Katsouras[1], Johannes Leidner[2], Andreia Maia Oliveira[2,4*], Fabrizio Murtas[2,5], Bart Peeters[1], Marco Silari[2]

[1] Holst Centre/TNO, High Tech Campus 31, 5656 AE Eindhoven, The Netherlands; [2] CERN, 1211 Geneva 23, Switzerland; [3] Institute of Radiation Physics, Lausanne University Hospital, Lausanne, Switzerland; [4] Albert Einstein Center for Fundamental Physics (AEC), Laboratory for High Energy Physics (LHEP), University of Bern, Hochschulstrasse 6, 3012 Bern, Switzerland; [5] INFN-LNF, 00044 Frascati, Italy.

*Corresponding author: andreia.cristina.maia.oliveira@cern.ch

ABSTRACT

Quality Assurance in hadron therapy is crucial to ensure a safe and accurate dose delivery to the patient. This requires fast and reliable detectors with high spatial resolution. Here we present a cutting-edge solution that combines a triple Gas Electron Multiplier and a highly pixelated readout based on a matrix of organic photodiodes coated on an oxide thin film transistor backplane. A first LaGEMPix prototype with an active area of 60 x 80 mm^2 has been successfully built and tested demonstrating promising results for quality assurance and treatment plan verification.

Keywords: Hadron therapy, dosimetry, quality assurance, GEM, optical readout.

1. INTRODUCTION

Hadron therapy is an advanced radiation modality for treating cancer, which at present uses protons and carbon ions. As of July 2020, there exist 97 particle therapy facilities worldwide and more than 30 centres are under construction [1]. Hadrons have the unique feature of increasing energy deposition with penetration depth, with a maximum at the end of their range followed by a sharp decrease (Bragg peak). Thus, hadron therapy offers considerable improvements to conventional radiation treatments by allowing better conformity of the dose to the tumour [2], but also requires a very accurate dose planning. A precise verification of the dose delivered to the patient with high spatial resolution is guaranteed by appropriate quality assurance (QA) procedures.

A proper set of detectors for measuring the important beam parameters, in particular the beam position and the delivered dose, is fundamental to achieve an efficient QA protocol [3]. Nowadays, there is still room for improvement towards a robust and complete solution providing accurate and real-time measurements with submillimetre spatial resolution and a uniform response to the beam energy.

A promising tool is the LaGEMPix detector. It consists of a triple-GEM (Gas Electron Multiplier) [4] coupled to a highly pixelated readout based on a matrix of organic photodiodes (OPDs). The potential of a triple-GEM detector combined with a high pixel granularity for QA in hadron therapy has already been demonstrated by its predecessor, the GEMPix [5]. Although promising, a wider sensitive area is required to cover the typical 20 x 20 cm^2 radiation field size The new readout, based on the detection of the scintillation photons generated in the GEM holes, allows the development of a compact detector for larger-area imaging, further scalable with an expected good spatial resolution.

In this paper we report on the development of the first LaGEMPix prototype with a six times larger active area compared to the GEMPix (6 x 8 cm^2). The detector is described in Section 3. The first results obtained using an X-Ray irradiator are reported in Section 4. Finally, Section 5 discusses the next steps of the project.

2. STATE OF THE ART

One of the advantages of hadron therapy is the possibility of driving the beam to accurately conform the dose to the tumour. To achieve this, it is critical to monitor the beam characteristics and the delivered dose. In routine QA checks, different kinds of dosimeters are employed to measure the 2D dose distribution [6].

International dosimetry guidelines propose the use of an array of ionization chambers for the weekly QA checks in a water phantom, due to their well-known performance and their accuracy and stability (small variation in

response with energy, dose and dose rate) [7]. However, ionization chamber-based systems have a poor spatial resolution limited by the size of the currently available detectors. The OCTAVIUS® Detector 1600 SRS, for example, consists of a matrix of 1521 vented plane-parallel ion chambers, with a spacing in the central area of 2.5 mm and 5 mm [8].

Films such as radiochromic EBT3 are generally used due to their very good spatial resolution down to 25 μm [9], but they provide an off-line response, which is also highly dependent on the particle energy [10].

Optical readout-based detectors are ideally suited for online monitoring of the beam. Scintillating screens coupled to CCD cameras with high spatial resolution for 2D dosimetry have been developed [11]. Other examples, such as the Lynx® commercial detector, which consists of a gadolinium-based plastic material, is only appropriate for relative 2D dosimetry measurements due to the strong energy dependence [12].

3. BREAKTHROUGH CHARACTER OF THE PROJECT

GEM detectors have been used in the past in particle therapy. In particular, the feasibility of optical-readout GEM-based detectors was previously investigated with CCD/CMOS cameras [13-15]. However, the degradation of the camera due to radiation requires placing it outside the beam, needing a more complex system with e.g. mirrors or lenses. In contrast to CCD/CMOS-based detectors, the highly pixelated readout of the LaGEMPix is adjacent to the GEM anode. This allows a more compact, easily scalable and low material budget set-up.

The LaGEMPix combines a triple-GEM detector with an area of 10 x 10 cm^2 and an optical readout based on three main building blocks: a Thin Film Transistor (TFT) backplane, a light sensitive OPD frontplane and a transparent thin-film encapsulation, serving as a protection against ambient conditions [16].

The triple-GEM detector includes a 20 μm thick Mylar window used as the cathode at 3.5 mm from the first GEM. The distance between the first and the second GEM is 1 mm and between the second and the third GEM is 2 mm. Each GEM foil consists of a 50 μm Kapton layer electroplated with a 5 μm thick Cu layer on both sides and pierced with holes of 70 μm diameter and 140 μm pitch. On the bottom of the third GEM, an ITO (Indium Tin Oxide) coated glass anode, with a thickness of 1.1 mm and resistivity of 100 Ω/sq, is placed at 1.9 mm distance to collect the electrons produced during the amplification process while allowing the optical photons to pass through [14, 17].

The sensor array has a resolution of 200 pixels per inch (ppi). It comprises 640 x 480 pixels, resulting in a total sensor area of 60 x 80 mm^2. The OPD frontplane is directly deposited on the TFT backplane by slot-die coating. The backplane is a self-aligned dual-gate oxide thin-film transistor array [18]. The sensor shows a dark current density of 10^{-7} mA/cm^2 at -2 V and a linear behaviour in a wide range of light intensities [19]. The OPD has a maximum external quantum efficiency (EQE) of ca. 50% at 550 nm, and about 25% at 640 nm (peak of the visible band emitted by the GEMs using an Ar:CF_4 (90/10) gas mixture).

4. PROJECT RESULTS

A first LaGEMPix prototype (Fig. 1) has been successfully built and tested as a preliminary step towards the development of a 20 x 20 cm^2 detector.

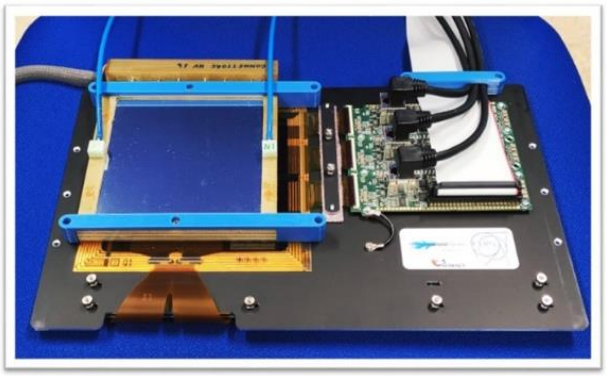

Fig. 1. The first LaGEMPix prototype.

We initially tested the triple-GEM detector at proton fluxes corresponding to high clinical beam intensities before coupling it to the optical matrix. We performed a current scan with 18 MeV protons at beam intensities up to 1.5 nA at the cyclotron at Inselspital in Bern [20]. We measured a linear behaviour between 2 pA and 1.5 nA with the sum of the GEM voltages equal to 500 V as shown in Fig. 2.

Later, the LaGEMPix was placed inside a custom made black PMMA box to shield the ambient light and provide a well aligned set-up. The readout was set to the highest sensitivity level of 0.5 pC, so that the least significant bit (LSB) of the 16-bit readout corresponds to a charge of approximately 70 electrons. The frame rate was 1 fps.

4.1. Dose response to Cs-137 photons

We performed a gain scan at the CERN Radiation Calibration Facility [21] with a 3 TBq Cs-137 source at 93.9 cm from the detector. The sum of the GEM voltages varied from 0 to 1030 V. The results are shown in Fig. 3. Each point is the average of the sum of all pixels for 10 recorded images. The light intensity vs high voltage gain follows an exponential trend. This was expected since the gain, i.e. the ratio of the number of electrons produced over the number of primary electrons, depends

exponentially on the applied GEM voltages. The number of scintillation photons increases proportionally with the number of secondary electrons, hence increasing exponentially with the gain [13].

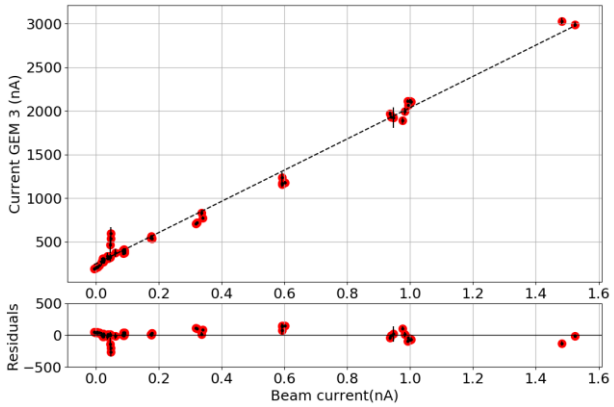

Fig. 2. Current at the last GEM vs the proton beam current of the 18 MeV cyclotron. The black dashed line represents a linear fit to the data. The bottom plot shows the residuals.

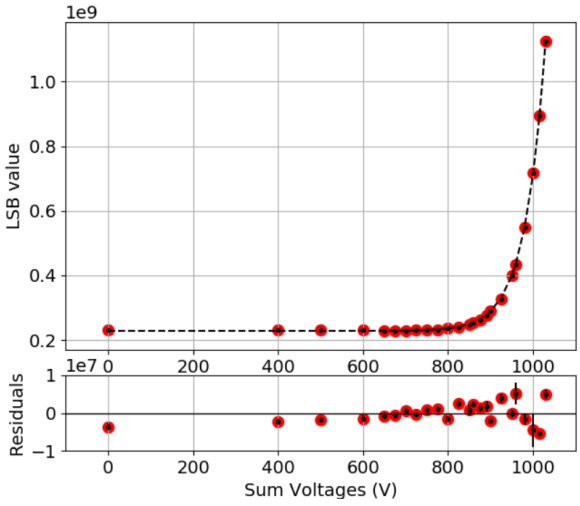

Fig. 3. Light intensity vs high voltage gain of the LaGEMPix using a 3 TBq Cs-137 source. The black dashed line represents an exponential fit to the data. The bottom plot shows the residuals.

4.2. Spatial Resolution

The spatial resolution of the LaGEMPix has been evaluated with 40 kV x-rays from an X-Ray irradiator, Model X80-320kV from Hopewell Designs, Inc. To ensure that undesirable effects such as readout inhomogeneities or noise are not affecting the results, a threshold per pixel was applied and dead pixels were removed. A background image was obtained by averaging each LSB pixel value over 200 background images. Then, each image was processed offline and the background subtracted. The final image was obtained by averaging each pixel over 200 background corrected images and the ROI (region of interest) selected.

To estimate the spatial resolution, we used two methods: the "edge response" and the "hole" response [22]. For the former method, we placed a lead block of 10 x 20 x 2.5 cm^3 size in front of the PMMA box covering half of the active area of the detector, while for the latter we used a 1 mm thick copper plate placed on the inner wall of the box at 3.3 cm from the Mylar window. Various holes of different sizes from 1.3 to 6 mm spaced by 2.5 to 17 mm were drilled in the plate. Results for both methods are shown in Figs. 4 and 5. The spatial resolution obtained by the first method is 8.40 ± 1.93 mm (FWHM). The spatial resolution measured by the second method varied between 6.67 ± 0.47 mm for the 6 mm hole and 5.35 ± 0.70 mm for the 3 mm holes (FWHM).

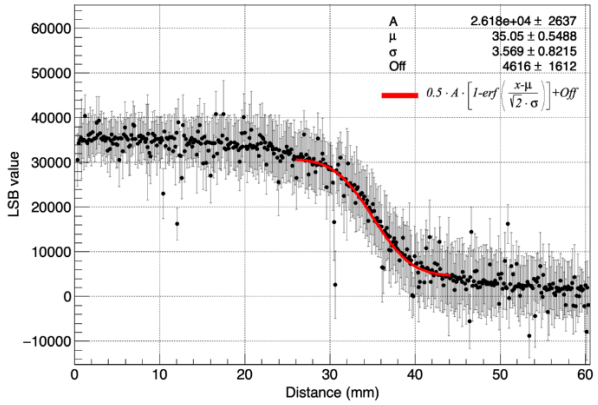

Fig. 4. Edge response profile for 40 kV x-rays using a lead block. The red line represents an error function fit to the data.

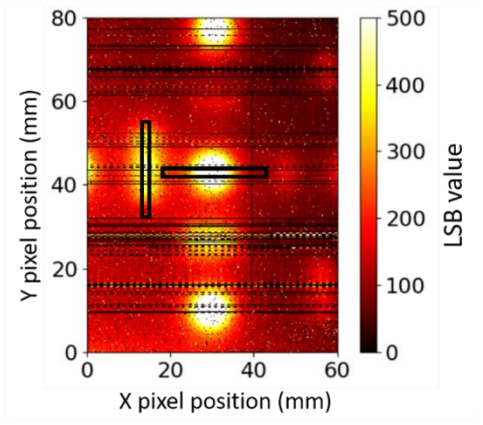

Fig. 5. Heat map of the Cu mask for 40 kV x-rays. Two ROIs (black lines) were set on the 6 mm and 3 mm holes. The spatial resolution is estimated by fitting the integrated profile in the ROIs by a Gaussian function.

5. FUTURE PROJECT VISION

During the ATTRACT phase 2, we would focus on the development of a compact and sealed 20 x 20 cm^2

LaGEMPix. Our intention is, independently of ATTRACT Phase 2 funding, to start its development on a shorter time scale, seeking for alternative funding sources and including additional partners. For the detector part, CERN has some funds already secured from the Medical Application section of the KT (Knowledge Transfer) group.

5.1. Technology Scaling

The ATTRACT project allowed us to develop the first LaGEMPix prototype (TRL 3 to 4) as a preliminary step for the development of a 20 x 20 cm^2 detector. The results show that the required sub-millimeter spatial resolution is not yet achievable. Two possible modifications on the detector are here briefly discussed. Decreasing the distance between the last GEM and the readout plane could reduce the dispersion of the light before reaching the readout. To increase the light detection efficiency, the OPD active layer could be replaced by another one with a better match between the emitted light and the OPD's quantum efficiency. An alternative solution to this readout system would be to eliminate the OPD layer leaving a TFT-only electronic readout. With this approach, secondary electrons produced in the electron avalanche would be directly measured by the readout, yielding an even more compact and possibly more efficient device with a higher signal-to-noise ratio. Additional options are currently being assessed.

In order to reach TRL 5, we would need to perform tests in clinical proton and carbon ion beams, to define the exact specifications for machine and patient QA. CERN RP group has an open collaboration with CNAO (the Italian Centre for Oncological Hadron Therapy). However, due to the COVID-19 pandemic, travelling to CNAO was not possible during the timeframe of this project.

To demonstrate the application of the LaGEMPix in QA for hadron therapy, we need to scale up the present prototype. Based on the experience with coupling the current OPD-TFT readout with the GEMs, we do not expect major issues to increase the detector size. The major efforts will be devoted to achieve the required spatial resolution of about 0.5 mm, and to prove the radiation hardness of the detector in clinical ion beams. A further planned step is to develop a sealed version of the LaGEMPix, which would avoid the installation of a gas system inside the treatment room thus simplifying the detector setup.

5.2. Project Synergies and Outreach

We are currently exploring the possibility of extending the CERN-TNO consortium mostly to secure funding for the development of the new TFT-only readout. Preliminary contacts have been established with the University of Groningen and the University of Delft in The Netherlands and CNAO in Italy.

We also plan to merge the results of this project with those of the ATTRACT GEMTEQ project, which has developed a version of the GEMPix for microdosimetry. Very interesting results have been achieved [23] paving the way to structural track microdosimetry. We also had an informal discussion with the ATTRACT project H2I2, (Hybrid high-precision in vivo imaging in particle therapy), which we plan to deepen in the future.

5.3. Technology application and demonstration cases

Merging a 20 x 20 cm^2 LaGEMPix imagining detector with the microdosimetric capability of the GEMPix demonstrated by the ATTRACT GEMTEQ project, and integrating such innovative device in a motorised water phantom (already built and tested outside the ATTRACT framework [5]), would yield an exceptional quality assurance tool for treatment planning and dose delivery in particle therapy, driven by a detailed knowledge of the radiobiological effectiveness (RBE) of the radiation. This approach, which has never been implemented until now, would bring a contribution to "personalised medicine" in cancer therapy.

5.4. Technology commercialization

For the commercialisation of a final product, we will need a dosimetry company or a medical instrumentation company with the required competences for industrialising the prototype. Some interest has been shown by a vendor of medical equipment, Philips, with whom we have established a preliminary contact.

5.5. Envisioned risks

The project started on a very solid basis, as the GEMPix was thoroughly studied by CERN RP group, specifically for medical applications, and TNO has a solid knowledge of TFT backplanes. Large area TFT backplanes are extensively used, generally as active electronic switching elements.

A preliminary risk analysis has been carried out leading to the identification of different types of risk, technological and organizational. The key risks concerning the technology development are: 1) radiation damage to the electronics; 2) delay in the development of the new TFT-only readout; 3) insufficient performance of the new readout; 4) insufficient performance of the new detector such as an insufficient spatial resolution. The lack of successful collaboration among partners or the withdrawal of one of the partners has been identified as a low-likelihood risk.

5.6. Liaison with Student Teams and Socio-Economic Study

The project has involved one Portuguese trainee (AMO), initially funded by the CERN-Portugal trainee program,

who subsequently enrolled as doctoral student at the University of Bern. She will use the work performed during ATTRACT for her PhD thesis, that will be completed in the coming 18 months within CERN doctoral student program.

An ATTRACT Phase 2 project will involve a larger consortium; a mixture of research institution and companies. It will offer very interesting opportunities for master and doctoral theses, to train experts in advanced dosimetric instrumentation who will later be able to work either in research institutions, in the private sector or in hospitals. With an estimated 3-year duration of a Phase 2 project, we envisage to organise annual scientific workshops in order that all partners can regularly meet. These workshops will also provide the occasion to organise training courses for the students involved in the project. A typical format of such workshops may include: 1) scientific meetings to discuss work progress; 2) a training course on one of the research areas of the project, during which experts will deliver seminars on recent progress in the field. The courses will be open to external researchers and local PhD students; 3) one full "Outreach day" dedicated to e.g. an Hackathon or an outreach event with students from local high schools, organised by the hosting organisation, where EU's role in supporting young scientists and in promoting research will also be explained; 4) an open discussion with the general public.

6. ACKNOWLEDGEMENTS

We wish to thank S. Braccini and colleagues at the University of Bern for the test at the Inselspital.

This project has received funding from the ATTRACT project funded by the EC under Grant Agreement 777222. The project has also been supported by CERN's Budget for Knowledge Transfer to Medical Applications.

7. REFERENCES

[1] Particle therapy facilities in clinical operation (last update: July 2020), https://www.ptcog.ch/index.php/facilities-in-operation, accessed on 18 July 2020.

[2] Ishikawa et al., H., 2019. Particle Therapy in Cancer Treatment - Current and Future Perspective, Gan to Kagaku Ryoho, Cancer & Chemotherapy, 46(8): pp. 1219-1225.

[3] Rana, S. et al., 2019. Development and long-term stability of a comprehensive daily QA program for a modern pencil beam scanning (PBS) proton therapy delivery system, Journal of Applied Clinical Medical Phys., 20(4):pp. 29-44.

[4] Sauli, F. 2016. The gas electron multiplier (GEM): Operating principles and applications, Nuclear Instruments and Methods in Physics Research Section A: Accelerators, Spectrometers, Detectors and Associated Equipment, 805: pp. 2-24.

[5] Leidner, J. et al., 2020. A GEMPix-based integrated system for measurements of 3D dose distributions in water for carbon ion scanning beam radiotherapy, Medical Physics, 47(6): pp. 2516-2525.

[6] Grevillot, L. et al., 2018. Implementation of dosimetry equipment and phantoms at the MedAustron light ion beam therapy facility, Medical Physics, 45 (1): pp.352-369

[7] Journal of the ICRU Vol 7 No 2 (2007) Report 78, Oxford University Press.

[8] OCTAVIUS® Detector 1600 SRS, Detector array for patient plan verification and quality control of SRS applications,https://www.ptwdosimetry.com/en/products/octavius-detector-1600-srs/, accessed on 4 August 2020.

[9] GAFChromic™ EBT3 film specifications, www.gafchromic.com, access on 18 July 2020.

[10] Spielberger, B. et al., 2001. Experimental investigations of the response of films to heavy-ion irradiation, Physics in Medicine and Biology, 46 (11): pp. 2889-2897.

[11] Safai, S. et al., 2004. Development of an inorganic scintillating mixture for proton beam verification dosimetry, Physics in Medicine and Biology, 49(19): pp. 4637-4655

[12] Russo, S. et al., M., 2017. Characterization of a commercial scintillation detector for 2-D dosimetry in scanned proton and carbon ion beams, Physica Medica, 34 (2017): pp. 48-54.

[13] Seravalli, E., 2009. 2D dosimetry in a proton beam with a scintillating GEM detector, Physics in Medicine and Biology, 54: pp. 3755–3771

[14] Brunbauer, F., 2018. Applications of gas scintillation properties in optically read out GEM-based detectors. CERN-THESIS-2018-106.

[15] Klyachko, A., 2012. A GEM-based dose imaging detector with optical readout for proton radiotherapy, Nuclear Instruments and Methods in Physics Research Section A: Accelerators, Spectrometers, Detectors and Associated Equipment, 694: pp. 271-279

[16] Weijer, P. van de et al., 2019. Spotless hybrid thin-film encapsulation stack for organic light-emitting diodes on organic foils, Organic Electronics, 66: pp. 43-46

[17] ITO Glass - Conductive Coated Glass Slides & Sheet. http://www.visionteksystems.co.uk/ito_glass_datasheet.htm on 25 February 2020.

[18] Kronemeijer, A. J. et al., 2018. Dual-gate self-aligned IGZO TFTs monolithically integrated with high-temperature bottom moisture barrier for flexible AMOLED, SID International Symposium: Digest of Technical Papers, 49(1): pp. 1577-1580.

[19] Tordera, D. et al., 2019. A High-Resolution Thin-Film Fingerprint Sensor Using a Printed Organic Photodetector, Advanced Materials Technologies, 4(11): 1900651.

[20] Auger, M., et al., 2015. Low current performance of the Bern medical cyclotron down to the pA range, Measurement Science and Technology, 26(9): pp. 094006.

[21] Brugger, M. et al., 2014. New radiation protection calibration facility at CERN. Radiation Protection Dosimetry, 161(1-4): pp. 181-184.

[22] Smith, S. W., 1997, Special Imaging Techniques. In The Scientist and Engineer's Guide to Digital Signal Processing. California Technical Publishing, San Diego, California, USA, pp. 423-432.

[23] GEMTEQ: GEMPix detector for microdosimetry with tissue-equivalent gas, ATTRACT final report, 2020.