GEMTEQ: GEMPix detector for microdosimetry with tissue-equivalent gas

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ABSTRACT
Microdosimetry is the study of the temporal and spatial distributions of absorbed energy in biological matter and is crucial for the understanding of the relative biological effectiveness (RBE) of radiation on human tissue, for example of a carbon ion beam used in cancer treatments. During the ATTRACT GEMTEQ project we introduced a new technology – the combination of Gas Electron Multipliers and a highly pixelated readout – to the field of microdosimetry. Prototypes of the GEMTEQ detector were built and their performance tested in various radiation fields, paving the path to track-structure microdosimetry and application to clinical ion beams.

Keywords: microdosimetry, GEM, GEMPix, Timepix, radiation therapy

1. INTRODUCTION

Microdosimetry is the 'systematic study of the spatial and temporal distributions of absorbed energy in irradiated matter' [1]. While the absorbed dose is the standard reference quantity in radiation physics and radiation protection, it is a macroscopic quantity insufficient to explain the effects of ionizing radiation at the cellular level and the relative biological effectiveness (RBE) of different types of radiation. For example, damage to the DNA of a cell and therefore the possible cell death does not only depend on the absorbed dose but also requires knowledge of microdosimetric quantities. This knowledge is crucial for improvements in radiation therapy, one of the main cancer treatment modalities. Microdosimetric measurements are limited by the spatial resolution and the size of adequate detectors.

With this ATTRACT project we used a new detector technology of radically different design – the GEMTEQ – as a small gaseous detector filled with tissue-equivalent (TE) gas and highly pixelated readout to build a novel type of microdosimeter. While Gas Electron Multipliers (GEMs [2]) had been used before in microdosimetry, the combination with a highly pixelated readout is unique to the GEMTEQ.

The particle track imaging capability of the GEMTEQ is completely new to microdosimetry: in this project, measurements were performed in different radiation fields recording tracks from various particles. The usual microdosimetric spectra were obtained and compared to those measured with standard microdosimetric detectors. The GEMTEQ detector was operated as a Time Projection Chamber (TPC) registering 3D particle tracks. The detector design was improved by exchanging the radiation entrance window made of Mylar with a window made of TE material. Finally, a major upgrade was just undertaken to obtain a sealed and low-pressure version of the detector.

In this paper we report on the development of the GEMTEQ and the microdosimetric results obtained in several radiation fields. The detector is described in Section 3. The most important results are reported in Section 4. Finally, Section 5 discusses the next steps of the project.

2. STATE OF THE ART

The golden standard in microdosimetry is the Tissue-Equivalent Proportional Counter (TEPC). A TEPC is a detector consisting of an active volume filled with TE gas, with TE walls and a thin anode wire. The gas pressure is only a few percent of the normal atmospheric pressure and therefore the ionization of a particle in the active volume is the same as in a small piece of tissue. Both the lineal energy and the absorbed dose to tissue can be measured [3]. It is a well-established technology, but it has important limitations that the present project aims to overcome. For example, the equivalent volume size in human tissue can be selected by adjusting the operational pressure, but it is typically of a few micrometres, with a lower limit of operation of 0.3 µm in case of special design [4], which is not enough to obtain details on the particle track structure. Detectors with the best spatial resolutions tend to be complex and bulky [5].

There are other, more recent detector technologies such as silicon microdosimeters [6]. The advantage of this technology is the possibility to fabricate matrices of small physical sensitive volumes, such as right cylinders with 10 µm diameter. In this way, they are suitable for

spatially resolved measurements in clinical beams. However, the main limitation of this technology is that the silicon is not tissue-equivalent. Therefore, a conversion factor between silicon and TE material is needed, which depends on the energy of the incoming particle.

3. BREAKTHROUGH CHARACTER OF THE PROJECT

TEPCs are well-established detectors that can measure the microdosimetric distributions accurately and reliably. However, conventional TEPCs feature only a single readout channel in a detection volume of fixed dimensions. Their equivalent spatial resolution in tissue is typically of a few micrometres. They also tend to be bulky when featuring highest spatial resolution, which makes their use in hadron therapy beams difficult. Silicon microdosimeters overcome some of these issues but introduce a new challenge: the accurate conversion of the response in silicon to the TE response.

The GEMTEQ (Fig. 1) introduces the technology of combining a triple-GEM setup and a highly pixelated readout for microdosimetry. The GEMTEQ is a small gaseous detector with maximum outer dimensions (excluding support and cables) of 22 x 10 x 5 cm^3, based on the GEMPix detector [7] recently developed at CERN, which has already found applications in several domains. It is operated with tissue-equivalent gas at standard pressure, featuring four highly pixelated Timepix ASICs [8] as readout to obtain a mean simulated unit-density tissue chord length of 1 µm. Electrons from primary ionizations are amplified in a series of three GEMs and detected in the ASICs with in total 512 x 512 pixels with a physical area of 55 x 55 $µm^2$ each.

In case of the GEMTEQ detector, it is possible to achieve a resolution down to the scale of tens of nanometres due to the following considerations: the inherently good spatial resolution (pixel pitch of 55 µm) is scaled down using a gas instead of a solid material by a factor of approximately 1000. A gas-tight version of the GEMTEQ that allows for low-pressure operation is being developed and the magnification will be further increased. In contrast to a conventional TEPC, a spatially resolved signal is obtained and the volume size of interest can be chosen and adjusted offline due to the pixelated readout and the storage of the pixels' signals. Table 1 compares the main characteristics of a conventional TEPC and the GEMTEQ.

4. PROJECT RESULTS

During phase 1 of the GEMTEQ ATTRACT project, two detector prototypes were built by ARTEL based on CERN design. One of them was equipped with a radiation window made of A150 TE plastic (Fig. 2). This represents a first step to increase the use of TE material in the detector. For the first time, a detector based on GEMs and a highly pixelated readout was used for microdosimetric measurements. The GEMTEQ was calibrated using an Fe-55 source and its performance was tested in various radiation fields (photons from an X-ray generator and from radioactive sources, neutrons from a neutron generator and a mixed photon/neutron field from an AmBe radioactive source). Fig. 3 shows the GEMTEQ detector setup for measurements in a neutron field. Results obtained in this project are the first milestone for performing microdosimetric measurements with the GEMTEQ. This work shows that standard microdosimetric data analysis can be performed with data obtained with the GEMTEQ: dose spectra, frequency-mean and dose-mean lineal energies were obtained and compared to results obtained with standard TEPCs. A dedicated FLUKA [9,10] Monte Carlo simulation of the GEMTEQ was developed and the results were used for comparison with experimental data and for optimization of the experimental setup.

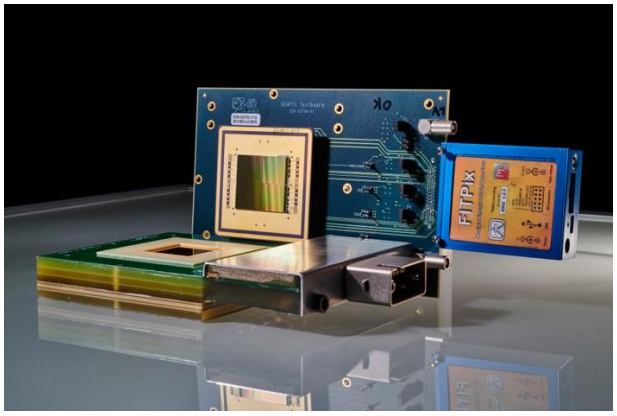

Fig. 1. The open GEMTEQ, showing the four Timepix ASICs.

Tab. 1. Comparison of standard TEPCs and GEMTEQ.

Feature	TEPC	GEMTEQ
Spatially resolved results	*Not available*	Available thanks to the highly pixelated readout with 512 x 512 pixels
Equivalent spatial resolution	*Typically a few micrometres*	Pixel edge length equivalent to 100 nm at standard pressure, low pressure version being developed
Microdosimetric volume	*Defined by detector volume and pressure*	Defined offline by software
Number of active volumes in a detector	*Typically 1*	Many, e.g. more than 2500 for 1 µm equivalent mean chord length
Track structure microdosimetry	*Impossible*	Possible

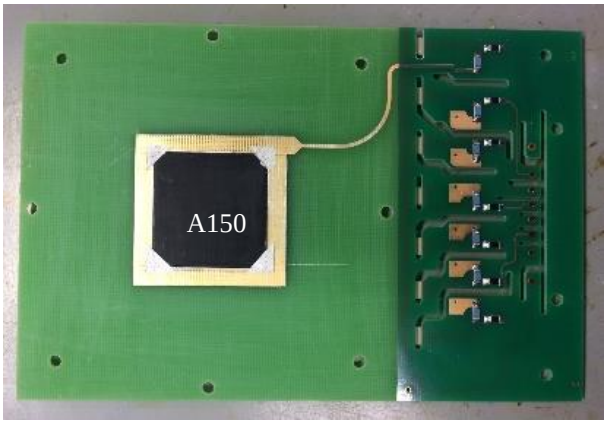

Fig. 2. A component of the GEMTEQ detector prototype including the radiation window made of A150 TE plastic (the black material in the image).

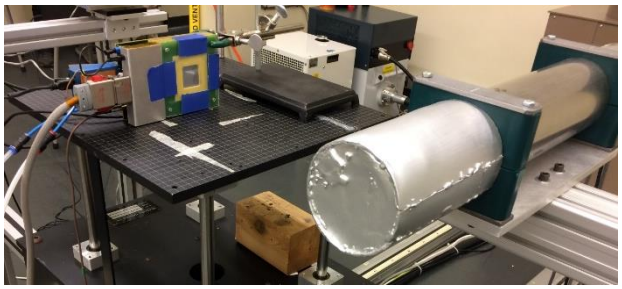

Fig. 3. The GEMTEQ detector placed on a support table and facing the neutron generator.

The Monte Carlo simulation provides energy deposition values in the sensitive volume. In order to emulate the detector response, models for the diffusion of secondary electrons, the energy threshold of the readout and the energy resolution were applied to the simulated data. Fig. 4 shows dose spectra obtained with a neutron generator emitting 2.5 MeV neutrons. The distributions are similar and differences either are due to differences in the shape of the sensitive volumes or are understood as effects related to the detector response. This demonstrates the good performance of the GEMTEQ.

Furthermore, 2D particle track images were obtained from the measurements using the same data set as for the dose spectra (Fig. 5). This is impossible with conventional TEPCs and opens the door for many new applications in microdosimetry. These include: particle tracks can be studied in detail (track structure microdosimetry), particle identification becomes possible (helping to disentangle contributions from different types of radiation in a mixed field) and effects of the size of sensitive volumes can be studied offline on a single data set. For the first time, another GEMTEQ prototype was operated with TE gas in a TPC mode and 3D particle tracks could be reconstructed (Fig. 6).

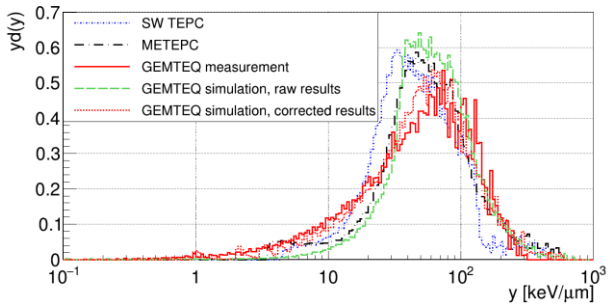

Fig. 4. Dose spectra for neutron irradiation obtained from measurements with the GEMTEQ and two TEPCs (called SW TEPC – a commercial TEPC manufactured by Far West Technology Inc., USA – and METEPC [11]). The simulated spectrum for the GEMTEQ is also shown before and after application of corrections emulating the detector response.

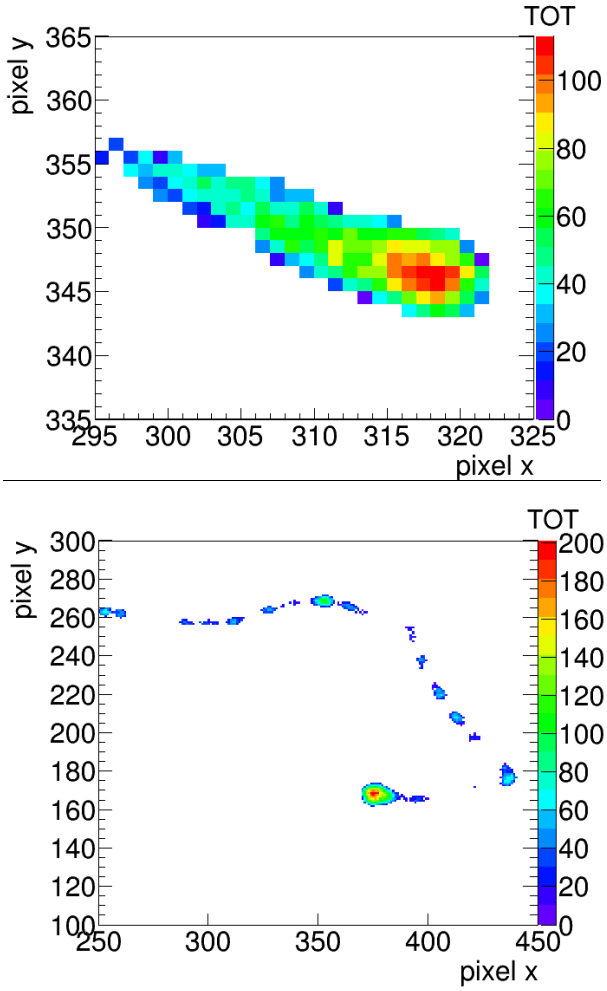

Fig. 5. Particle tracks of a proton (top) and an electron (bottom) in the GEMTEQ: the x and y axes are the spatial coordinates given as pixel numbers, while the energy deposition is colour coded in units of Time over Threshold (TOT), which corresponds to energy when the detector is calibrated.

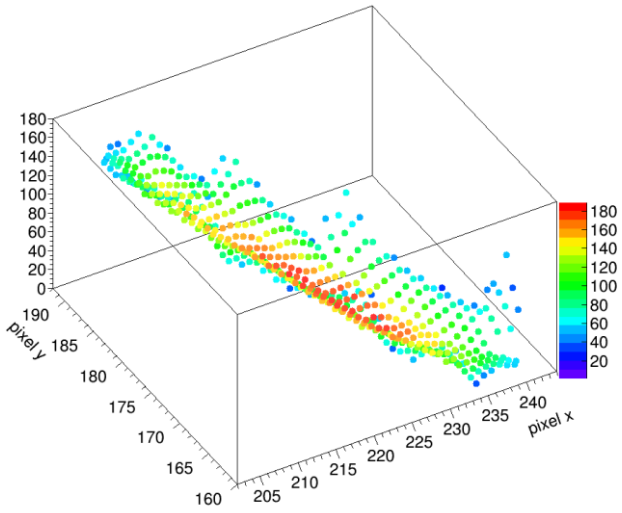

Fig. 6. A 3D particle track reconstruction of an alpha particle: the x and y axes are the spatial coordinates based on the pixelated readout, the z axis is based on the reconstruction from the measured time of arrival information and the energy deposition (before energy calibration) is colour coded.

In conclusion, these results demonstrate the capabilities of the compact GEMTEQ detector in microdosimetry. While being more complex than a conventional TEPC, the GEMTEQ offers spatially resolved measurements of the energy deposition, which are not possible with TEPCs.

5. FUTURE PROJECT VISION

During the ATTRACT phase 2, we would focus on the development of a compact, sealed, low-pressure and tissue-equivalent GEMTEQ detector with a larger active area of 20 x 20 cm^2. The final goal is the development of a detector that can be used in radiation therapy for quality assurance involving microdosimetric quantities. Our intention is, independently of potential ATTRACT Phase 2 funding, to pursue the development of the GEMTEQ on a shorter time scale, seeking for alternative funding sources and including additional partners.

5.1. Technology Scaling

The ATTRACT project allowed us to develop the first GEMTEQ detector prototypes (TRL 3 to 4). The results show that it is possible to perform microdosimetric measurements with the GEMTEQ. The detector is more complex than a standard TEPC but offers new possibilities like particle track analysis and offline definition of the volume of interest. The development of a sealed and low-pressure version has just started and will be pursued after the present ATTRACT project. A measurement of the electron drift velocity would be needed for the accurate 3D particle track reconstruction. This is a rather complex measurement and indeed experimental data are not available for propane-based TE gas. The use of TE material for the detector has been preliminarily investigated using a TE plastic cathode as the radiation entrance window. We envision to increase the use of TE material in the next version of the GEMTEQ.

In order to reach TRL 5, we would need to test the performance of the detector in clinical proton and carbon ion beams and check its capabilities to perform microdosimetric measurements. CERN RP group has an open collaboration with CNAO (the Italian Centre for Oncological Hadron Therapy), where these measurements can be performed.

5.2. Project Synergies and Outreach

We plan to merge the results of this project with those of the ATTRACT LaGEMPix project, which has developed a version of the GEMPix with a larger readout area. Very interesting results have been obtained [12], paving the way to achieving an area large enough to cover typical clinical field sizes. The LaGEMPix project also included 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 the microdosimetric capability of the GEMTEQ with a 20 x 20 cm^2 LaGEMPix imagining detector of the LaGEMPix ATTRACT project, and integrating such an innovative device in a motorised water phantom (already built and tested outside the ATTRACT framework [13]), 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 and will for industrialising the prototype and producing a commercial version. 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 developed and thoroughly characterised by CERN RP group, specifically for medical applications, and

ARTEL has a solid knowledge of producing GEMPix detectors.

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) the detector being more complex than conventional TEPCs, making it e.g. more difficult to find the best settings for a certain type of measurement; 2) the needed in-depth understanding of the charge production and movement in the detector for a complete exploitation of the gathered data; 3) the challenge of developing a detector withstanding a clinical beam while still being capable of performing microdosimetric measurements. Due to our experience with the GEMPix and more specifically the successful completion of the ATTRACT GEMTEQ and LaGEMPix projects, we are confident to meet the technological specifications. Technical difficulties encountered in one or more of the above aspects may delay the project but should not prevent its successful completion. 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

In the second half of 2020, the project will involve a Danish student from Aarhus University helping with the design of a sealed and low-pressure detector version, during five months at CERN.

An ATTRACT Phase 2 project will involve a larger consortium, a mixture of research institutions 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. a 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.

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7. REFERENCES

[1] Rossi, H., et al., 1996, Microdosimetry and Its Applications, Springer-Verlag, Berlin and Heidelberg, Germany.

[2] Sauli, F., 1997, GEM: A new concept for electron amplification in gas detectors, NIM A, 386(2–3): pp. 531-534.

[3] Lindborg, L., et al., 1999, The use of TEPC for reference dosimetry, Radiation Protection Dosimetry, 86(4): pp. 285–288.

[4] Bortot, D., et al., 2018, A novel TEPC for microdosimetry at nanometric level: response against different neutron fields, Radiation Protection Dosimetry, 180(1-4): pp. 172-176.

[5] Banstar, A., et al, 2017, State of the art of instrumentation in experimental nanodosimetry, Radiation Protection Dosimetry, 180: pp. 177-181.

[6] Rosenfeld, A.B., 2016, Novel detectors for silicon based microdosimetry, their concepts and applications, NIM A, 809: pp. 156-170.

[7] Murtas, F., 2014, Applications of triple GEM detectors beyond particle and nuclear physics, Journal of Instrumentation, 9(01): p. C01058.

[8] Llopart, X., et al., 2007, Timepix, a 65k programmable pixel readout chip for arrival time, energy and/or photon counting measurements. NIM A 581(1–2): pp. 485-494.

[9] Böhlen, T., et al., 2014, The FLUKA Code: Developments and Challenges for High Energy and Medical Applications, Nuclear Data Sheets, 120: pp. 211-214.

[10] Ferrari, A., et al., 2005, FLUKA: a multi-particle transport code. CERN-2005-10, INFN/TC_05/11, SLAC-R-773.

[11] Waker, A.J., et al., 2011, Design of a multi-element TEPC for neutron monitoring, Radiation Protection Dosimetry, 143(2-4): pp. 463–466.

[12] Oliveira, A.M., et al., 2020, LaGEMPix: a large area GEMPix detector with optical readout for hadron therapy, Public deliverable for the ATTRACT Final Conference.

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