A simple approach for experimental characterization and validation of proton pencil beam profiles

Paulina Stasica[1,2], Jakub Baran[1], Carlos Granja[3], Nils Krah[4], Grzegorz Korcyl[5], Cristina Oancea[3], Monika Pawlik-Niedźwiecka[1,5], Szymon Niedźwiecki[5], Marzena Rydygier[1], Angelo Schavi[6], Antoni Rucinski[1], Jan Gajewski[1*]

[1] *Institute of Nuclear Physics PAN, Krakow, Poland*
[2] *AGH University of Science and Technology, Krakow, Poland*
[3] *ADVACAM, Prague, Czech Republic*
[4] *CNRS/CREATIS, UMR 5220, Lyon, France*
[5] *Institute of Physics, Jagiellonian University, Krakow, Poland*
[6] *Sapienza University of Rome, Italy*

Correspondence*:
Jan Gajewski
jan.gajewski@ifj.edu.pl

ABSTRACT

A precise characterization of therapeutic proton pencil beams is essential for commissioning of any treatment planning system (TPS). The dose profile characterization includes measurement of the beam lateral dose profile in the beam core and far from the beam core, in the so called low-dose envelope, and requires a sophisticated detection system with a few orders of magnitude dynamic range. We propose to use a single-quantum sensitive MiniPix Timepix detector, along with an in-house designed holder to perform measurements of the pencil beam dose profile in air and in water. We validated the manufacturer calibration of the MiniPix Timepix detector in proton beams of various energies and compared the deposited energy spectra to Monte Carlo (MC) simulations. The precision of the lateral dose profile measurements has been systematically validated against Krakow proton facility commissioning data and dose profile simulations performed with MC codes Gate/Geant4 and Fred. We obtained an excellent agreement between MiniPix Timepix measurements and simulations demonstrating the feasibility of the system for a simple characterization and validation of proton pencil beams. The proposed approach can be implemented at any proton therapy facility to acquire experimental data needed to commission and validate analytical and MC based TPS.

Keywords: Proton therapy; Dose; Semiconductor pixel detector; Timepix detector; Monte Carlo simulation

1 INTRODUCTION

The dosimetric advantage of proton beams in radiotherapy is due to their depth-dose distribution (Bragg curve), which enable to minimize dose deposited in healthy tissues and to maximize it in the tumor region [1, 2]. After many years of research and development, a growing interest in proton radiotherapy is observed.

According to data provided by the Particle Therapy Co-Operative Group (`https://www.ptcog.ch/`, 2020) there are 91 proton (or proton and carbon ion) radiotherapy facilities in operation, 33 under construction, and 27 in the planning stage, all around the world. At the start-up of each new proton facility, for the purpose of launching a treatment planning system (TPS), a commissioning of the proton pencil beam is required. The beam commissioning that includes, i.a., an experimental characterization of lateral and longitudinal beam profiles, is a demanding and time-consuming experimental procedure. In this paper we propose a new approach for characterization of lateral beam profiles in air and in water to simplify the procedure of commissioning of TPS and its validation.

The state-of-the-art experimental approach for proton beam commissioning is to measure lateral dose profiles in air with a scintillating screen [3]. This method allows only to measure the major component of the lateral beam dose profile characterized by a Gaussian distribution. In fact, primary particles scatter on the passive components of a beam delivery system, such as gantry nozzle equipment and range shifters/compensators, building up an additional dose envelope of the lateral beam profiles [3], which is recognized as a nuclear halo. The nuclear halo is often approximated in TPS by double Gaussian model of proton pencil beam. The accurate characterization of pencil beam lateral dose profiles is particularly important for facilities using very small spot sizes as the uncertainty of the nuclear halo modeling is propagated over a greater number of spots [3, 4]. Also, the effect is pronounced for small, shallowly located targets that are irradiated with a limited number of spots because the uncertainties are not averaged [4]. Still, the measurements of the dose envelope are often neglected, because characterization of pencil beam nuclear halo requires dedicated detector technology with sufficient sensitivity and accuracy.

In order to compensate for the uncertainties in the beam modeling caused by the dose envelope some of the proton centers investigate and develop new detection techniques for characterization of the lateral beam profile far from the beam core. For instance, in Krakow proton facility, passive dosimetry [5, 6] or single particle sensitive methods like scCVD diamond detectors [7] have been investigated. Refer to a review of Karger et al. and references for description of other approaches [8].

After commissioning stage, a validation of the beam model implementation in TPS is required, and it is typically performed by means of experimental measurements in water. Usually, the dose in complex radiation fields consisting of several pencil beams is measured and, if necessary, field size factors are applied to correct for experimental and computational uncertainties of the pencil beam modeling. The introduction of Monte Carlo (MC) tools in the clinical routine offers computational accuracy allowing consideration of nuclear halo in patient treatment plan simulations. However, the experimental validation of single pencil beam dose profiles in water, including the nuclear halo, is even more demanding than in air, because requires operation of the detector in water. There is still a necessity to provide more accurate, fast, and easy-to-use experimental methods for characterization of the low-dose envelope of proton pencil beams.

Here, we propose a simple approach for experimental characterization and validation of lateral and longitudinal dose profiles including the dose envelope. We used a commercial semiconductor pixel detector, MiniPix Timepix, for fast and high-precision particle-by-particle measurements of a therapeutic proton beam. We present an experimental setup consisting of the MiniPix Timepix detector, in-house developed detector holder, and water phantom, that can be used for both, commissioning measurements in air and validation measurements in water. We measured pencil beam profiles and compared the results to the facility commissioning data, TPS calculations, and Monte Carlo (MC) simulations, demonstrating the feasibility of the approach.

2 MATERIALS AND METHODS

2.1 Proton radiotherapy facility

The Krakow proton beam facility is in clinical operation since October 2016, offering protons for radiation therapy treatment, as well as for physics and radiobiology experiments. The Krakow facility offers stable beam intensities ranging from 1 to 300 nA and scanning pencil beam in energy range from 70 to 226 MeV, which corresponds to range in water from 4.2 cm to 31.8 cm. The lateral beam size (1σ) ranges depending on the proton beam energy and application of a range modulator (range shifter - RS) from about 3 to 15 mm. The RS made of 4.2 cm thick PMMA material, mounted at the gantry nozzle is used to modulate proton range.

In Krakow, Eclipse TPS from Varian (version 13.6), commissioned against experimental data, is used for treatment planing. Longitudinal dose profile measurements were performed in water using a Bragg Peak Chamber (from PTW). Lateral dose profiles in air were measured using LYNX scintillating screen (IBA Dosimetry) and thermoluminescence detectors (TLDs) in the primary Gaussian and the dose envelope regions, respectively. Eclipse TPS was used to compute 3D pencil beam dose profiles in water. In addition to clinical TPS, the dose profiles were simulated using a secondary dose computation tool, FRED MC code [9] that was commissioned and validated for quality assurance purposes in Krakow [10]. The proton beam model used by clinical TPS and FRED have been adopted for GATE/Geant4 simulations performed in this work.

2.2 MINIPIX TIMEPIX Detector and data acquisition software

In this study we propose using the technology of pixel semiconductor detectors, TIMEPIX from ADVACAM (`https://advacam.com`), for characterization of therapeutic proton pencil beams and validation of TPS and MC simulations. Due to the single-quantum sensitivity and particle tracking capability, TIMEPIX technology enables particle-by-particle dosimetry of proton pencil beams. TIMEPIX is a commercial version of MEDIPIX detector developed at CERN and is widely used for radiation research, e.g., in ion beam therapy [11, 12], in radiation dosimetry [13, 14, 15], in particle accelerator environments [16] or for space radiation characterization on board of the International Space Station [17, 18, 19].

In this work a compact MINIPIX TIMEPIX detector was used (figure 1, left). The entire MINIPIX TIMEPIX has dimensions of $77\times21\times10$ mm and its total weight is 25 g. The sensitive volume of the semiconductor silicon sensor ($14.08\times14.08\times0.3$ mm) consists of a 2D array of 256×256 pixels, each has dimensions of 55×55 μm. The ionizing particle penetrating the sensitive volume of the MINIPIX TIMEPIX produces electric charge, which is collected by adjacent electrode pixels forming a cluster. The signal read-out is performed in each pixel individually in single frame acquisition time of typical length of about 1-100 ms. The MINIPIX TIMEPIX frame readout dead-time is 22 ms. Data acquisition electronics is fully integrated, connected to the computer via USB port and does not require a dedicated cooling system. For more details on the TIMEPIX detector technology refer to [20, 21, 22] and references.

The MINIPIX TIMEPIX detector is equipped with a data acquisition and real-time visualization software, PIXET PRO, which also provides data processing tools for cluster morphology analysis. Figure 1 (right) shows an example of data frame acquired in Krakow. The morphology of each cluster, consisting of the signal amplitude in a number of adjacent pixels, is characterized by a list of cluster parameters, including: the position of the cluster center of mass, the total energy deposited, the cluster length, and the angle at which the particle enters the detector. The cluster analysis enable identification of impinging particle type [21]. The analysis of multiple clusters enables particle-by-particle experimental characterization of the mixed radiation fields consisting of primary and secondary protons, secondary electrons, photons, etc. Depending on the primary particle fluence, the single frame acquisition time need to be adjusted for each measurement individually, in order to minimize the overlapping of the clusters. The cluster overlapping effect occurs when different particles at short time intervals produce clusters which are so close to each other that they overlap and are recognized by PIXET PRO software as a single cluster of larger energy deposition. The overlapping effect does not influence the total energy deposited in the detector.

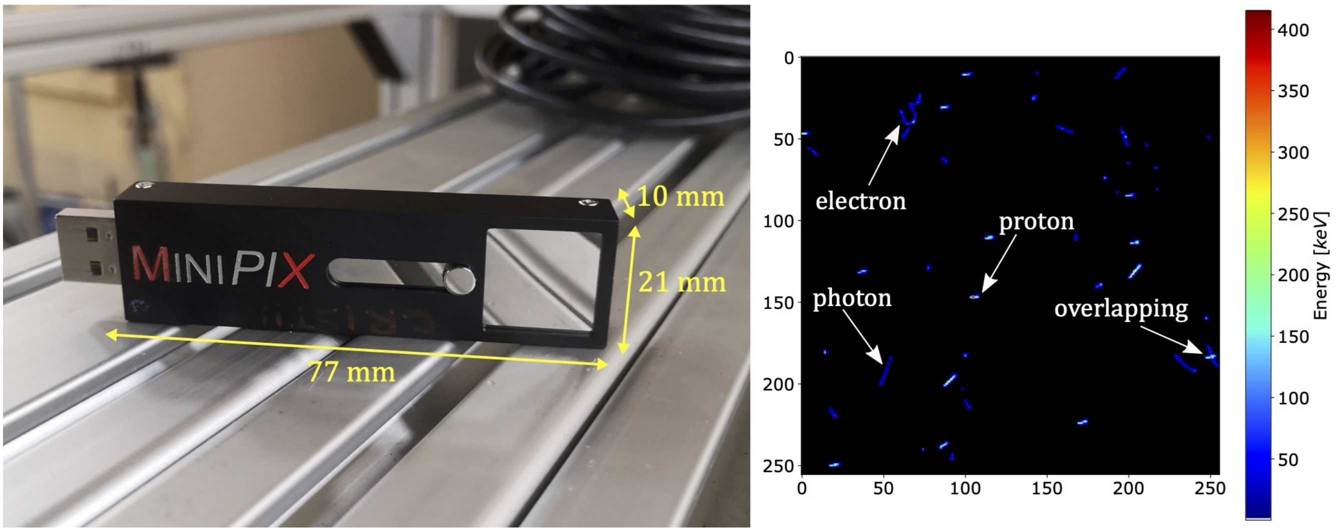

Figure 1. The MINIPIX TIMEPIX detector equipped with a ASIC and 300 μm thick silicon sensor (left) and an example frame obtained form the measurements (right). Clusters are produced by different particles in mixed radiation field of proton pencil beam in water. Low-LET, narrow, curly tracks are typical for electrons, high-LET, wide, straight tracks for energetic heavy charged particles such as protons, while low-LET, straight tracks are characteristic for photons. In the right side of the frame an example of overlapping clusters is shown.

2.3 Dose calculation engines

In this work, the dose distributions were calculated using clinical TPS Eclipse, as well as two MC toolkits: GATE/Geant4 (version 8.2), interfaced to Geant4 (version 10.4.p2) [23] and FRED MC (version 3.0.18) [9]. GATE/Geant4 is a full MC simulation engine transporting all the primary and secondary particles contributing to the dose deposition. FRED is a fast, GPU-accelerated MC tool transporting primary and secondary protons, deuterons, and tritons, whereas the energy from gammas and delta-electrons is deposited at their production point.

2.4 Calibration measurements

The MINIPIX TIMEPIX detector is calibrated by the manufacturer aiming at a uniform response of each individual pixel to energy depositions from X-rays source [22, 24, 25]. In principal, primary and/or secondary particles can enter the detector surface at any angle, which specially occurs measuring mixed radiation field produced by a proton beam in water. In this work, we performed a validation of the detector response to proton beams impinging the detector surface at different angles by comparing the energy deposition spectra obtained experimentally to MC simulations.

Experimental setup and data acquisition

The MINIPIX TIMEPIX was exposed to proton pencil beams of nominal energies E70, E100, E150, and E200, corresponding to proton mean energies and energy spreads (standard deviation) at the detector position of 70.5(0.6) MeV, 100.1(0.8) MeV, 149.9(1) MeV, and 199.6(1) MeV, respectively. For each nominal energy the detector was positioned at the isocentre in air (in the beam core) at β angles ranging from 27° to 83°. We defined β as the angle between the normal to the silicon sensor surface and the proton beam axis (cf. figure 2). The accelerator dark current was used allowing to keep the particle fluence low enough to avoid saturation of the detector and to minimize the cluster overlapping.

Monte Carlo simulations

We performed MC simulations of the calibration setup in GATE/Geant4 toolkit. The MINIPIX TIMEPIX detector active volume was simulated as a $14.08{\times}14.08{\times}0.3\,\mathrm{mm}^3$ cube made out of silicon ($\rho = 2.33\,\mathrm{g/cm}^3$, $\mathrm{I_{pot}} = 173\,\mathrm{eV}$ [26]). The detector was positioned at the isocentre at β angles mimicking the experimental conditions. For simulations of proton pencil beams, the MC implementation of the clinical beam model based on Krakow proton facility commissioning measurements was used. We used the QGSP_BIC_HP_EMZ physics list with production cuts in the active volume of 10 $\mu\mathrm{m}$ for protons, electrons, and gammas. For each individual calibration simulation the total number of 10^6 primary particles were simulated. Using a phase space actor in GATE/Geant4 we scored the type, energy, angle, and position of the incidence of each primary particle crossing the detector surface. The history of the interactions and energy depositions of primary and secondary particles of unique identification number (UID) was scored using a GATE/Geant4 sensitive volume.

Data analysis

The results scored by the phase space actor and the GATE/Geant4 sensitive volume were merged based on the primary particle UID. The total energy deposited in the detector by a single primary proton was calculated as a sum of all energy depositions from the primary and secondary particles scored inside the GATE/Geant4 sensitive volume.

For each primary proton energy and detector angular position (β), the energy deposition distributions obtained from the MINIPIX TIMEPIX measurements were compared to the GATE/Geant4 simulations. In order to account for differences in experimental and MC simulation setups, we applied filtering of experimental data. The list of clusters obtained with MiniPix Timepix was filtered for the measured angle at which the particle entered the detector with the condition $\beta \pm 3°$. In addition we compared the mean deposited energy measured by the MiniPix Timepix detector and simulated in Gate/Geant4 to the deposited energy calculated based on PSTAR data of proton stopping power in silicon [26].

2.5 Dose profile characterization

The experimental setup was used for two types of dose profile measurements. We performed lateral dose profile measurements in air to demonstrate the capability of the MiniPix Timepix detector to be used for commissioning and characterization of proton therapeutic pencil beams. Next, we performed lateral and longitudinal dose profile measurements in water to validate the pencil beam propagation performed by TPS and MC simulations.

Experimental setup, beam conditions, and data acquisition

The MiniPix Timepix detector was positioned in a dedicated, waterproof, in-house designed PMMA holder mounted inside the water phantom (BluePhantom^2 by IBA). We enclose the technical sketch of the PMMA holder in supplementary materials. The detector sensitive volume was positioned at isocentre using water phantom step motors and laser patient positioning system. The MiniPix Timepix was positioned at an angle $\beta = 45°$. See figure 2 middle panel for the detector placed in the phantom (in air) without the waterproof cover and figure 2 right panel for detector placed in water.

The lateral proton pencil beam profiles in air and in water were acquired for proton beams at nominal energies E100, E150, E200, with and without range shifter. All the measurements were performed using the lowest possible accelerator beam current of 1 nA to keep the beam current stable between measurements. For the 1 nA beam current we did not perform measurements with the detector placed in the beam core (0-20 mm away from the isocentre) because at such current the primary proton yield leads to detector saturation for a single acquisition time frame. For dose profile measurements, the time frame duration was set by the software operator based on a real-time visual assessment of the data in the Pixet Pro software. Before starting the data acquisition, while beam was on, the most optimal time frame duration was selected allowing acquisition of the maximal possible number of clusters in one frame and avoiding cluster overlapping effect. The total acquisition time of each measurement in single point of radiation field depends on particle fluence, and it was from 20 to 40 s resulting in the order of 10^4-10^6 registered single particle events (clusters). In total, we performed 26 proton pencil beam lateral and longitudinal dose profile measurements.

For measurements in air, MiniPix Timepix was positioned at the gantry room isocentre, and lateral profiles were acquired at the distance from 30 to 180 mm away from the isocentre. Following the measurements in air, BluePhantom^2 was filled with water. See figure 3 for simulated 2D dose distributions of proton pencil beams in water with and without range shifter for three investigated nominal proton beam energies. The dose distributions are overlapped with lines indicating which lateral and longitudinal dose profiles were measured. We measured lateral dose profiles at three depths, at 1/2 and 3/4 of the proton beam range, as well as in the Bragg peak position. For 150 MeV proton beam, the longitudinal profiles were measured at the distance of 25, 37, 49, and 61 mm away from the isocentre.

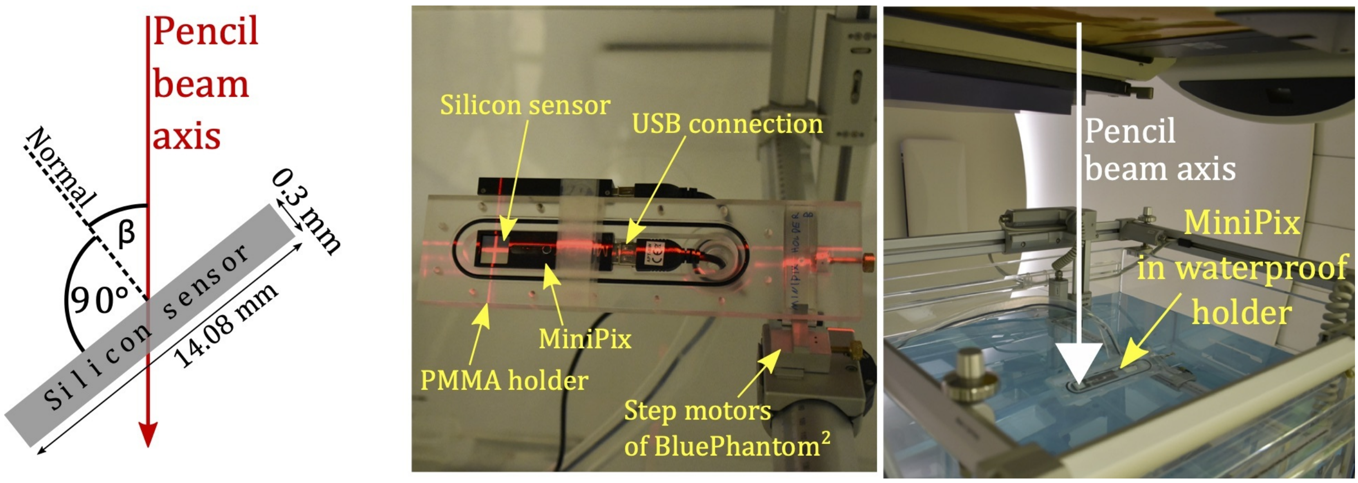

Figure 2. Schematic illustration of MINIPIX TIMEPIX detector silicon sensor and the definition of β angle between the normal to the silicon sensor surface and proton pencil beam axis (left panel), MINIPIX TIMEPIX placed in the PMMA holder positioned in water phantom without the waterproof cover (middle panel), and immersed in the water phantom filled with water for profile measurements (right panel).

Monte Carlo simulations

The dose distributions in water for the nominal energies used in the experiment with and without the RS were calculated using clinical TPS (analytical dose computation algorithm), as well as simulated in GATE/Geant4 and FRED MC engines. In GATE/Geant4, we used the QGSP_BIC_HP_EMZ physics list with 1 mm production cut for gammas, electrons, and positrons and 10 μm for protons. In both MC engines, a high statistics of 10^9 primaries were simulated in order to obtain the beam dose envelope in water up to 150 mm far from the beam core. The dose was scored in water in $2\times2\times2\,\mathrm{mm}^3$ voxels.

2.6 Data analysis

The data pre-processing was performed using PIXET PRO track processing tool, which provided a list of clusters and their parameters for each measurement performed at the given point of radiation field. For analysis of the dose profiles we extracted from PIXET PRO: (i) the total energy deposition in each cluster, (ii) the cluster position in the detector sensor as well as (iii) the total number of frames and (iv) the frame duration time for each measurement point. For each measurement point we calculated the relative dose rate D as:

$$\mathrm{D} = \frac{1}{\mathrm{t_{acq}} \cdot \mathrm{n}} \cdot \frac{\sum_\mathrm{i} \mathrm{E_i}}{\mathrm{m}}\ [\mathrm{Gy/s}], \tag{1}$$

where $\mathrm{E_i}$ is the total energy deposited by a particle in a cluster, m is the mass of the detector silicon sensor, $\mathrm{t_{acq}}$ is the frame acquisition time (constant within one measurement point), and n is the total number of frames acquired in one measurement point.

The visualization and comparison of the lateral dose profiles obtained experimentally in air and in water to simulations was performed as follows. The maximum value of the lateral beam dose profile simulated in GATE/Geant4, FRED, and TPS were normalized. The dose experimental profiles were adjusted to the corresponding simulated profiles using least mean square algorithm. This was necessary because the dose rate at the profile maximum varies depending on primary beam energy and on measurement depth. The value of relative dose rate obtained experimentally was not modified between the measurement points within a single profile.

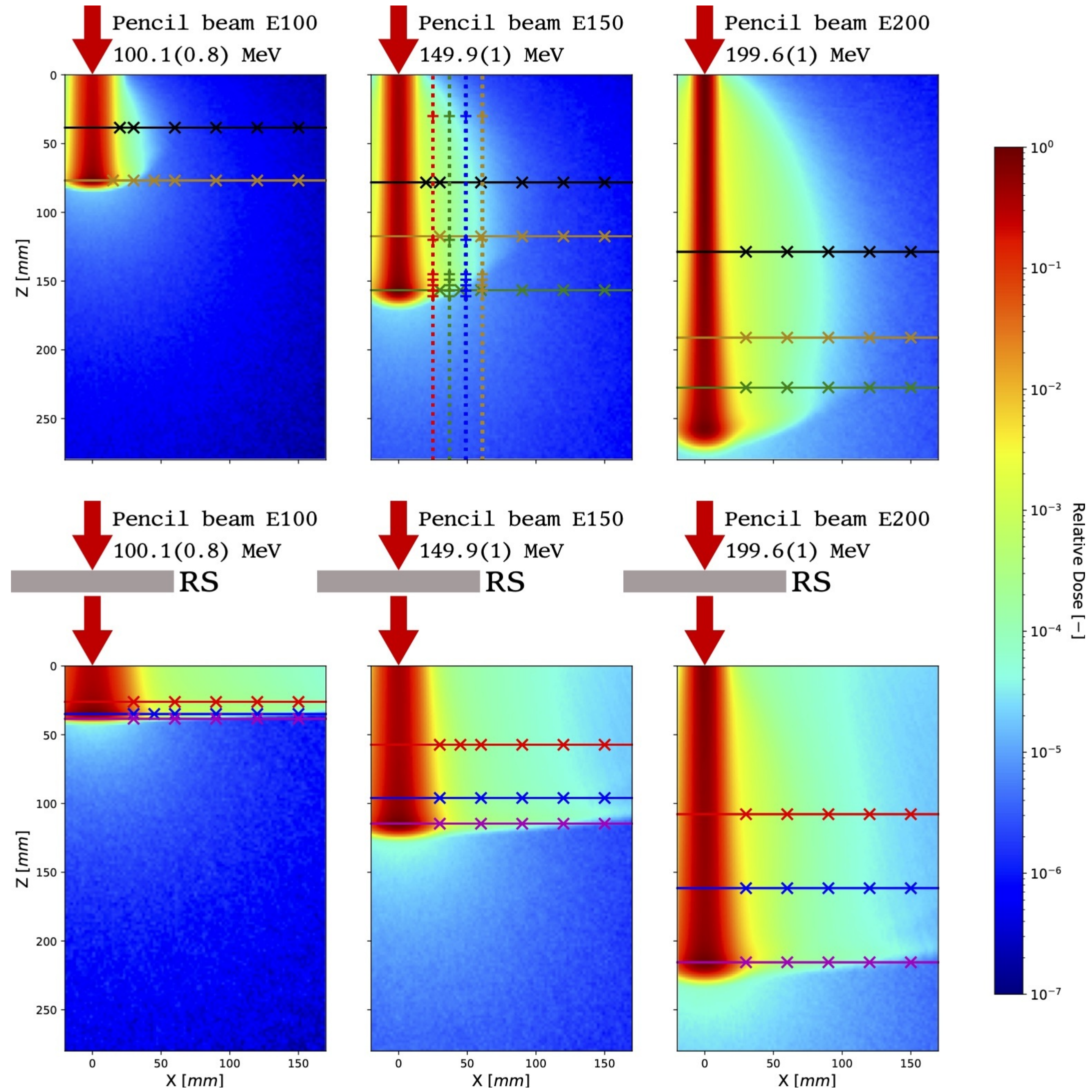

Figure 3. 2D dose profiles obtained from MC simulation of proton beams at three nominal energies with (bottom) and without (top) the RS. The lateral and longitudinal dose profiles measured with MINIPIX TIMEPIX are shown, and the measurement points are marked with crosses. The color convention used to illustrate measured dose profiles is the same as the one used in the figures in the results sections 3.3 and 3.4.

Next, we compared lateral and longitudinal dose profiles measured with MINIPIX TIMEPIX in water with the simulations of 3D dose profiles performed with clinical TPS, fast MC code FRED, and full MC code GATE/Geant4. A median filter with kernel size of 5 was used for lateral GATE/Geant4 profiles at the distance larger than 50 mm from the beam core to compensate for the statistical fluctuations of MC simulation.

For the purpose of visualization of the longitudinal dose profile measurement in water, the maximum value of the 3D dose distribution simulated in GATE/Geant4, FRED, and TPS was normalized to 1. The longitudinal profiles simulated at the distance from beam core are plotted according to the normalization, and the MINIPIX TIMEPIX measurement results were adjusted to the simulations using the same least mean square algorithm.

3 RESULTS

3.1 Calibration measurements

Figure 4 (left panel) shows an example of energy deposition spectra for detector angle β=57° (cf. figure 2 left panel) and nominal proton energy E150. The spectrum obtained experimentally (raw data) exhibits considerable amount of clusters with low energy depositions (below 0.4 MeV) and particles incoming at significantly smaller angles than β. These clusters are produced mostly by photons originating from the gantry nozzle equipment (plane-parallel and multiwire ionisation chambers), which are not explicitly simulated in the GATE/Geant4. The main energy deposition peak, with the maximum of about 0.5 MeV, is produced by the protons entering the detector at angle 57±3°. The peaks to the right, with the maximum of about 1 MeV and 1.6 MeV, result from the overlapping effect, where respectively two or three primary protons overlap creating a single clusters with the doubled or tripled energy deposition. The overlapped clusters exhibit larger incident angles than the primaries in the main energy deposition peak. The overlapping effect is not taken into account in GATE/Geant4 simulations. In order to compare the spectra obtained experimentally with the MC simulations, all the particles incoming at angles different than 57±3° were filtered out. Figure 4 (left panel) shows the spectra obtained experimentally before and after filtering, spectra obtained from simulations, and measured angle of the incoming particles as a function of deposited energy.

Figure 4 (middle panel) shows energy deposition spectra for nominal energy E150 and various β angles. The main energy deposition peak shapes and positions are comparable with the simulations. The mean deposited energy obtained from MINIPIX TIMEPIX measurements (after filtering), simulated in GATE/Geant4 MC and calculated based on PSTAR stopping power data are presented in figure 4 (right panel). The best agreement is achieved for detector angles β up to 73°. For angles higher than 73°, the mean energy deposition obtained from simulations is consistent with the PSTAR data but it is higher for measurements. This might be an effect of registering particles scattered on the MINIPIX TIMEPIX case made of aluminum, which produce long clusters of large energy depositions. Therefore, for the beam profile measurements in water and in air, the detector angles of 45° or 60° were chosen.

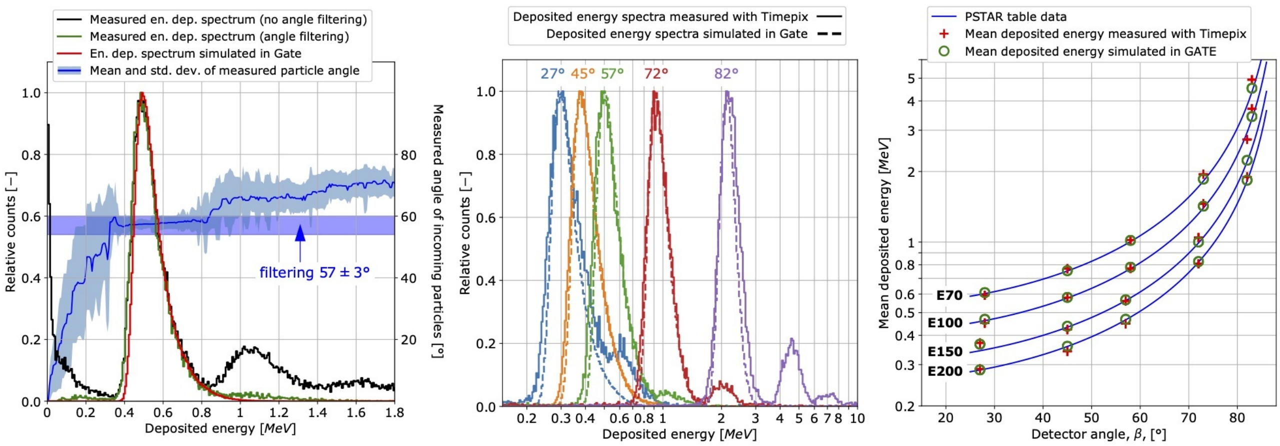

Figure 4. Example of energy deposition spectrum for proton beam at the nominal energy E150 measured with MINIPIX TIMEPIX positioned at angle β=57° before and after filtering for the particles incidence angle (±3°) as well as the one obtained from GATE/Geant4 MC simulation (left panel). Energy deposition spectra after applying the cluster filtering procedure for nominal energy E150 and various β detector angles (middle panel). Mean energy deposited in MINIPIX TIMEPIX exposed to nominal proton energies E70, E100, E150, and E200 when positioned at various angles. The measurement results are compared to MC simulations and data calculated based on PSTAR stopping power tables (right panel).

3.2 Beam spot profiles in air

Figure 5 shows proton pencil beam lateral profiles measured for nominal energies E100, E150, and E200 in air, at the isocentre, without and with the RS. The profile shapes measured with MiniPix Timepix correspond well to TPS beam model data obtained during the facility commissioning. The high sensitivity of MiniPix Timepix allowed to perform measurements in significant distance from the beam core (from 30 mm up to 180 mm) in relative dose range of 3 orders of magnitude. This allowed to measure the build up of the nuclear halo.

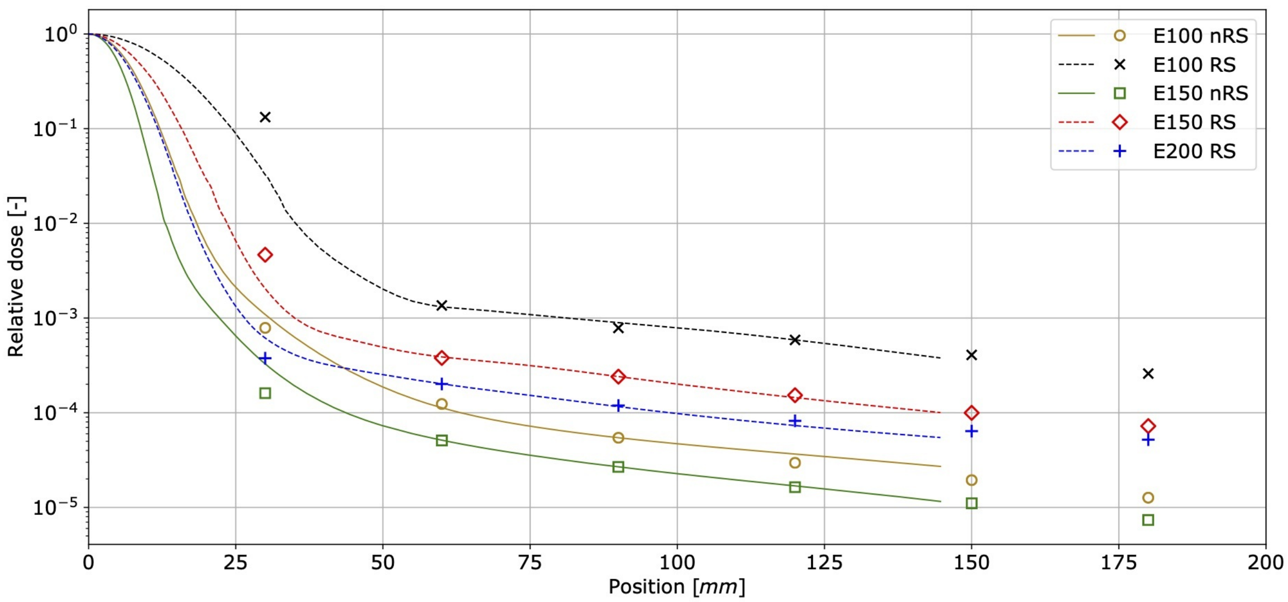

Figure 5. Lateral pencil beam dose profiles measured at the gantry room isocentre in air for primary proton beams at three nominal energies. Points correspond to MiniPix Timepix measurement results, whereas solid and dashed lines are the data obtained from TPS beam model without RS (nRS) and with RS, respectively.

3.3 Lateral profiles in water

Figure 6 shows MiniPix Timepix results in water performed with and without the RS for three nominal beam energies E100, E150, and E200. The measurement results of (i) the first Gaussian term obtained with the Lynx scintillating screen and (ii) the low-dose envelope (nuclear halo) obtained with MiniPix Timepix are compared with Gate/Geant4 and Fred MC simulations.

We observed an excellent agreement between the shape of the profiles obtained experimentally with Lynx and MiniPix Timepix and simulated with full MC code Gate/Geant4 up to 150 mm far from the beam core. The shape of the lateral dose profiles were also accurately reproduced at different depths in water and behind the RS. In Fred simulations, the shape of the lateral dose profiles in comparison to MiniPix Timepix measurements is well mimicked up to 4 orders of magnitude. The disagreement for more distant measurement points is due to the fact the Fred code does not transport secondary gammas and electrons.

3.4 Longitudinal profiles in water

Figure 7 presents proton pencil beam longitudinal dose profiles in water for beam nominal energy E150. The beam range measured with MiniPix Timepix is in agreement with the Gate/Geant4 simulations, even at the distance of 61 mm from the beam core, whereas TPS does not predict any dose at this distance.

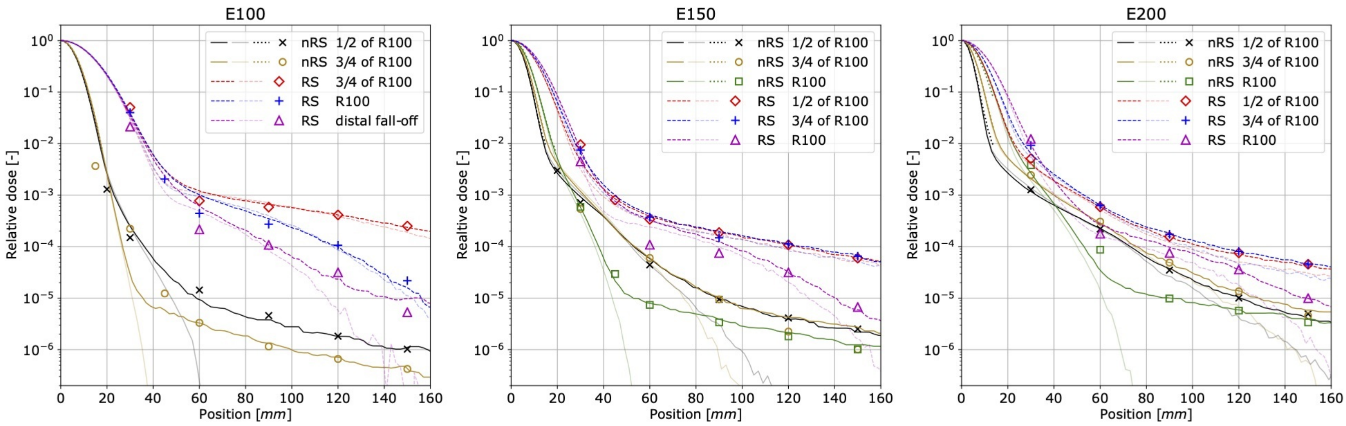

Figure 6. Lateral beam dose profiles measured in water at different depths for three beam nominal energies. Points correspond to MINIPIX TIMEPIX measurement results, dotted lines are results of measured with LYNX detector, whereas solid and dashed lines are the GATE/Geant4 data without (nRS) and with RS, respectively. Corresponding transparent lines presents FRED simulations result.

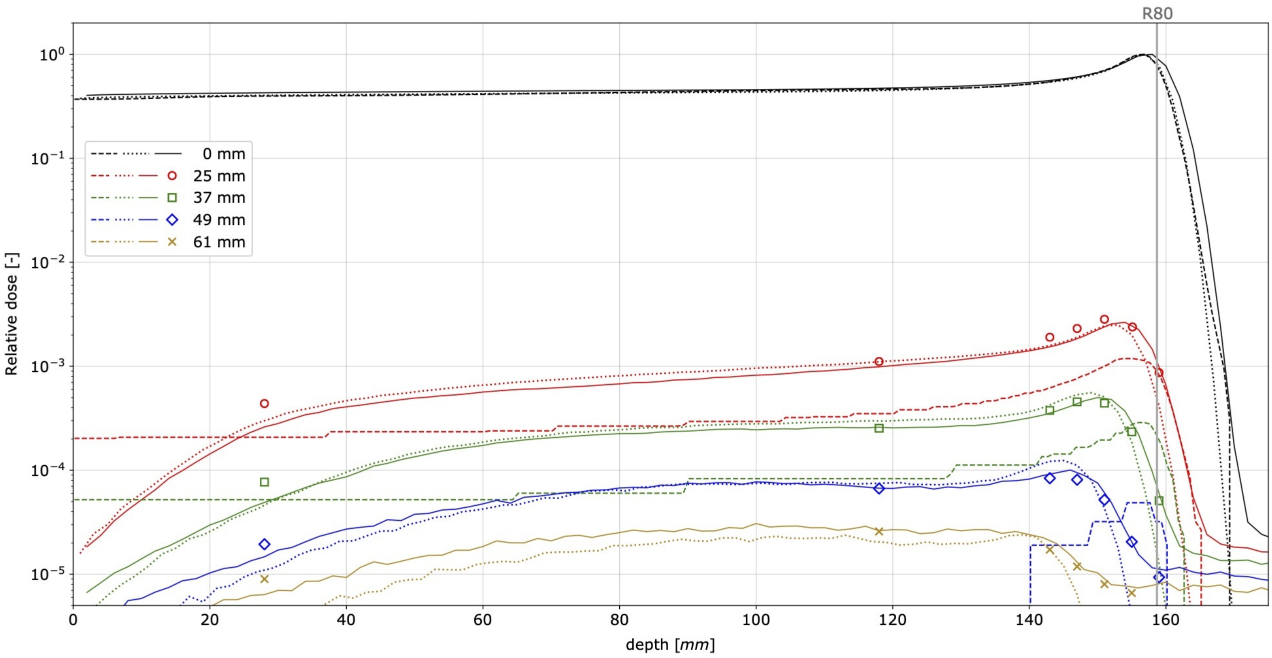

Figure 7. Longitudinal pencil beam dose profiles measured in water for proton beam nominal energy E150. Points correspond to MINIPIX TIMEPIX measurement results, whereas solid, dotted, and dashed lines to GATE/Geant4, FRED, and TPS simulations, respectively. The mean proton range of 158.7 mm is marked by a vertical line (R80).

4 DISCUSSION

In the frame of this work we performed a validation of the detector calibration for protons, and the measurements of the beam dose profiles in air and in water. The comparison of the calibration measurements and MC simulations demonstrate that the MINIPIX TIMEPIX accurately measures energy deposited by proton beams. The comparison of the mean energy deposition in the detector to MC simulation results and PSTAR data indicates that positioning of the detector at 45° with respect to the beam axis is the most optimal for the measurements. Here we performed only the validation of the calibration for protons in energy range from 70 to 200 MeV, whereas in the mixed radiation field in water, a wider energy spectrum of particles can be registered by the detector. The response of the MiniPix Timepix detector to other radiation types was studied elsewhere [27].

The measurements of the lateral and longitudinal pencil beam dose profiles performed with the MiniPix Timepix detector show its capability to measure the dose with the dynamic range of up to 4 orders of magnitude. The measurements of the beam lateral profiles in air correspond well to the TPS beam model data obtained during the facility commissioning. The beam lateral and longitudinal profiles measured in water are in an excellent agreement with Gate/Geant4 simulations. Because of the limited time resolution of the MiniPix Timepix detector, it was not possible to perform measurements in the beam core, where the fluence of particles was high, causing detector saturation. A new generation of the Timepix detectors, the MiniPix Timepix 3 (ADVACAM), offers time resolution better than the MiniPix Timepix used in this work. MiniPix Timepix 3 will allow for measurements in the beam core and in therapeutic fields, where the particle fluence is high. In order to minimize the fraction of particles scattered on the aluminum detector case, an alternative, e.g., PMMA case, should be considered.

Since MiniPix Timepix provides information about a single particle energy deposition and its track length, it is possible to calculate the linear energy transfer (LET) value of each particle penetrating the detector sensor. Future work will focus on an experimental characterization of the energy deposition and the LET spectra in mixed radiation fields produced by therapeutic proton beams in water. The results will be used for validation of MC codes and TPS, aiming at improved physical and biological modeling in proton radiotherapy.

CONFLICT OF INTEREST STATEMENT

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

AUTHOR CONTRIBUTIONS

PS, AR, JG, CG, GK, CO, MPN, SN, MR performed the experiments. PS and JG made the experiment data analysis and prepared figures. CG and CO provided expertise in MiniPix Timepix data analysis. JG performed the MC simulations, analyzed the data and prepared figures. MPN and JB provided expertise in Gate/Geant4 MC simulations and data analysis. AS developed and made substantial improvements in Fred source code required to enable presented studies. PS, AR, and JG drafted the manuscript. NK extensively reviewed the manuscript. AR and JG designed the project and AR acquired funding.

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