TIME-RESOLVED PROTON BEAM DOSIMETRY FOR ULTRA-HIGH DOSE-RATE CANCER THERAPY (FLASH)

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Abstract

A new radiotherapy modality, known as FLASH, is a potential breakthrough in cancer care as it features a reduced damage to healthy tissues, resulting in the enhancement of the clinical benefit. FLASH irradiations are characterized by ultra-high dose-rates (>40 Gy/s) delivered in fractions of a second. This represents a challenge in terms of beam diagnostics and dosimetry, as detectors used in conventional radiotherapy saturate or they are too slow for the FLASH regime. In view of the FLASH clinical translation, the development of new dosimeters is fundamental. Along this line, a research project is ongoing at the University of Bern aiming at setting-up new beam monitors and dosimeters for FLASH. The proposed detection system features millimeter scintillators coupled to optical fibers, transporting light pulses to a fast photodetector, readout by high bandwidth digitizers. First prototypes were exposed to the 18 MeV proton beam at the Bern medical cyclotron. The new detectors have been found to be linear in the range up to 780 Gy/s, with a maximum time resolution of 100 ns. These characteristics are promising for the development of a new class of detectors for FLASH radiotherapy.

INTRODUCTION

FLASH radiotherapy is a novel radiation delivery modality characterized by very fast irradiations (< 300 ms) and ultra-high dose rates (> 40 Gy/s). By comparison, conventional radiotherapy treatments are performed in a few minutes at dose rates of the order of 0.1 Gy/s. Since the first pioneering work by Favaudon et al. [1], many experiments have shown that FLASH irradiations drastically reduce normal tissue toxicity, while keeping the same effectiveness on the cancer cells as of the conventional radiotherapy [2]. This striking sparing effect on healthy tissue, also termed as FLASH effect, has been observed with more than one radiation type, including electrons, protons, photons, and carbon ions [3]. The dosimetry and beam monitoring of FLASH irradiations are challenging owing to the peculiar characteristics of FLASH beams. Ionization chambers are the gold standard for the dosimetry in conventional radiotherapy; however, these detectors feature relatively slow response and saturation at high dose rates [4]. Consequently they cannot be used for FLASH beams, without corrections. Along this line, a research project is ongoing at the University of Bern aiming at the proof-of-principle of a new detection system for dosimetry and beam monitoring in FLASH radiotherapy. The first dosimeter prototypes, based on plastic scintillators coupled to optical fibers, have been tested at the Bern cyclotron laboratory located at the Bern University Hospital (Inselspital).

MATERIALS AND METHODS

This work reports on two measurements aimed at evaluating the feasibility of the proposed innovative system for ultra-high dose rate beams, namely: 1) the study of the detector response as a function of the average dose rate and 2) the time trend of the proton beam at high time resolution. This section describes the proposed innovative detection system and the specific dosimetry method tested at the Bern medical cyclotron.

The Innovative Detection System

The new detection system for ultra-high dose rate measurements is depicted in the schematic of Fig. 1.

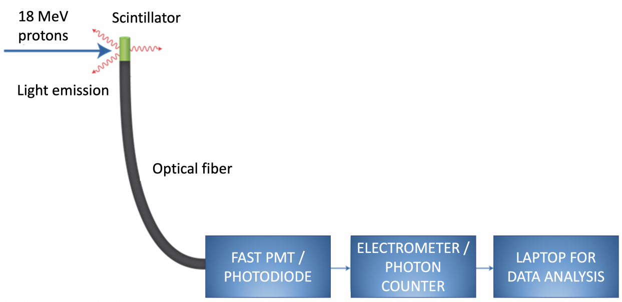

Figure 1: Schematic of the FLASH detection system.

Its main element is a scintillator of millimeter or submillimeter size coupled to an optical fiber. The light pulses are delivered to the data acquisition (DAQ) through the optical fiber. In this work, we used a $(0.5\times0.5\times2)$ mm^3 polystyrene scintillator, and two different DAQs, one for the study of the linearity of the dose rate response and another for the beam monitoring at high time resolution. The former comprises a high speed response PhotoMultiplier Tube (PMT) and a Keysight B2985A electrometer; the latter comprises a single-photon detector module based on a silicon avalanche photodiode and a Ortec Multi-Channel Scaler (MCS). The MCS allows for measurements with 65536 chan-

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nels and a variable dwell time down to 100 ns. In this measurement, the dwell time was set to 50 µs.

The Bern Cyclotron Laboratory

The characterization of the detection system for ultra-high dose rates was performed with the IBA 18 MeV medical cyclotron located at the Bern University Hospital (Inselspital). The cyclotron is used overnight for the production of radioisotopes for nuclear medicine, in particular for the ^{18}F production for Positron Emission Tomography (PET) imaging. During the day, the cyclotron is used by the group of medical application of particle physics of the University of Bern for multidisciplinary research activities [5, 6]. Part of these activities are possible thanks to a 6 meter long Beam Line Transfer (BTL), equipped with beam focusing, steering and diagnostic systems, which connect the cyclotron to a second bunker with independent access to the experimental area. The cyclotron allows for irradiations in a wide beam current range from a few pA to 10^2 µA. For the measurements reported in this work, we used an independent dosimetry system based on Faraday cup and collimators, which was recently validated for radiation damage studies [7]. The dosimetry on the scintillator position has been verified with radiochromic films [8, 9]. A picture of the experimental setup is shown in Fig. 2.

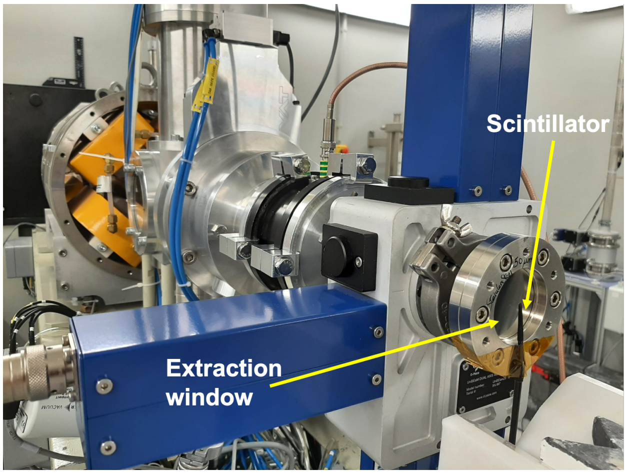

Figure 2: Beam Transfer Line of the Bern medical cyclotron. The optical fiber, with the scinitillator, is directly exposed to the proton beam, which is extracted in air.

The beam is extracted in air through a 50 µm stainless steel window. A 2-D beam monitor based on Ce-doped scintillation optical fibers [10] provides accurate measurements of the beam profile downstream the extraction window. The beam energy in the BTL, (18.3±0.3) MeV, was accurately measured in previous works [11–13]. The beam energy in the scintillator position was evaluated with energy loss calculations based on the SRIM/TRIM package [14]. It was found to be (17.5±0.3) MeV and the corresponding water stopping power $S_W=2.9\,\frac{\text{keV}}{\mu\text{m}}$. A fast beam stopper positioned at the center of the cyclotrons, can provide proton beams of a few seconds.

RESULTS

The study of the response of the detection system as a function of the average dose rate has been performed with the high speed PMT and the electrometer, as discussed in the Methods section. Figure 3 shows the electrometer current I_{PMT} as a function of the proton beam average dose rate $\dot{D}$ in the range (30-780) Gy/s. The data are well fitted a straight line, with a coefficient of determination R^2=0.996. The values of the fitting parameter, namely the slope m and the intercept I_0, are reported in the inset of Fig. 3.

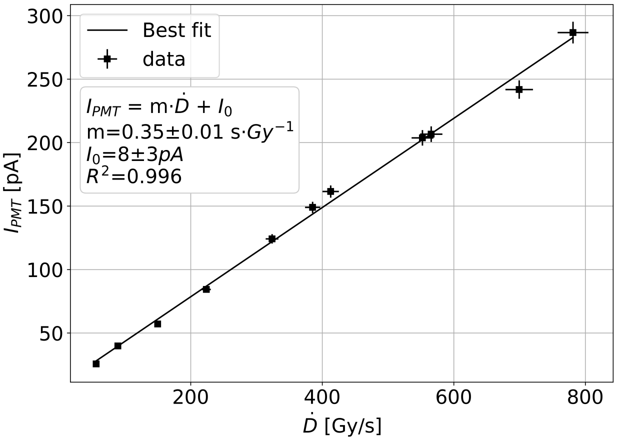

Figure 3: Photomultiplier current I_{PMT} as a function of the proton beam average dose rate $\dot{D}$. The inset reports the values of the fitting parameters and of the coefficient of determination R^2.

The time trend of the proton beam at high time resolution has been performed with a DAQ system comprising of the single-photon detector module and the MCS, as discussed in the Methods section. Figure 4 shows the photon counts with 50 µs dwell time as a function of the time for 1.5 seconds.

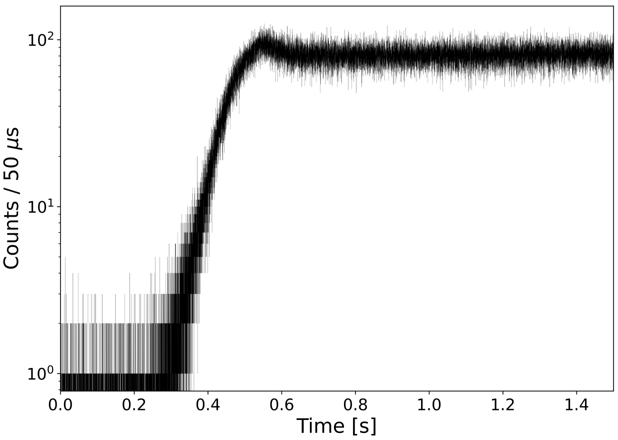

Figure 4: Time trend of the proton beam with 50 µs dwell time.

The plot of Fig. 4 can be divided in three parts corresponding to the beam stopper position: 1) the beam is stopped during the first 200 ms, 2) the beam stopper is released and the counts detected by the single-photon detector module rapidly increase, 3) the beam is delivered to the scintillator and the counts reach a fixed average value. In order to evaluate the dark counts contribution, we measured the dark count rate in absence of beam. The dark count rate was found to be (5730±90) Hz.

CONCLUSION AND OUTLOOK

This work demonstrates the feasibility of a detection system based on fast scintillators and optical fibers for the ultra-high dose rate dosimetry for FLASH radiotherapy. In particular, we found that the response of a polystyrene scintillator is linear in the dose rate range (30-780) Gy/s. Furthermore, we successfully measured the proton beam for 1.5 seconds with a 50 µs dwell time. Even if such time resolution is enough for many clinical applications, higher time resolutions can be achieved by changing the dwell time. The Multi-Channel Scaler used in this work allows measurements down to 100 ns for a maximum of 655 ms. The spatial resolution is given by the scintillator size. In this first tests, we used a (0.5×0.5×2) mm^3 polystyrene scintillator. The findings reported in these work are very promising for the definition of a new class of detectors to be used in several applications for FLASH radiotherapy, including beam monitoring, quality control, and in-vivo dosimetry. Further steps of this project will be devoted to the test of scintillators featuring higher radiation resistance than polystyrene, and to study of the response of the system to pulsed electron beams.

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