SpotOn+

Center for Proton Therapy :: Paul Scherrer Institut :: #23_08/2021

Dear Reader,

It is my pleasure to introduce you this month's Newsletter dedicated to ultra-high dose rate or FLASH irradiation, as it is commonly known. I have the honor to do so on behalf of my Team, including but not limited to Serena Psoroulas and David Meer, and the one of CHUV lead by Marie-Catherine Vozenin, who has co-signed this editorial. This has been a productive collaboration, partly sponsored by Proton Solutions/Varian Medical Systems (VMS). Initial pre-clinical studies by Vozenin et al. and others have shown that irradiation at dose rates far exceeding (i.e. › 40 Gy/sec) those currently used in clinical contexts reduce radiation-induced toxicities whilst maintaining an equivalent tumor response. While MC Vozenin team at CHUV has initially developed the FLASH effect concept using an experimental electron beam of 6MeV (eRT6, Oriatron), she is now working in collaboration with PSI to foster applicability of FLASH-RT to deep-sited tumors using proton beam at ultra-high dose rate. The use of protons might also give the opportunity to enhance further the benefits of the FLASH-RT given the ability to more accurately control dose deposition profiles coupled with dose-conformality that can be achieved by superimposing the Bragg peak over the tumor volume. Combining the well-known advantages of proton beams to enhance the therapeutic ratio with their capability to deliver ultra-high dose rates may hasten the clinical translation of these innovative technologies in the near future. The mechanism responsible for reduced tissue toxicity following FLASH radiotherapy is yet to be elucidated, and may not be the prominent hypothesis of acute oxygen depletion occurring within the irradiated tissue. Vozenin's team is working hard on that. In this edition we present the quality assurance of FLASH delivery using a Faraday cup performed in our experimental Gantry 1. Another article on the dose assessment of biological samples (Zebra Fish) using optically stimulated luminescence detectors has been written by Christensen et al. Finally, Dr Togno reports the combination of the FC measurements with measurements of integral depth-dose curves and beam phase space using the 250 MeV beam delivered with a transmission paradigm. With the proposed experimental setup, PSI was able to reach a reproducibility of the delivered dose better than 1% for all the investigated dose rates (up to 9'000 Gy/sec!). These dosimetry-driven measurements are of paradigm importance as one has to assure that the challenging ultra-dose rate are indeed delivered correctly. Only time (and many other experiments) will tell if the FLASH effect will revolutionized radiation therapy and will berry for the last time › 100 years of conventional fractionation and dose rate. These are definitively exciting times for the radiotherapy community. That being said, I hope that this newsletter was of interest to you and I wish all of you all the best for the rest of this wet & cold summer.

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Physics News

Faraday cup for commissioning and quality assurance for proton pencil beam scanning beams at conventional and ultra-high dose rates

Introduction

The Faraday Cup is a dosimetry device which measures the deposited charge of the proton beam, and as such directly “counts” the number of delivered protons. It has been used for over 40 years for monitor commissioning and quality assurance in proton therapy. Recently, there has been a renewed interest in dosimetry with the Faraday cup for ultra-high dose rate (FLASH) experiments. In this experimental study, we therefore investigate the dose rate dependency of the Faraday cup. Additionally, the influence of different Faraday cup settings on the measured signal has been quantified for the clinical range of initial proton energies.

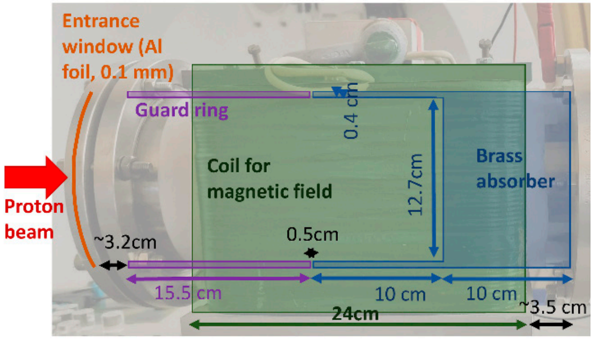

Figure 1: Schematic drawing of the PSI Faraday cup

Materials & Methods

Figure 1 shows a schematic drawing of the PSI Faraday cup. It consists of a brass absorber (marked in blue in the schematic drawing), which stops the proton beam. Subsequently, the charge collected in the absorber is measured to determine the number of delivered protons. The device is set under vacuum (closed off by an aluminium vacuum window, marked in orange). Additionally, magnetic field coils (green) and an electric field (guard ring marked in violet) are applied to divert secondary electrons, which might escape the brass absorber or originate in the vacuum window, aiming to minimize their influence on the Faraday cup signal.

The Faraday cup signal has been measured for 3 clinical proton energies (70 MeV, 150 MeV, 230 MeV) and a range of combinations of electric and magnetic fields. Additionally, the Faraday cup current has been measured as a function of the cyclotron current (cyclotron currents up to 800nA, corresponding to dose rates along the central axis of up to 1000 Gy/s).

Results & Discussion

When applying the maximum magnetic field (24mT) to the Faraday cup, the measured signal is independent of the applied voltage (voltages between -1000V and +1000V, figure 2), indicating that all secondary electrons are stopped by the magnetic field. When applying a voltage (-1000V) only, the signal is however lower compared to the signal with maximum magnetic field, with an energy dependent offset of up to 1.3%. Without magnetic or electric field, the signal is up to 1.3% higher compared to the signal with maximum magnetic field, with this offset again depending on the initial proton energy. This might indicate that a magnetic field is necessary to reach a Faraday cup accuracy below 1-2%. The observed effects and the magnitude of the effects might depend on the exact geometry of the Faraday cup, and detailed Monte Carlo simulations of the whole setup are necessary to determine the exact contributions of all secondaries to the Faraday cup signal.

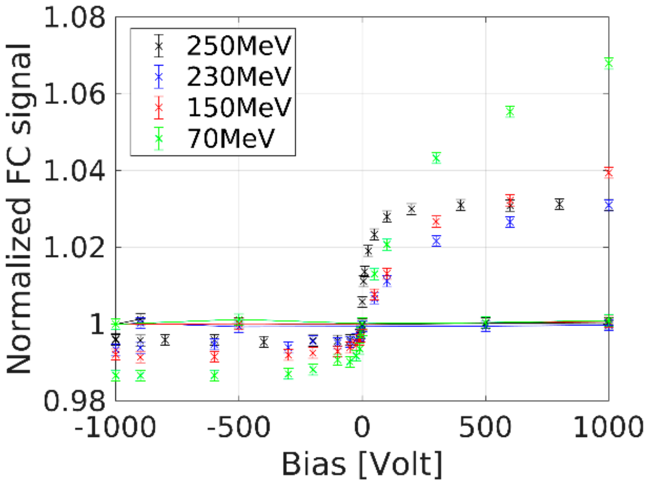

Figure 2: Normalized Faraday cup signal as a function of applied voltage (with magnetic field, lines, and without magnetic field, crosses)

The Faraday cup measured signal rises linearly with cyclotron currents up to 800nA (residuals within 5%). This shows that the Faraday cup measurements do not substantially depend on the dose rate of the initial proton beam. As such, the Faraday cup can be used for the commissioning and quality assurance of proton beam monitors up to ultra-high dose rates, and for dosimetry during FLASH experiments.

Conclusion

This experimental study shows that thorough commissioning of the Faraday cup is crucial for accurate dosimetric results, and it indicates that caution might be necessary when using a Faraday cup without a magnetic field. In summary, the Faraday cup is a promising dosimetry tool up to ultra-high dose rates, and as such a valuable device for FLASH experiments.

The results of this work have been recently published (Winterhalter et al. 2021)

Physics News

Al_2O_3:C optically stimulated luminescence dosimeters (OSLDs) for ultra-high dose rate proton dosimetry

Optically stimulated luminescence detectors (OSLDs) have been used for decades to measure ionizing radiation. OSL is widely applied in fields as luminescence dating (e.g. to date natural sediments or archaeological artifacts), personal dosimetry, temperature sensing, and increasingly, also for medical dosimetry. Particularly, aluminum oxide detectors doped with carbon (Al_2O_3:C OSLDs) are of particular interest for dosimetry given their ability to measure doses ranging from tens of μGy to kGy, versatility of form (chips, films, powder) and use.

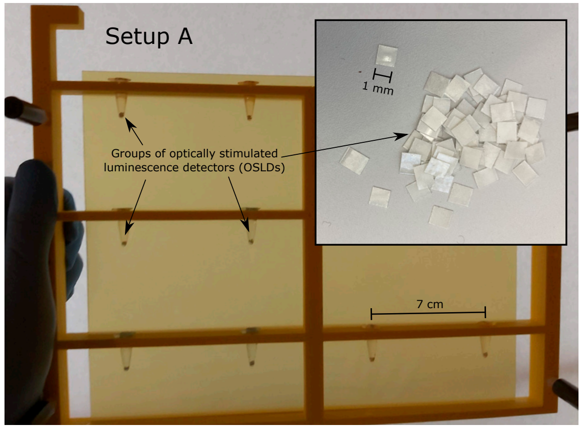

Figure 1: Groups of OSLDs (also shown in the insert) placed in 12 water-filled tubes. The tubes accommodate either biological samples or OSLDs and are irradiated one-by-one.

The working principle of OSL is based on the trapping of charges in the lattice's defects upon exposure to ionizing radiation. The trapped electron and hole pairs can recombine upon stimulation by light (OSL) in each case emitting a detectable photon. The amount of emitted light is therefore related to the absorbed dose. Another attractive property of Al_2O_3:C OSLDs is that the crystal powder can be mixed with a binder to form a sheet of ~50 um thickness. If the OSL sheet is cut to sub-mm sized pieces, the OSLDs may almost serve as waterproof point-like detectors with a dose sensitivity spanning many orders of magnitude. Although only few studies have investigated the use of OSLDs in dose rates above 40 Gy/s in photon and electron beams, none of them have shown indications of a dose-rate dependency in doses assessed using Al_2O_3:C. Hence, the Al_2O_3:C OSLDs were chosen as monitors for the proton FLASH experiments at PSI as the OSLDs can be irradiated under the nominally same radiation conditions as the biological samples. Ultimately, the experiments can further the understanding how treatments with high dose rates affect the biological response.

An example of a frame containing 12 water-filled vials is shown in figure 1, referred to as setup A, where each vial contains either 5 OSLDs or biological samples.

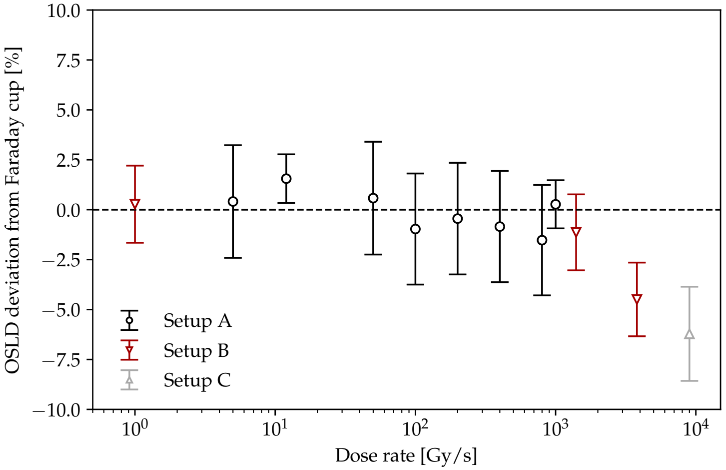

Figure 2: The response of the OSLDs relative to the Faraday cup derived doses as a function of dose rate.

Other irradiation setups B and C relied on OSLDs or samples in water-filled plexiglass (PMMA) cylinders or aligned in a grid, respectively. The doses measured by the OSLDs floating in the vials or cylinders hence reflect the variation of doses to the biological samples in the vials with all sessions monitored by a Faraday cup.

Around 400 OSLDs were irradiated at Gantry 1 at PSI during the FLASH experiments for doses between (2 - 33) Gy and dose rates (1 - 9000) Gy/s with the aim of investigating the accuracy of the dose delivery to the samples. The deviation between the OSLD measured doses and the dose derived from the Faraday cup measurement is shown in figure 2 as a function of dose rate. The agreement is within 2% for dose rates below 1000 Gy/s, where the single pencil beam is somewhat wide. A discrepancy is observed for higher dose rates as the pencil beam is smaller and a signal averaging effect over the OSLD surface causes an underestimation of the dose. The signal averaging at ultra-high dose rates, however, is different from a dose rate effect of the OSL material.

It is thus concluded that Al_2O_3:C OSLDs are suitable to support the accurate dose assessment of biological samples irradiated within the framework of FLASH experiments in both water and air.

This work has been recently published (Christensen et al. 2021)

Physics News

Ultra-high dose rate dosimetry for pre-clinical experiments with mm-small proton fields

Introduction

Recently, a number of studies reported on the feasibility of radiotherapy (RT) with ultra-high dose rates, also known as FLASH-RT, using electron, photon and proton beams. While the potiential of FLASH-RT and its fundamental mechanisms are still under research, several technical challenges need to be tackled in order to safely implement this technique into clinical scenarios. A major challenge concerns the possibility to perform accurate and reliable dosimetry in non-conventional, ultra-high dose rate radiation beams. Indeed, traditional active dosimeters such as ion-chambers, diodes and diamond detectors, may exhibit severe saturation problems when the dose rate is increased beyond the typical values of standard RT. Moreover, no specific dosimetry protocols have been designed yet for FLASH-RT conditions. We have investigated the response of different dosimeters in mm-small, ultra-high dose rate proton beams. The characterization of field detectors relies on the use of a Faraday cup (FC), a dose rate independent device, as reference. All the tests have been performed at the CPT Gantry 1, which was commissioned for radiobiological FLASH research in 2020. For such experimental campaign, the FC has been used as on-line verification monitor of the dose delivered to biological samples.

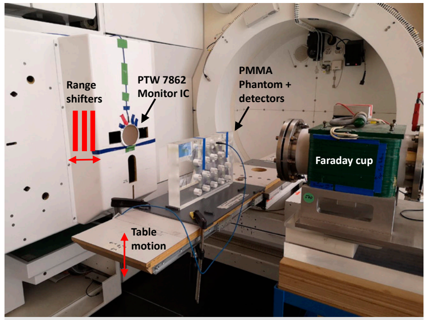

Figure 1. Gantry 1 setup for FLASH experiments. Biological samples and detectors are positioned in phantoms onto a robotic table. The FC downstream the detectors acts as on/line monitor system as well as beam stopper.

Material & Methods

The dedicated research setup of Gantry 1 (Fig. 1) allows to irradiate small biological samples and detectors with a 250 MeV transmission proton pencil beam at currents up to ~700 nA (~9000 Gy/s). In our experiments, the size of biological samples is typically ‹ 3 mm (volume ‹ 0.1 cm^3). The samples and the detectors can be accommodated in either a tank filled with water or in dedicated PMMA holders which are then insterted into a PMMA phantom.
To model the delivered dose, FC measurements have been combined with measurements of integral depth-dose curves and beam phase space. During the experiments, the FC was positioned downstream the detectors or samples to be examined, which were then exposed to a wide range of dose rates. Several detectors have been investigated: a Monitor ion-Chamber 7862 (PTW, Freiburg, DE), a microDiamond 60019 (PTW, Freiburg, DE), EBT3 Gafchromic™ films (Ashland Speciality Ingredients, Bridgewater, US) and Gd_2O_2S scintillating screens.

Results

With the proposed setup, we were able to reach a reproducibility of the delivered dose better than 1% for all the investigated dose rates. As expected, the Monitor ion-Chamber 7862 exhibits strong ion-recombination, with a consequent drop in response larger than 30% at ~9000 Gy/s. Similar results have been reported in literature for small-volume ionization chambers used as field detectors. Notwithstanding the large efficiency drop, the chamber 7862 demonstrated to be highly reproducible, which allow for the possibility to introduce empirical correction factors based on FC measurements.
EBT3 Gafchromic™ films and scintillating screens were found to be independent on the dose rate within the measurement uncertainty, in the range 1-9000 Gy/s.
The microDiamond detector was also found to be dose rate independent (response within ± 0.7%), althought tested up to only 1800 Gy/s. Additional experiments are planned to further extend the investigated range of dose rates with this type of detector.

Conclusions

FLASH RT poses challenges to the performance of conventional detectors, as it was shown for ionization chambers, and the characterization of detectors' response up to FLASH dose rates is of paramount importance for an accurate dosimetry. This characterization shall be performed by means of dose rate independent instruments, such as Fraday cups. Alongside with the confirmation of dose rate independence of EBT3 films and plastic scintillators, we found the microDiamond to be a promising detector for relative and absolute dosimetry of small, ultra-high dose rate proton beams.

This work will be presented at the 1st FLASH Radiotherapy and Particle Therapy (FRPT) conference in December 2021.

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Imprint

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Villigen PSI, August 2021