ISBN: 978-3-95450-227-1 ISSN: 2673-5490 doi:10.18429/JACoW-IPAC2022-THPOMS007

BEAM DIAGNOSTICS FOR FLASH RT IN THE VARIAN PROBEAM SYSTEM

M. Schedler, S. Busold
Varian Medical Systems Particle Therapy GmbH & Co. KG, Troisdorf, Germany
M. Bräuer, Siemens Healthcare GmbH, Erlangen, Germany

Abstract

FLASH RT is a novel ultra-high dose rate radiation therapy technique with the potential of sparing radiation induced damages to healthy tissue while keeping tumor control unchanged. Recent studies indicate that this so-called FLASH effect occurs when applying high doses of several Grays in a fraction of a second only, and thus significantly faster than with conventionally available radiation therapy systems today.

Varian's ProBeam system has been enabled to deliver ultra-high beam currents for FLASH treatments at 250 MeV beam energy. The first clinical trial is currently conducted at Cincinnati Children's Hospital Medical Center and all involved human patients have been successfully irradiated at FLASH dose rates, operating the system at cw cyclotron beam currents of up to 400 nA. With these modifications, treatment times could be reduced down to less than a second.

First automated switching between conventional and FLASH operation modes has been demonstrated in non-clinical environment, including switching of the dose monitor system characteristics and all involved beam diagnostics. Furthermore, for an improved online beam current control system with full control over dose rate in addition to dose Varian has demonstrated first promising results that may improve future applications.

FLASH RT

In conventional IMPT[1], three-dimensional dose distribution in the patient target volume is applied and controlled by the radiotherapy system. With pencil-beam scanning technique, a treatment plan is a set of energy layers, each containing a set of individual spots, defined by 2D beam position at isocenter plane and accumulated proton beam charge. Typical treatment times for a single treatment fraction vary in the range of 30 s up to several minutes.

Recent studies discovered a sparing effect of radiation induced damage to healthy tissue under influence of ionizing radiation at ultra-high dose rates of $> 40\,\mathrm{Gy\,s^{-1}}$ [1], approximately two orders of magnitude above conventional dose rates. This effect is refered to as FLASH effect. The resulting treatment time of a single treatment field is reduced to < 1 s.

The pencil-beam dose rate $\dot{D}_{\mathrm{PB}}$ can be defined based on the stopping power $-\frac{\mathrm{d}E}{\mathrm{d}x}\big|_{\mathrm{water}}$ of the pencil beam on a circular detector of radius r for a given particle flux $\dot{n}$ as

$$\dot{D}_{\mathrm{PB}} = -\frac{\mathrm{d}E}{\mathrm{d}x}\bigg|_{\mathrm{water}} \frac{\dot{n}\left(1 - \mathrm{e}^{-\frac{r^2}{2\sigma^2}}\right)}{\pi r^2} \tag{1}$$

assuming a gaussing beam shape with a standard deviation of σ. For the Varian ProBeam system, this yields to nozzle dose rates of up to $2400\,\mathrm{Gy\,s^{-1}}$ at maximum beam energy and current.

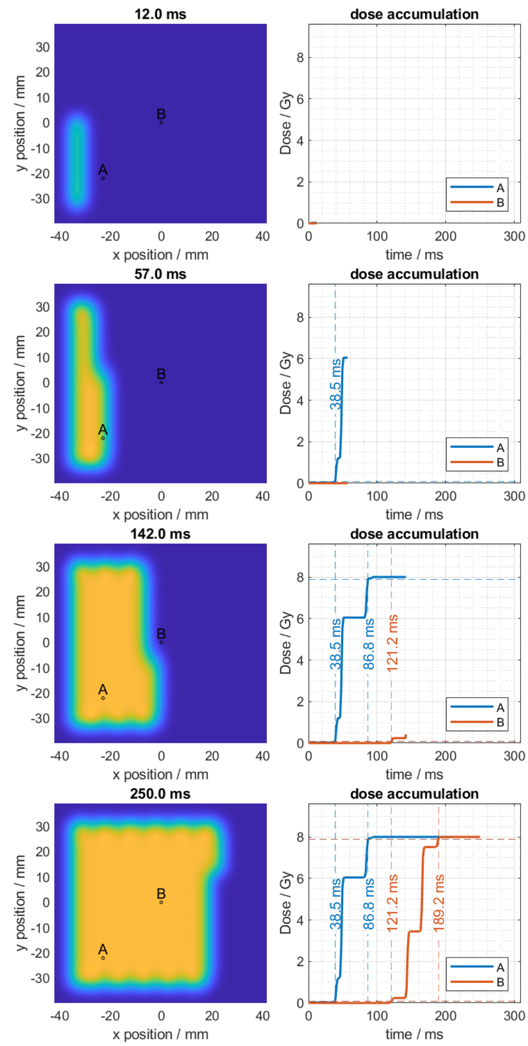

Figure 1: Dose accumulation in a clinical 2D FLASH treatment field calculated for four different time slices. Detailed dose accumulation dynamics is shown for two voxels *A* and *B*.

[1] IMPT: **I**ntensity **M**odulated **P**roton **T**herapy

ISBN: 978-3-95450-227-1 ISSN: 2673-5490 doi:10.18429/JACoW-IPAC2022-THPOMS007

In a scanned field however, several treatment spots contribute to the dose of a single voxel in the field, thus the dose rate per voxel depends on the dynamics of the moving pencil-beam [2]. For a given threshold dose D_{thr}, the voxel dose rate can be expressed as

$$\dot{D}_{\text{voxel}} = \frac{\bar{D} - 2\,D_{\text{thr}}}{t_1 - t_0} \tag{2}$$

where t_0 is the time when the voxel dose reached D_{thr} and t_1 describes the time where the voxel dose exceeded $\bar{D} - D_{\text{thr}}$, based on an integrated voxel dose $\bar{D}$.

Figure 1 shows the dose accumulation curves for two voxels A and B in the 2D dose distribution for a clinical FLASH treatment plan. As several scan lines contribute to the dose accumulation per voxel, also the dose rate strongly depends on the voxel location and the spot order.

A Varian ProBeam system has been successfully modified for a clinical study as part of an investigational device exemption at CCHMC[2], treating human patients with FLASH dose rates [3]. In the future, clinical studies will typically have to take place in parallel to conventional patient treatment, thus a FLASH enabled treatment room has to be capable of both FLASH and conventional treatments without the need for hardware changes or recommissioning and recalibration inbetween treatments.

VARIAN PROBEAM SYSTEM

The Varian ProBeam systems features a proton beam of variable beam energy in the range of 70 MeV to 250 MeV at the patient's site in the individual treatment room. The superconducting cyclotron is set up to deliver a fixed-energy proton beam of 250 MeV with intensities of up to 800 nA. In order to provide range modulation, the proton beam energy is reduced to its target value in an adjacent graphite degrader in the beamline. After energy degradation and the corresponding degradation of beam emmittance, a double-bend achromat filters the selected beam energy to a configurable energy spread and provides a well-focussed beam to the treatment area. As a result of energy selection, the beam intensity is also reduced as a function of selected beam energy. The ratio between beam intensity available at the patient site and the cyclotron output intensity is refered to as beamline transmission.

Typical beamline transmission of a ProBeam system reach from > 0.5 at cyclotron output energy, down to $< 3 \times 10^{-4}$ at lowest clinically available beam energy. Thus, only at highest beam energies of 250 MeV ultra-high dose rates can be achieved in the patient target volume.

While restricting the beam delivery to 250 MeV beam energy, the three-dimensional dose modulation is reduced to a two-dimensional dose control, where the water-equivalent range of the proton beam is fixed to 37.9 cm. As a result, the maximum stopping power and thus the Bragg peak will not be achieved in the patient target volume but the beam is fully transmitted through the patient and dumped in an external beam stop.

Compared to conventional irradiations, the intended nozzle proton current will be increased by two orders of magnitude, up to 215 nA at the patient site. The present ProBeam dose and beam diagnostics system in the scanning nozzle can only handle currents up to 4 nA, thus a redesign of the beam flux and fluence monitor system will be discussed below.

DUAL-MODE IONIZATION CHAMBER SYSTEM

In the present ProBeam system, the redundant beam flux and fluence monitor system is located in the scanning nozzle, providing signals to control and monitor the beam delivery to the patient target. The present ionization chamber system inclduding readout path is optimized for a maximum nozzle proton current of 4.5 nA at a beam energy of 244 MeV. As the ion collection efficiency f of the ionization chamber at ionized charge density S depends on the high voltage U applied to the IC[3] electrodes and the gap size d between the active elctrodes as per [4] to

$$f = \frac{1}{1 + \frac{\xi^2}{6}}, \tag{3}$$

where

$$\xi = 2.1 \times 10^7\,\sqrt{\text{Cm/s}}/\text{V} \cdot \frac{d^2\sqrt{S}}{U}, \tag{4}$$

the conventional ProBeam IC will introduce a $< 1\,\%$ electrical signal loss. In order to decrease recombination losses and thus to maintain linear responses over the entire dynamic range, the FLASH IC is operated at smaller gap sizes and adjusted operation voltages.

In order to avoid the need for recommissioning and recalibration of the dose monitor system for FLASH treatments, a dual-mode flux and fluence monitor system is introduced to cover both conventional and FLASH operation ranges in one set of hardware. Figure 2 shows an image of the ProBeam IC system, consisting of two transmission ionization chambers for beam flux detection, as well of a set of MSICs[4] for beam position and shape reconstruction in both transverse planes. The IC is designed to cover a scanned beam field of a transverse size of 30 cm × 40 cm at isocenter plane.

The internal schematic of the dual-mode IC, has been modified with respect to the conventional ProBeam chamber in order to allow switching between conventional and FLASH mode by powering or grounding individual high voltage electrodes, depending on their gap sizes and operation voltages. In conventional mode, the invidivual ionization chamber sections with larger active volume are powered, whereas in FLASH mode only the low-gap sections are acting as ionization chambers.

Together with dynamically switching the gain of the preamplifier stage of the IC readout electronics based on operation mode, the current mapping and thus the control system

[2] CCHMC: **C**incinnati **C**hildren's **H**ospital **M**edical **C**enter

[3] IC: **I**onization **C**hamber

[4] MSIC: **M**ulti-**S**strip **I**onization **C**hamber

13th Int. Particle Acc. Conf. IPAC2022, Bangkok, Thailand JACoW Publishing
ISBN: 978-3-95450-227-1 ISSN: 2673-5490 doi:10.18429/JACoW-IPAC2022-THPOMS007

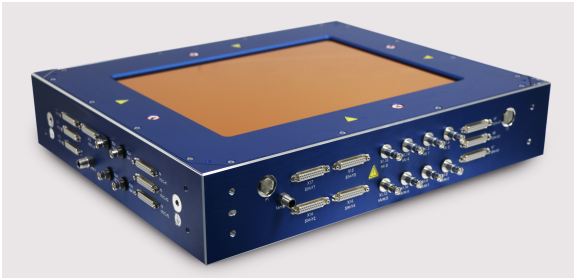

Figure 2: Varian ProBeam IC.

input signals stay unchanged while the dynamic range of nozzle beam currents change by two orders of magnitude. With this setup, a software controlled switching between conventional and FLASH mode can be achieved within several minutes.

SPOT-WISE BEAM CURRENT VARIATION

In the current ProBeam system, each energy layer is irradiated with a fixed nozzle beam current. As beam diagnostics and control system processing are subject to latency and processing time, the irradiation time per spot shall not fall below a pre-configured minimum value of 3 ms. Thus, the spot with the lowest equivalent charge defines the maximum beam intensity per layer. In order to optimize dose rate and delivery time, a spot-wise current modulation is under consideration for FLASH operation mode. In this mode, a closed-loop control is active, providing stable and highly dynamical beam intensity modulation between the spots in a layer. First measurements were executed at the Holland Proton Therapy Center with a conventional ProBeam system.

Figure 3 shows the measured transfer function of the ProBeam system with all components included involved in spot-wise current modulation. The linear phase advance in the measured transfer function points to a significant latency in the system. The measurements setup, especially the Beckhoff DAC module the actuator was found to mostly contribute to the overall latency, thus it can be removed from the calculations. The remaining amplitude and phase response can be expressed as a PT1 model and fits to the expected bandwidth limitations of the IC readout electronics. An updated readout electronics with optimized bandwidth is currently under testing.

Even though, the treatment time of an example treatment plan could be reduced from 276.3 s in conventional mode down to 40.7 s with close-loop modulated beam current. The irradiation time per spot for the example treatment is shown in Fig. 4.

CONCLUSION

Introducing a dual-mode ionization chamber system opens the possibility for clinical studies under FLASH dose rates in parallel to clinical operation in the same treatment room, without the need for hardware changes or recalibration. High-

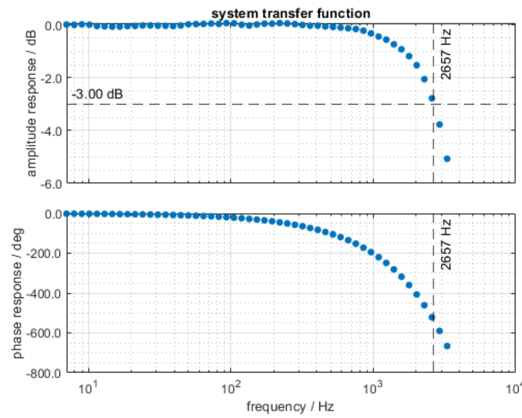

Figure 3: System transfer function measured in open-loop control between VDPS input voltage and nozzle rate output.

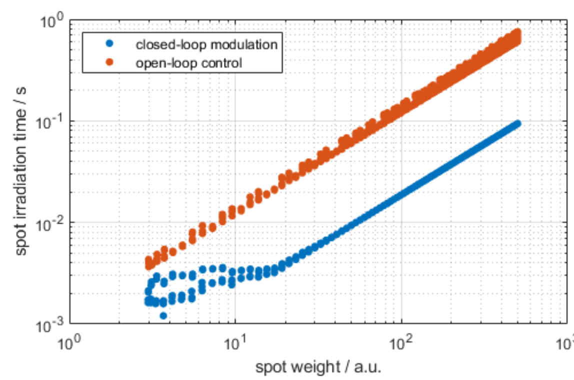

Figure 4: Irradiation time per spot for open loop fixed current and closed-loop current modulation.

est dose rates can be achieved when applying a spot-wise current modulation for modulated treatment fields.

REFERENCES

[1] V. Favaudon *et al.*, "Ultrahigh dose-rate flash irradiation increases the differential response between normal and tumor tissue in mice," *Science Translational Medicine*, vol. 6, no. 245, 245ra93–245ra93, 2014, doi:10.1126/scitranslmed.3008973

[2] M. M. Folkerts, E. Abel, S. Busold, J. R. Perez, V. Krishnamurthi, and C. C. Ling, "A framework for defining flash dose rate for pencil beam scanning," *Medical Physics*, vol. 47, no. 12, pp. 6396–6404, 2020, doi:https://doi.org/10.1002/mp.14456

[3] *Feasibility Study of FLASH Radiotherapy for the Treatment of Symptomatic Bone Metastases*, Clinical trial registration, submitted: October 5, 2020, 2021, https://clinicaltrials.gov/ct2/show/NCT04592887

[4] R. Tansho *et al.*, "Study of general ion recombination for beam monitor used in particle radiotherapy," in *Proc. of IBIC2014, Monterey, CA, USA*, paper WEPF30, 2014.