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Author(s):
Colizzi, Isabella; Maradia, Vivek; Kuenzi, Rene; Gabard, Alexander; Baumgarten, Christian; Weber, Damien Charles; Lomax, Antony John; Meer, David; Psoroulas, Serena

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UPGRADE OF A CLINICAL FACILITY TO ACHIEVE A HIGH TRANSMISSION AND GANTRY ANGLE-INDEPENDENT FLASH TUNE*

Isabella Colizzi[†,1], Vivek Maradia[1], Rene Kuenzi, Alexander Gabard, Christian Baumgarten, Damien Charles Weber[2,3], Antony John Lomax[1], David Meer, Serena Psoroulas
Paul Scherrer Institut, 5232 Villigen PSI, Switzerland
[1]also at ETH Zurich, Switzerland
[2] also at University Hospital Zurich, Switzerland
[3]also at Department of Radiation Oncology, Inselspital, Bern University Hospital, Switzerland

Abstract

In proton therapy, FLASH-RT, irradiation at ultra-high dose rates (>40 Gy/s) that can minimize radiation-induced harm to healthy tissue without reducing its ability to treat tumors, is a topic of great interest. However, in cyclotron-based proton therapy facilities, losses caused by the energy degradation process reduce the transmission to less than 1% for low energies, making it difficult to achieve high dose rates over the clinical range (70-230 MeV).

We will demonstrate how an already existing clinical beamline can be converted into a FLASH beamline by mainly beam optic changes. To achieve maximum transmission, we have developed a new optics that transports the undegraded 250 MeV beam from the cyclotron to the isocenter. However, this has a slightly asymmetric emittance in the transverse planes, leading to gantry angle-dependent beam characteristics at the patient.

Particle transport has been simulated with MINT (in-house matrix multiplication transport program with Monte Carlo simulations for scattering effects) and benchmarked with beam profile measurements. We used the optimization criteria for sigma matrix matching to achieve gantry angle-independent optics.

Simulations and beam profile measurements showed a good agreement**,** and with FLASH optics, we experimentally achieved 90% transmission at the patient, translating to a maximum current of 720 nA (>9000 Gy/s on-axis). Further, we demonstrate that using the matrix matching optimization criteria together with fine tuning of the magnets, we could achieve gantry angle-independent beam profiles at the patient location.

In conclusion, we have shown how an already existing cyclotron-based proton gantry can be adapted to achieve ultra-high dose rates at 250 MeV, enabling investigations of FLASH radiotherapy with protons, with the drawback of downstream energy modulation, if required. Since most of the modifications are performed on the beam optics, it is completely transparent to clinical operations, making the method transferable to other facilities.

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† isabella.colizzi@psi.ch

INTRODUCTION

The delivery of ultra-high dose rates (>40 Gy/s), also known as FLASH radiotherapy, has proven in preclinical investigation to allow tumour control while minimizing damage to surrounding healthy tissues [1]. In 2014, the effect was demonstrated on mice with a 4.5 MeV electron beam [2] and in 2018, the first human patient was successfully treated with electron-FLASH radiotherapy at the Lausanne University Hospital (CHUV, Switzerland) [3]. After that, many biological cell experiments and even a few clinical trials started to investigate the parameters that triggers the FLASH effect. Nowadays, the effect has been confirmed by different institutes and for different beam modalities (electrons, photons, proton and heavy ions [4]) and organs [5].

Some proton centres around the world have begun to look at whether it's possible to use current treatment equipment to achieve FLASH dose rates. The FLASH dose rate requirements can theoretically be met by cyclotron-based facilities, at least for high energies [6]. However, there is no conclusive proof that dose rates greater than 40 Gy/s cause the FLASH effect since this limit was derived in a limited number of experiments and tissues. Therefore, flexibility is required.

In this study we report how the clinical Gantry 2 [7] at the Paul Scherrer Institute could be adapted to achieve ultra-high dose rates at 250 MeV, without affecting clinical operations. The aim of this update is to enable clinical investigation of conformal FLASH radiotherapy using protons in scanning mode, hence a symmetric and gantry-angle independent beam is required.

METHODS AND MATERIALS

PSI Beamline and Gantry 2

In the PSI proton therapy center the proton beam is generated by the COMET cyclotron (Fig. 1). The extracted beam has an energy of 250 MeV and up to 800 nA intensity. For treatment, energies in the range 70-230 MeV are required and the energy modulation is done by mean of a degrader placed right after the cyclotron. We lose more than 99% of the particle for low energies due to the collimators following the degrader and the energy selection slits, resulting in a transmission of less than 1% at the isocenter [8, 9]. Consequently, in order to obtain ultra-high dose rates, we optimized the transport of the undegraded 250 MeV proton beam to the treatment room with the least amount of losses. However, PSI Gantry 2 dipole magnets [10] were designed to transport only energies up to 230 MeV and therefore an investigation of the flexibility of the power supplies as well as the magnet cooling system had to be conducted.

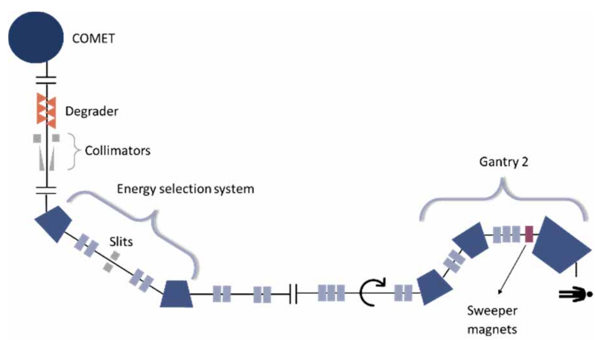

Figure 1: Schematic of the PSI beamline from the cyclotron (COMET) to Gantry 2. The light blue rectangles represent the quadrupoles, the blue trapezoid the dipoles.

Beam Transport

The particle transport was simulated with MINT [11], an in-house developed matrix multiplication program with Monte Carlo calculations of scattering effects, which occurs due to permanent monitors or foils placed along the beamline. The following criteria were used in the optimization of the beamline:

- Beam size smaller than magnets and collimators aperture.
- Three imaging point (after the energy selection system, at the coupling point between the beamline and the gantry and at the isocentre).

The isocenter beam parameters were optimized to account for the slightly asymmetric emittance in the transverse planes of the undegraded beam (6.1π mm mrad in y and 3.7π mm mrad in x, 1σ emittance), which might result in undesired gantry angle-dependent beam characteristics at the patient. We utilized the matrix matching approach [12] to achieve an angle independent and symmetric beam, which requires:

- Symmetric beam size at the gantry entrance.
- Beam waist at the gantry entrance.
- Diagonal transfer matrix from the gantry entrance to the isocentre.

Measurement

The beam profiles were measured with strip chamber monitors [13, 14] distributed along the beamline. The precision of the measured beam profile reduces for low current due to sensitivity and small beam sizes due to the strip resolution. The transmission at the treatment room was calculated with the ratio between the current monitor after the cyclotron and the two transmission monitors (plane parallel ionisation chambers) in the nozzle [15].

The beam size at the isocentre was measured with a scintillating foil connected to a charge coupled device (CCD) camera. The (pixel) resolution of the camera was 0.3 mm.

RESULTS

Hardware Adaptation for 250 MeV

The needed coil current of the gantry magnets at 250 MeV was determined by extrapolating the measured current from 70 to 230 MeV while accounting for saturation effects observable at high energies. We parametrize the hysteresis curve using a linear function for low current (energies) and a quadratic function for higher current (energies). Due to the limited amount of data, the parametrization of the saturation zone was sensitive to uncertainty. In Fig. 2 we show in red the maximum current that we could achieve with the previous power supply configuration (500 A) and in green the required current (518 A). The dashed lines represent the current with 10% and 25% error in the parametrization of the quadratic function. After ulterior measurements, we found the required current to be 515 A, which agrees with less than 1% with our extrapolation. The specifications were translated in a new configuration of the power supplies which was tested and implemented without affecting clinical operation. In particular, no adaptation to magnets operation conditions (such as cooling water flow etc.) was needed.

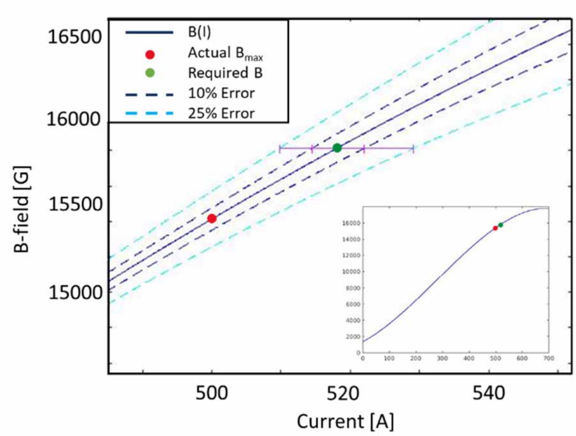

Figure 2: The interpolated hysteresis curve of the largest dipole magnet in the gantry is plotted for positive current in the smaller plot. The red point shows the actual maximum current achievable and the green the requirement for 250 MeV. In the larger plot we zoom in the region of interest, and we show with dashed lines 10% and 25% error in the parametrisation.

FLASH Optimized Beam Transport

Figure 3 shows a comparison between the simulated (and hand-tuned) particle transport and the measured beam profile at different position in the beamline. Hand-tuning was necessary for different reasons, for gantry misalignment due to the weight of the magnet when we change the gantry angle and, as will be discussed later, to produce a circular beam at the isocentre.

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The mean deviation lies around 12%, in particular, only 10% in the beamline and 17% in the gantry region. From the degrader until the gantry entry, the disagreement in x and y is nearly same (less than 1% difference). The agreement is however satisfactory for our purpose.

It is important to mention that the simulation's starting assumption of the phase space is an important factor in determining whether measurements and simulations match. By changing the initial parameters, the beam size at the monitor's position will vary even if the overall beam envelope (shape) stays constant.

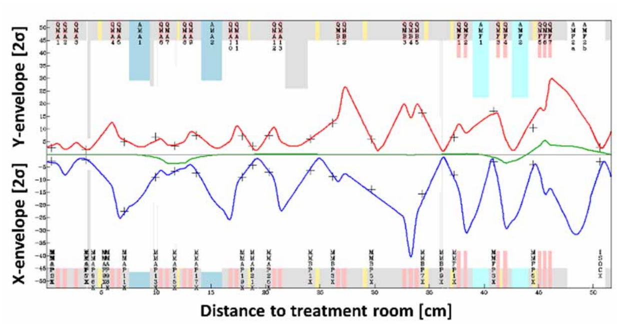

Figure 3: Comparison between the simulated particle transport (full red and blue line) and the measured beam profile (red dots). The lower half of figure shows beam envelope in X-plane (2σ) and the upper half shows envelope in Y-plane (2σ). The dispersion (mm per mil dp/p) is represented with the green line. The beamline and gantry quadrupoles are indicated in red and the diploes in blue.

We experimentally achieved a transmission of 90% from cyclotron to isocenter that can be translated to a maximum current of 720 nA (>9000 Gy/s peak dose rate on-axis, since the dose distribution in a proton beam is not uniform, we mention the dose on-axis defined as the dose on the proton beam's center axis), thus enabling investigations of FLASH radiotherapy with protons.

Beam Characteristics at the Isocentre

To demonstrate the independence of the tune on the gantry angle, we measured the beam size at different gantry positions, and we plot in Fig. 4 the results. The beam size variation is overall smaller than 10%. On average the beam size is 1.36 +/- 0.02 mm in y and 1.37 +/- 0.02 mm in x.

This result was obtained in two steps. Firstly, we optimised the magnetic settings using matrix matching optimization constraints in MINT. Secondly, fine-tuning the gantry's quadrupoles was the required step to experimentally achieve a symmetric and angle independent beam size at the isocentre.

We provide in Fig. 5 a spot map measurement for a scanning pattern of 16 cm x 12 cm. In the plane orthogonal to the bending plane (x) of the magnet we see a significant distortion and non-parallelism at the corner of the scanning area. However, in the central region, which is important for our purposes, we measured a regular grid with a round beam.

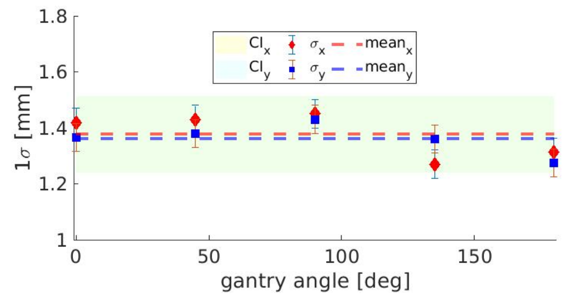

Figure 4: Measured beam size (1σ) as a function of the gantry angle. The dashed line is the mean value of the beam size in x (red) and y (blue). The orange and light blue band indicate 10% variation of the beam size.

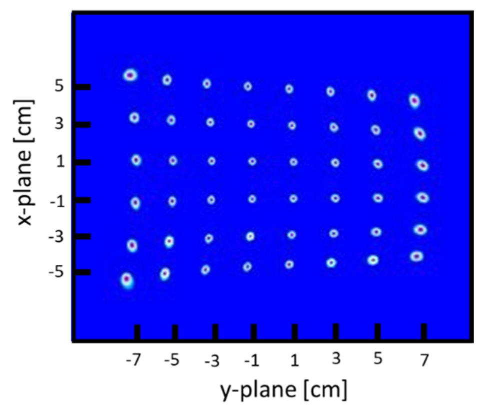

Figure 5: Measured spot map at the isocentre.

DISCUSSION

In this work, we demonstrate that we could upgrade PSI Gantry 2 to transport 250 MeV and achieve UHDR at the patient position. Even though the gantry was designed to transport proton beams with a maximum energy of 230 MeV, the flexibility of the design enables us to extend the power supply limits and transport 250 MeV without affecting clinical operations.

We simulate the particle transport in MINT, and we benchmarked the simulations with profile measurements. We achieved an overall agreement, and the small discrepancies can be explained by different reasons. Firstly, the initial beam size definition may not be accurate. It has been calculated a posteriori comparing profile measurements performed over months with simulations with varying initial beam parameters (beam size and divergence). Further, since we were operating at very low current (0.2 nA), due to radiation protection requirements, we observed deformation of the beam in y due to the vertical deflector in the cyclotron used to reduce the beam current. Since simulation tools assume a Gaussian beam, this could explain the minor deviation in the y-envelope in the first monitors. Additionally, the profile monitors along the beamline do not work optimally at low current and for very narrow beams with a width comparable to or smaller than the strip pitch, the width is usually overestimated. This would explain why there is a slight discrepancy when the beam size is very small. The inaccuracy of the simulation's definition of the gantry magnets' effective length in particular may be used to explain the discrepancy in the gantry. Lastly, missing second order terms might be in general a cause of discrepancy.

However, the simulations in MINT provided us a beneficial guide for beam line tuning, offering an important qualitative description of our beam transport.

We show that we could achieve a symmetric and gantry angle independent beam size at the patient position. The observed small discrepancy (<10%) is however negligible if we consider scattering in the patient. We noticed, according to a simple estimation of the multi-coulomb-scattering (using the Lynch and Dahl constants [16]), that the scattering in air and in the nozzle has a non-negligible contribution (30% of the beam size) in achieving a symmetric beam at the isocentre. However, a more detailed analysis is outside the scope of this study.

In the corner of the scanning region, the measured spot map reveals a non-parallel pattern and distortion. This can be explained by the final bending magnets' effective field edge curvature at the exit edge, which is bigger than 0.4 m-1 for 250 MeV [17], as well as by the large gap. However, FLASH clinical trials are usually conducted on small animals with small tumour sizes and since the tumour is usually located in the centre of scanning map, this distortion will affect only marginally the experiments.

We experimentally achieved a transmission of 90% meaning >9000 Gy/s peak dose rate on-axis, thus achieving the dose rate requirements for FLASH radiotherapy. Nevertheless, since there is no absolute evidence of the required parameters to achieve the FLASH effect, developing a versatile irradiation facility able to work under different dose rate conditions is crucial. Furthermore, with the objective of translating FLASH radiotherapy into the clinic, we will investigate FLASH proton beam scanning techniques rather than the transmission approach often utilized in clinical studies. For this, we must minimize the time necessary to change energies, for example, by modulating the beam with devices such as ridge filters [18] to increase the Bragg peak width from a few millimeters to a few centimeters.

CONCLUSION AND OUTLOOK

We have demonstrated how a cyclotron-based proton gantry can be modified to achieve ultra-high dose rates at 250 MeV and have achieved the desired beam quality (symmetric and small beam size at the isocenter, angle independent beam size) to enable investigations of FLASH radiotherapy using protons in pencil beam scanning mode. Since most of the modifications are performed on the beam optics, the method transferable to other facilities, too.

Further investigation of energy modulation techniques and monitoring systems for ultra-high dose rate will be the main topic of future studies.

In conclusion, PSI Gantry 2, an operating clinical gantry, will provide a unique setting for researching FLASH-PT and demonstrating FLASH's adaptability in the clinic.

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