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CURRENT STATUS OF MINIBEE: MINIBEAM BEAMLINE FOR PRECLINICAL EXPERIMENTS ON SPATIAL FRACTIONATION IN THE FLASH REGIME*

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Abstract

In vivo studies support that the combination of protons and spatial fractionation, the so-called proton minibeam radiotherapy (pMBT), enhances the protection of normal tissue for a given tumor dose. A preclinical pMBT facility for small animal irradiation at the 68 MeV cyclotron of Helmholtz-Zentrum Berlin (HZB) will improve the understanding of this method. A two-step energy-degrading system will first define the maximum energy of the beam and further degrading will occur before the target forming a spread-out Bragg peak (SOBP), if necessary. Beam size and divergence will be adjusted by slit systems before a 90-degree magnet bending the beam into the experimental room. At the current stage, a magnetic quadrupole triplet placed close to the target demagnifies the beam by a factor of ~ 5. The goal is to generate a magnetically focused minibeam of 50 micrometer sigma. Scanning magnets will enable a raster-scan application in the tumor. Conventional dose rate delivery will be allowed while FLASH applications can be accomplished with the possible use of a ridge filter. The results of beamline simulations by TRACE-3D and BDSIM will be presented.

INTRODUCTION

Cancer treatment relies on four pillars: surgery, chemotherapy, radiotherapy (RT) and immunotherapy. RT remains one of the most important modalities against cancer with almost half of the patients undergoing RT during their treatment scheme [1].

During the last years, novel modalities like proton minibeam radiation therapy (pMBT) and FLASH radiotherapy (FLASH-RT), have drawn the attention of the scientific community. pMBT exploits the advantageous properties of proton beams combined with spatial fractionation [2, 3]. In-vivo studies have shown that it can achieve better sparing of healthy tissues and possibly better tumor control [4–7]. In contrast to conventional proton therapy, in pMBT multiple sub-millimeter-sized beams separated by a constant interval (center-to-center,ctc) are used to irradiate a tumor creating a pattern of irradiated and non-irradiated regions at the entrance (see Fig. 1). While the minibeams transverse the matter, they scatter due to Multiple Coulomb Scattering (MCS) leading to a homogeneous coverage of the tumor when the ctc is adjusted for a certain tumor depth. FLASH-RT relies on the delivery of ultra-high dose rates (≥ 40 Gy/s) within a short irradiation time (≤ 500 ms). A plethora of animal experiments have shown that also this method reduces healthy tissue toxicity while preserving tumor control [8, 9]. Both modalities seem promising and further research is essential to enhance the understanding of the biological mechanisms and the effects of their synergy. The construction of a beamline for dedicated research in the field of pMBT with the option to also apply FLASH dose rates will allow systematic and intensive investigation of both irradiation schemes.

MINIBEE PROJECT

The MINIbeam BEamline for preclinical Experiments (MINIBEE) is a project about the construction of a preclinical facility for experiments in small animals and biological samples using proton minibeams. The beamline (see Fig. 2) will be hosted at the 68 MeV cyclotron of Helmholtz-Zentrum Berlin für Materialien und Energie (HZB) [10]. It will offer the possibility to generate magnetically focused proton minibeams with a beam size (σ) of 50 µm (in vacuum), a ctc in the mm range and current of ~ 1 nA, while also FLASH applications will be feasible.

Once the proton beam is extracted from the cyclotron, it is transported by dipoles and quadrupole triplets in the experimental room and the beam profiles are shaped, regarding the beam size and the divergence, by different slit pairs along the beamline. A last quadrupole triplet (QUATC) close to the isocenter will demagnify the beam by a factor of ~5 generating the minibeam. Furthermore, downstream of QUATC a pair of scanning magnets will deflect the beam to the target covering a maximum field size of ± 25 mm in both directions (x and y). In case of irradiation of shallower tumors where lower energies are required, the beam energy can be adapted by placing a degrader after the beam extraction from the cyclotron and additionally by a range shifter placed close to the isocenter, to minimize the beam enlargement, for the generation of the Spread-out bragg peak (SOBP). The use of a ridge filter for FLASH delivery is also investigated.

In this paper, a full simulation study of the beamline is presented demonstrating that at the isocenter the desired beam size, current and beam deflection can be achieved. TRACE-3D and the python library Georges have been used to find

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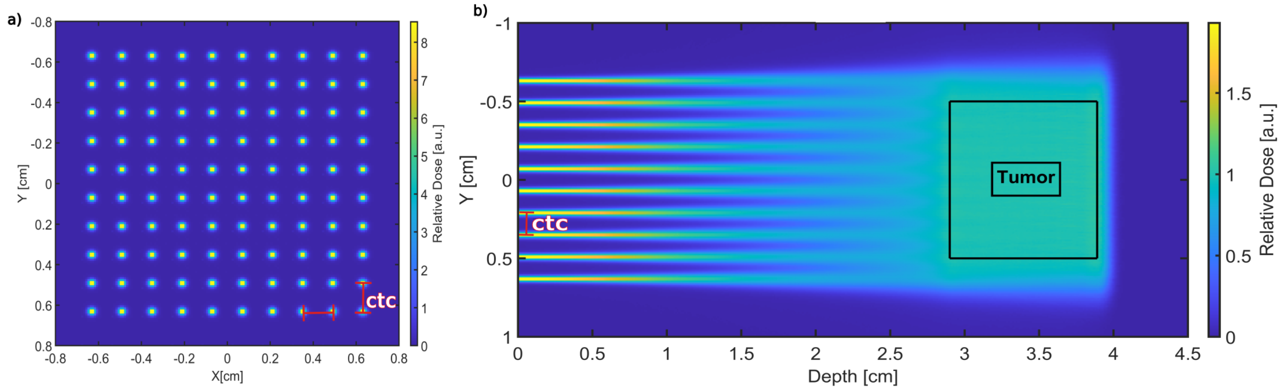

Figure 1: Dose distribution of pMBT in a water phantom assuming a tumor in 2.9 cm to 3.9 cm depth and ctc=1.4 mm (a: transversal cross-section at the entrance. b: longitudinal cross-section).

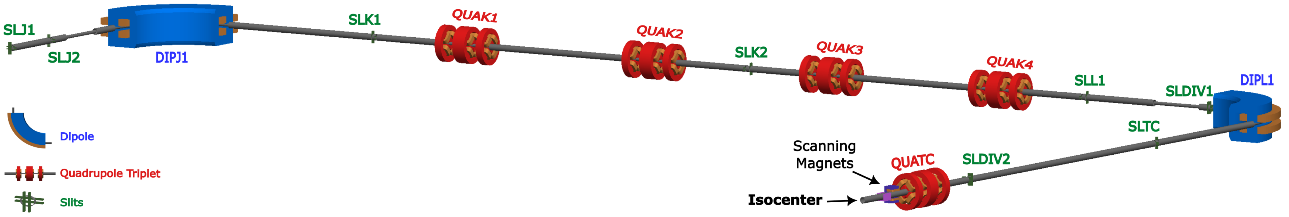

Figure 2: MiniBee beamline layout. The beamline starts from the slit pairs (SLJ1) and it is transported with dipole magnets and quadrupole triplets up the position of the isocenter. The slits are larger than in reality for visualization purposes. The slits pair SLDIV1 refers to a pair close to DIPL1 and therefore it is not visible in this figure.

the best values for the quadrupole strengths and the slits settings [11,12]. The simulations were repeated using the Beam Delivery Simulation (BDSIM) to study simultaneously the effects of the particle transport and their interactions with the materials of the beamline components [13]. The exiting nozzle will include a Kapton foil and between the nozzle and the isocenter there will also be a dose monitor and a few mm of air. However, these are not implemented in the presented simulations where only the effects of the beam transport are studied.

SIMULATION RESULTS

In the simulations using BDSIM, all the magnetic elements and the slit systems have been implemented and the proton beam (10^5 particles) was transported starting from the slits SLJ1 up to the isocenter, as plotted in Fig. 2. The beam emittance at slits SLJ1, which are downstream of the cyclotron (not presented in Fig. 2) has been measured [14]. Firstly, the beam was focused at the position (x,y) = (0,0) and in Fig. 3 the evolution of the beam size and the transmission along the beamline are presented. A beam size of about 50 µm (σ) is achieved at 2.3 % overall transmission. The beam parameters are also calculated when the beam is deflected at x,y =± 25 mm by scanning magnets of 200 mm magnetic length and field strengths of B_x= 152 mT and B_y= 217 mT. Fig. 4 shows the phase spaces of the beam at the positions (x,y) = (0,0), (x,y) = (-25 mm,-25 mm) and (x,y) = (25 mm,25 mm) and Table 1 shows the detailed values of the beam parameters (beam size and divergence) at the aforementioned positions.

The results about the beam parameters at the isocenter demonstrated in Fig. 3 and 4 and in Table 1 indicate that the wanted beam size (50 µm) can be accomplished at the isocenter plane while a slight enlargement is observed at the edges of the field. Furthermore, the proposed beamline can attain 2.3% transmission at the isocenter. The cyclotron of HZB can provide 100 nA and consequently the current requirements on the isocenter can be fulfilled. At the edges of the scanning field, the current was also preserved at the same levels as in the central position.

CONCLUSION

The simulation study showed that by transporting the beam along the presented beamline, the desired beam characteristics of a proton minibeam regarding the beam size and the current are fulfilled in the isocenter position. Furthermore, the results from the scanning field highlighted that these requirements are also valid at the edges of the field with only a minor beam enlargement. This should be further investigated including the Kapton foil, the dose monitor and the air for better evaluation of the effect of beam properties on the skin of the treated animals. Those results contribute to the design and construction of the pMBT facility at HZB and thus to the broadening of the research in the disciplines of proton minibean and FLASH.

Table 1: Beam Parameters at the Isocenter at the Positions (x,y)=(0,0), (x,y)=(25 mm,25 mm) and (x,y)=(-25 mm,-25 mm)

Position (x,y)	σ_x	$\sigma_x{}'$	σ_y	$\sigma_y{}'$
(25 mm,25 mm)	50.26 µm	5.3 mrad	52.82 µm	2.99 mrad
(0 mm,0 mm)	49.14 µm	4.6 mrad	50.28 µm	2.57 mrad
(-25 mm,-25 mm)	52.12 µm	5.14 mrad	54.59 µm	2.97 mrad

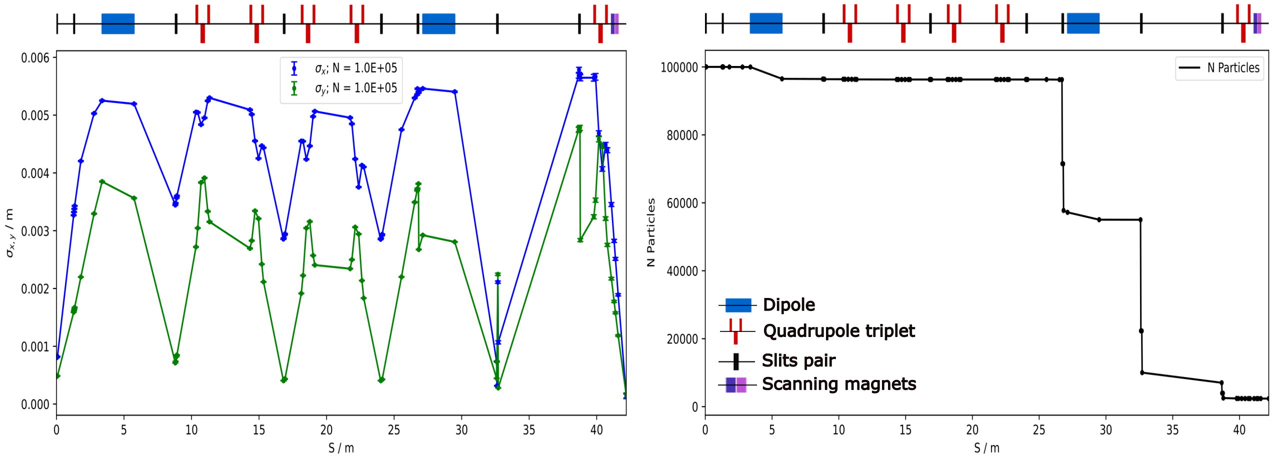

Figure 3: Right: Evolution of beam size (σ) along the beam transport (BDSIM), left: beam transmission (BDSIM).

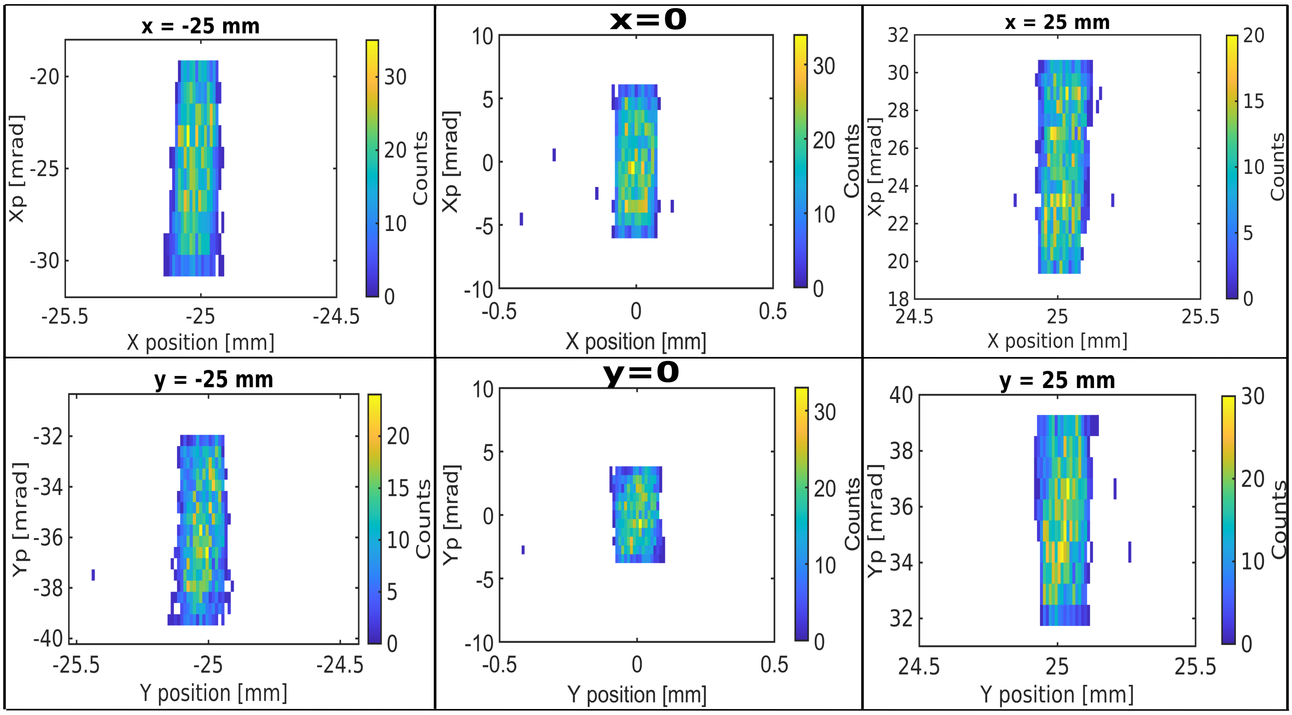

Figure 4: Beam's phase space at the isocenter at positions (x,y)=(0,0), (x,y)=(25 mm,25 mm) and (x,y)=(-25 mm,-25 mm).

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