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TECHNICAL PAPER

Measurements of in-air spot size of pencil proton beam for various air gaps in conjunction with a range shifter on a ProteusPLUS PBS dedicated machine and comparison to the proton dose calculation algorithms

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Abstract

The purpose of this study is to (i) investigate the impact of various air gaps in conjunction with a range shifter of 7.5 cm water-equivalent-thickness (WET) on in-air spot size of a pencil proton beam at the isocenter and off-axis points, and (ii) compare the treatment planning system (TPS) calculated spot sizes against the measured spot sizes. A scintillation detector has been utilized to measure the in-air spot sizes at the isocenter. The air gap was varied from 0 to 35 cm at an increment of 5 cm. For each air gap, a single spot pencil proton beam of various energies (110–225 MeV) was delivered to the scintillation detector. By mimicking the experimental setup in RayStation TPS, proton dose calculations were performed using pencil beam (RS-PB) and Monte Carlo (RS-MC) dose calculation algorithms. The calculated spot sizes (RS-PB and RS-MC) were then compared against the measured spot sizes. For a comparative purpose, the spot sizes of each measured energy for different air gaps of (5–35 cm) were compared against that of 0 cm air gap. The results of the 5 cm air gap showed an increase in spot size by ≤ 0.6 mm for all energies. For the largest air gap (35 cm) in the current study, the spot size increased by 3.0 mm for the highest energy (225 MeV) and by 9.2 mm for the lowest energy (110 MeV). For the 0 cm air gap, the agreement between the TPS-calculated (RS-PB and RS-MC) and measured spot sizes were within ± 0.1 mm. For the 35 cm air gap, the RS-PB overpredicted spot sizes by 0.3–0.8 mm, whereas the RS-MC computed spot sizes were within ± 0.3 mm of measured spot sizes. In conclusion, spot size increment is dependent on the energy and air gap. The increase in spot size was more pronounced at lower energies (< 150 MeV) for all air gaps. The comparison between the TPS calculated and measured spot sizes showed that the RS-MC is more accurate (within ± 0.3 mm), whereas the RS-PB overpredicted (up to 0.8 mm) the spot sizes when a range shifter (7.5 cm WET) and large air gaps are encountered in the proton beam path.

Keywords Spot size · Pencil beam scanning proton therapy · Range shifter · Air gap · Dose calculation algorithms

Introduction

The spot size of a pencil proton beam is typically defined in the air at the isocenter of the machine. A number of studies have characterized the in-air spot sizes on different proton machines, such as ProteusOne (Ion Beam Applications, Louvain-la-Neuve, Belgium) [1], ProteusPLUS (Ion Beam Applications, Louvain-la-Neuve, Belgium) [2, 3] ProBeam (Varian Medical Systems, Palo Alto, CA, USA) [4], and ProBeat (Hitachi Ltd., Tokyo, Japan) [5]. It is well known that the in-air spot size is energy dependent such that it increases with a decrease in energy [6, 7]. The in-air spot size is primarily dictated by multiple Coulomb scattering (MCS) and beam emittance, which is a function of quadrupole tuning,

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dipole field uniformity, and energy spread of the pencil beam. The lower energy protons have a lower probability of forward beam emittance, thus undergoing a higher probability of wide-angle scattering. As the energy of a proton beam increases, the probability of nuclear interaction and forward beam emittance is increased [7, 8].

Currently, commercially available PBS proton machines can deliver minimum energy of 70 MeV, which has approximately 4 cm range in water. Hence, for the treatment of shallower targets (e.g., breast and chest wall cases), a downstream pre-absorber material (also known as range shifter) is added after the nozzle exit. The addition of range shifter at the end of the nozzle exit reduces the beam energy, and this allows to achieve full dose modulation of the tumor volume that may be extended close to the skin. At the same time, the range shifter creates an air gap between its downstream and patient surface. The air gap increases the in-air spot size at the isocenter due to the angular distribution of a pencil proton beam after traversing the range shifter and translation of angular distribution into a geometric spread of proton beam's cross-section at the detector/patient surfaces as a function of distance [7, 8].

Several authors have investigated the use of a range of shifter in PBS proton therapy. For example, Titt et al. [7] studied the effect of a range shifter (or, pre-absorber) on lateral and longitudinal spot size using Monte Carlo simulations of PBS treatment head of Hitachi synchrotron. Shirey et al. [9] quantified the effect of range shifter and air gap on the absolute dose by performing measurements on an IBA ProteusOne PBS system. However, the effect of the air gap on the spot size was not included in the study [9]. Both et al. [10] reported the use of a universal bolus to replace the range shifter to maintain a smaller spot size on an IBA ProteusPLUS PBS system. The results from Both et al. [10] demonstrated the decrease in in-air spot size at the isocenter using a universal bolus (5.5 cm WET) for air gaps of 2 and 8 cm when compared against using a range shifter (7.5 cm WET) for an air gap of 34.5 cm. From the above studies [7, 10], it was shown that the decrease in the air gap between the range shifter and patient surface will decrease the spot size, but comprehensive measurements characterizing the effect of various air gaps on spot size is yet to be reported in a scientific literature, especially for a modern IBA ProteusPLUS proton therapy system with a PBS dedicated nozzle. Additionally, to the best of our knowledge, there is no available literature that focuses on spot size prediction accuracy of proton dose calculation algorithms implemented within commercial RayStation treatment planning system (TPS) (RaySearch Laboratories, Stockholm, Sweden).

The goal of this study is twofold. First, we investigated the impact of various air gaps in conjunction with the range shifter (7.5 cm WET) on in-air spot size (1 sigma) at the isocenter and two off-axis points for various energies using a high-resolution scintillation detector. Second, we mimicked the experimental setup in the RayStation TPS and compared the spot sizes calculated by analytical pencil beam (RS-PB) and Monte Carlo (RS-MC) dose calculation algorithms against the measured spot sizes.

Methods and materials

Proton beam delivery system

Our proton center is equipped with ProteusPLUS (Ion Beam Applications, Louvain-la-Neuve, Belgium), which includes PBS in all three gantries. A schematic of the PBS dedicated nozzle of our ProteusPLUS system is shown in Fig. 1. The description of the IBA PBS dedicated nozzle has been previously published [11, 12]. In brief, an ionization chamber 1 (IC1) verifies the alignment of the proton beam at the nozzle entrance. A set of two focusing quadrupole magnets focus the proton beam at the isocenter. Ionization chambers 2&3 (IC2/3) monitor beam characteristics and dose just before the proton beam exit the nozzle. At our proton center, we currently use 7.5 cm WET range shifter made up of lucite for clinical treatment of tumors that are situated at a shallower depth. A range shifter can be placed in the accessory

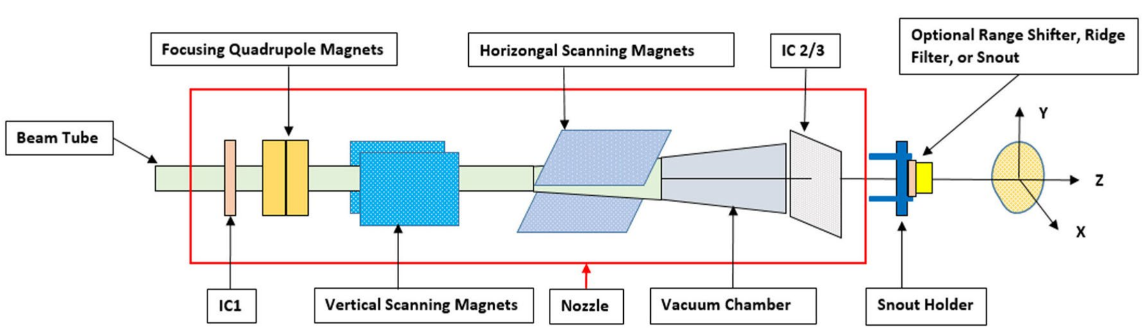

Fig. 1 Schematic representation of the Beam Delivery System (BDS) equipment in the PBS treatment mode for an IBA ProteusPLUS gantry-based system. [IC1 = Ionization Chamber 1, IC 2/3 = Ionization Chambers 2 & 3]

drawer, which moves with the retractable dedicated nozzle snout holder (DNSH) (Fig. 2).

Detector and software

The Lynx (IBA Dosimetry, Schwarzenbruck, Germany) has been utilized to measure the in-air spot sizes at the isocenter. The Lynx is a gadolinium-based scintillation detector with an active surface area of 300 mm × 300 mm and a pixel resolution of 0.5 mm. Readers are advised to read a publication by Russo et al. [13] for a detailed description of the Lynx. For spot profile acquisition and data analysis, the Lynx plug-in within myQA software (IBA Dosimetry, Schwarzenbruck, Germany) was used to calculate the in-air spot sizes (1 sigma).

Experimental setup

Figure 3 shows the schematic of the experimental setup of the current study. The Lynx was placed at the isocenter such that proton beam (gantry angle 270°) is perpendicular to the detector plane. The air gap was varied from 0 to 35 cm

Fig. 2 A range shifter (7.5 cm WET) is placed in the accessory drawer, which moves with the retractable dedicated nozzle snout holder (DNSH). [WET = Water Equivalent Thickness]

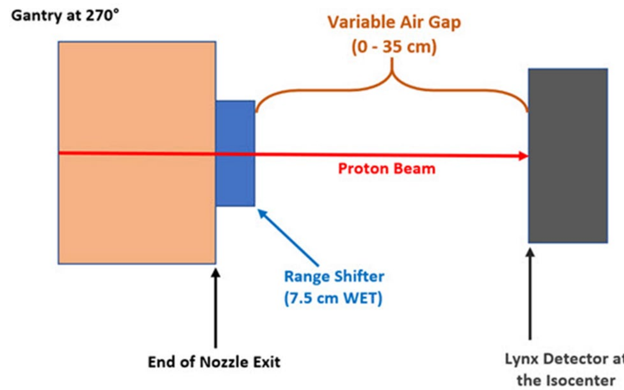

Fig. 3 Schematic of the experimental setup with variable air gap thicknesses (0–35 cm) between downstream of range shifter/solid-water blocks and Lynx detector situated at the isocenter. [WET = Water Equivalent Thickness]

with an increment of 5 cm. Specifically, air gaps of 15, 20, 25, 30, and 35 cm were created by moving the DNSH with range shifter (7.5 cm WET) inserted in the beam path at different snout positions. For example, a snout position of 41.5 cm, in this case, corresponds to an air gap of 35 cm between the downstream of the range shifter and surface of the Lynx (Fig. 4). For the DNSH in our PoteusPLUS system, the smallest achievable air gap between downstream of the range shifter and Lynx surface is about 11 cm. Hence, in order to create the air gaps of 0, 5, and 10 cm, we placed a total of 7.3 cm thick solid-water blocks (7.5 cm WET) in the beam path at the distance of 0, 5, and 10 cm, respectively, from the Lynx surface (Fig. 4). The WET of the lucite range shifter and solid-water blocks were measured using a Giraffe, a multi-layer ionization chamber (IBA Dosimetry, Schwarzenbruck, Germany). For the sake of simplicity, solid-water blocks will be referred to as range shifter from here onward. The in-air spot size measurements at the isocenter (X, Y, Z = 0 cm, 0 cm, 0 cm) were performed by delivering a single spot pencil beam of energies ranged from 110 to 225 MeV at an increment of 2.5 MeV. Additionally, the measurements were done at two off-axis points (Fig. 5) (top left (TL) at X = − 12 cm, Y = 12 cm, Z = 0, and bottom right (BR) at X = 12 cm, Y = − 12 cm, Z = 0) for energies ranged from 110 to 150 MeV at an increment of 5 MeV. Both sets of measurements included the air gaps of 0, 5, 10, 15, 20, 25, 30, and 35 cm.

TPS setup

The experimental setup was mimicked by importing a virtual phantom (30 × 30 × 30 cm^3) in RayStation TPS (version 6.1.1.2). The phantom was manually overridden with the physical density of air. A treatment plan was created

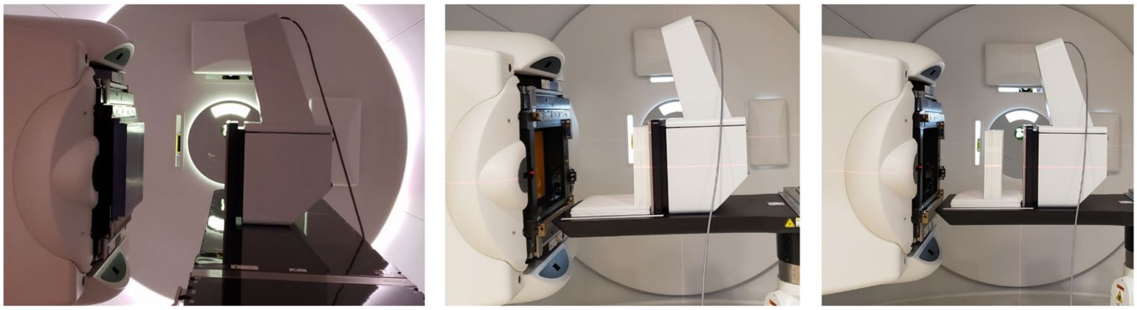

Fig. 4 An experimental setup showing 35 cm air gap (left), 0 cm air gap (middle) and 10 cm air gap (right). For 35 cm air gap setup, the range shifter is in the beam path. For 0 and 10 cm air gaps setup (middle and right, respectively), the range shifter is out of beam path. The air gap in the middle and right figures is defined by the distance from the downstream of solid-water blocks (7.5 cm WET) to the surface of the Lynx detector. [WET = Water Equivalent Thickness]

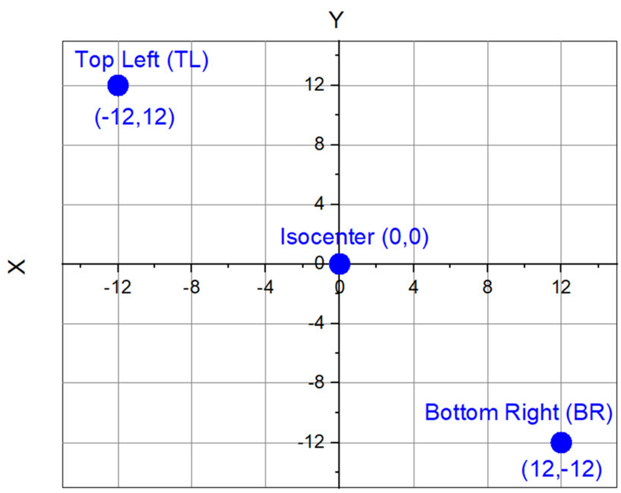

Fig. 5 A map displaying the coordinates (X and Y) of the spots at the isocenter and off-axis points. [TL = Top Left, BR = Bottom Right]

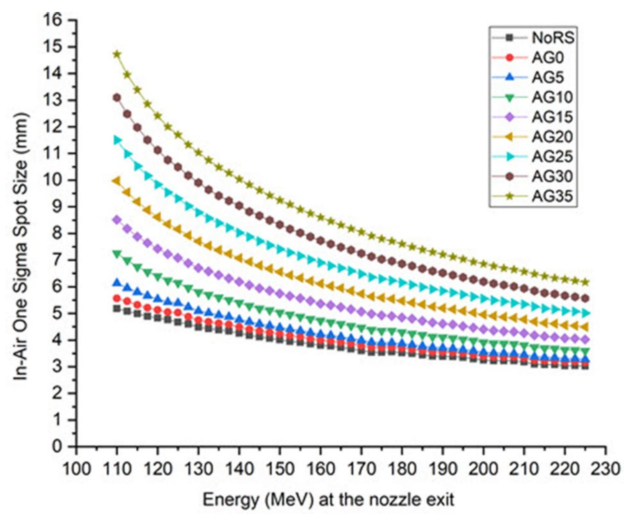

Fig. 6 The in-air spot size (1 sigma) at isocenter for air gaps of 0 cm (AG0), 5 cm (AG5), 10 cm (AG10), 15 cm (AG15), 20 cm (AG20), 25 cm (AG25), 30 cm (AG30), and 35 cm (AG35). The air gap was created by placing the pre-absorber (range shifter or solid water) of 7.5 cm WET in the beam path. [WET = Water Equivalent Thickness]

using a single lateral field (gantry 270^0) with an isocenter at the surface of the phantom. For air gaps of 15, 20, 25, 30, and 35 cm, a range shifter (7.5 cm WET) was inserted in the beam path. For the air gaps of 0, 5, and 10 cm, a block of 7.5 cm WET was placed in the beam path. Dose calculations were performed using a grid size of 1 mm. Specifically, for each scenario as outlined in "Experimental setup" section, a treatment plan was calculated using PB and MC algorithms for a single spot of a given energy. The monitor unit (MU) of each spot was assigned to 5. Once the dose calculations (RS-PB and RS-MC) were completed, in-air 1 sigma was calculated based on the PB- and MC-calculated line dose profiles at the isocenter and off-axis points (TL and BR). For the RS-MC, a 0.5% statistical uncertainty was used for the dose calculations. Details on the RS-PB and RS-MC algorithms have been provided elsewhere [14].

Results

Measurements at the isocenter

The in-air 1 sigma spot size (hereafter simply referred as spot size) results presented herein are based on 504 measurements at the isocenter and two off-axis points (TL & BR) (Fig. 5). Figure 6 illustrates the spot sizes measured at the isocenter for energies 110–225 MeV at various air gaps of 0–35 cm. For a comparative purpose, the average spot sizes of each energy for different air gaps of 5–35 cm are compared against that of 0 cm air gap (Fig. 7). Furthermore, in order to observe the impact of air gap on the spot size at different energies, a total of 47

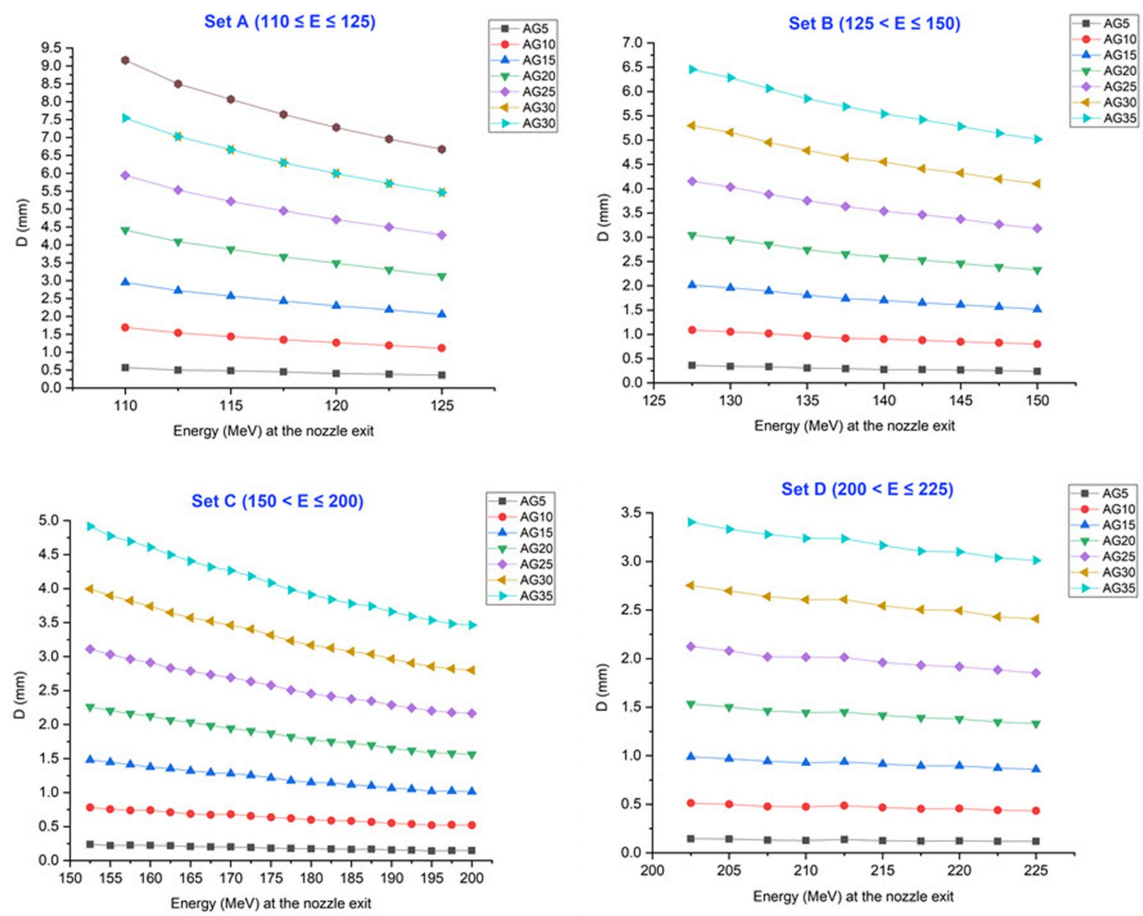

Fig. 7 The difference (D) in spot sizes for energy sets A–D. The D is calculated by comparing the spot sizes at various air gaps (5, 10, 15, 20, 25, 30, and 35) with that of 0 cm air gap. [AG = Air Gap]

energies (110–225 MeV, an increment of 2.5 MeV) are sub-grouped into: (a) Set A: 110 MeV ≤ E ≤ 125 MeV (b) Set B: 125 MeV < E ≤ 150 MeV (C) Set C: 150 MeV < E ≤ 200 MeV, and (d) Set D: 200 MeV < E ≤ 225 MeV.

The results of the 5 cm air gap showed an increase in spot size by ≤ 0.6 mm for all sets (A – D). The results of the 10 cm air gap showed an increase in spot size by average of 1.4 mm for Set A, 0.9 mm for Set B, and 0.5–0.6 mm for Sets C and D. Similarly, the results of the 15 cm air gap showed an increase in spot size by average of 2.5 mm for Set A, 1.7 mm for Set B, 1.2 mm for Set C, and 0.9 mm for Set D. For the 20 cm air gap, on average, the increase in spot size was 3.7 mm for Set A, 2.7 mm for Set B, 1.9 mm for Set C, and 1.4 mm for Set D. For the 25 cm air gap, on average, the increase in spot size was 5.0 mm for Set A, 3.6 mm for Set B, 2.6 mm for Set C, and 1.9 mm for Set D. The results of the 30 cm air gap showed an increase in spot size by average of 6.4 mm for Set A, 4.6 mm for Set B, 3.3 mm for Set C, and 2.5 mm for Set D. For the largest air gap (35 cm) in the current study, the spot size increased by 9.2 mm at the lowest energy (110 MeV) and by 3.0 mm at the highest energy (225 MeV). Additionally, on average, the increase in spot size for the 35 cm air gap was 7.8 mm for Set A, 5.7 mm for Set B, 4.1 mm for Set C, and 3.1 mm for Set D.

Comparison of measurements versus TPS at the isocenter

Figures 8 and 9 show the effect of range shifter (7.5 cm WET) and various air gaps on the measured and TPS-calculated spot sizes for different energies (110–225 MeV at an increment of 5 MeV). For the 0 cm air gap, the agreement between the TPS-calculated (RS-PB and RS-MC) and measured spot sizes were within ± 0.1 mm. For the air gaps of 5–35 cm in the current study, spot sizes calculated by the RS-PB were found to be larger than the ones calculated by the RS-MC. The agreement between the RS-MC and measurements is within ± 0.1 mm for the air gaps of 5–30 cm and within ± 0.2 mm for the 35 cm air gap. In contrast, the RS-PB always overestimated the spot sizes when compared to the measured spot sizes. Specifically, spot size overestimation by the RS-PB was by

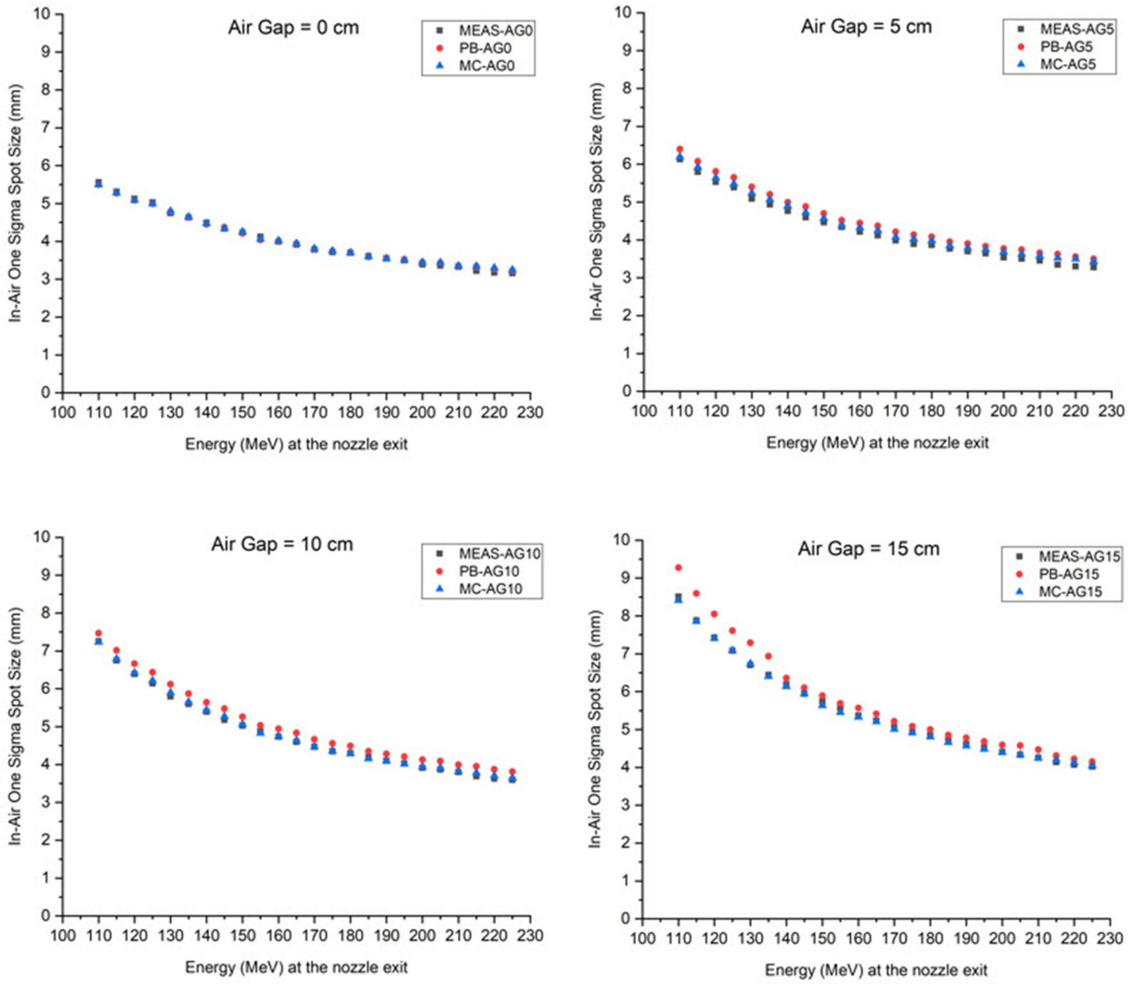

Fig. 8 The in-air spot size at isocenter for energies 110–225 MeV on a ProteusPLUS PBS dedicated nozzle. The results shown are for air gaps of 0–15 cm air gap in conjunction with 7.5 cm WET range shifter. [AG = Air Gap, MEAS = Measurement, RS-PB = RayStation Pencil Beam Algorithm, RS-MC = RayStation Monte Carlo Algorithm]

0.1–0.3 mm for the 5 cm air gap, 0.2–0.3 mm for the 10 cm air gap, 0.1–0.5 mm for the 15 cm air gap, 0.1–0.4 mm for the 20 cm air gap, 0.2–0.5 mm for the 25 cm air gap, 0.3–0.6 mm for the 30 cm air gap, and 0.3–0.8 mm for the 35 cm air gap.

Comparison of measurements versus TPS at the off-axis points

Figures 10 and 11 illustrate the difference (mm) in the spot size between the TPS (RS-PB and RS-MC) and measurements. For both the off-axis points (TL and RB), the accuracy of the RS-MC predicting more accurate spot size was distinct for the air gaps ≥ 5 cm. In comparison to the measurements, the RS-PB overpredicted the spot size by up to 0.8 mm, whereas the RS-MC computed spot sizes were within ± 0.3 mm.

Discussion

The current study was designed to understand how the combination of a range shifter and various air gap thicknesses affect the spot size of a pencil proton beam. The study was focused on a modern ProteusPLUS machine with a PBS dedicated nozzle. To our best knowledge, this is the first study to include comprehensive measurements on a ProteusPLUS machine to characterize the spot size change due to the combination of the range shifter and various air gaps (0–35 cm). Additionally, the current study investigates the accuracy of spot size prediction by the RS-PB and RS-MC when the range shifter and air gaps are involved in the proton beam path.

From the results presented in the current study, it is evident that the increase in air gap will increase the spot size. The spot size increment is more pronounced at the lower energies for all the air gaps, but the largest air gap showed

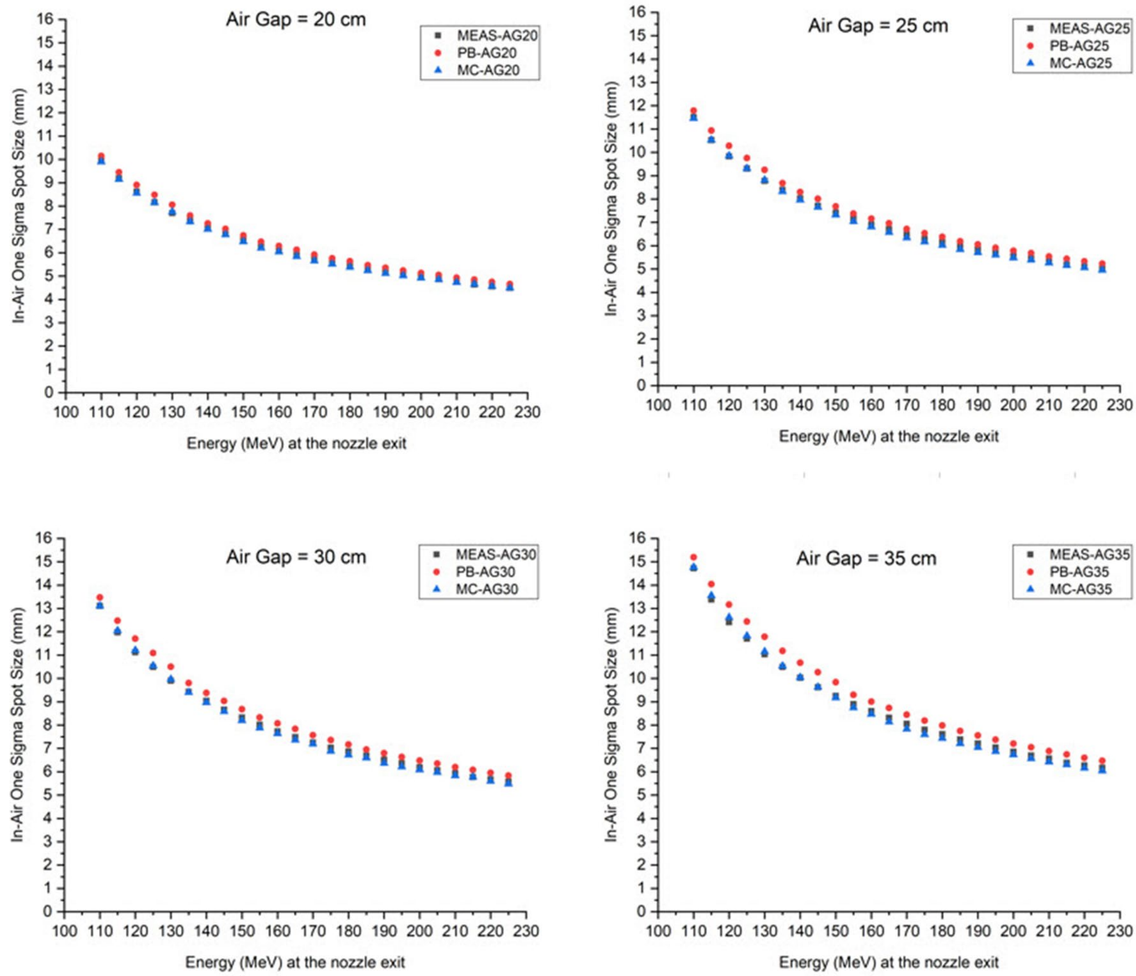

Fig. 9 The in-air spot size at isocenter for energies 110–225 MeV on a ProteusPLUS PBS dedicated nozzle. The results shown are for air gaps of 20–35 cm air gap in conjunction with 7.5 cm WET range shifter. [AG = Air Gap, MEAS = Measurement, RS-PB = RayStation Pencil Beam Algorithm, RS-MC = RayStation Monte Carlo Algorithm]

the highest increment. For example, at 200 MeV, when compared to the air gap of 0 cm, the spot size is increased by 0.2 mm for the 5 cm air gap and by 3.5 mm for the 35 cm air gap. At lower energy of 115 MeV, when compared to the air gap of 0 cm, the spot size is increased by 0.5 mm for the 5 cm air gap and by 8.1 mm for the 35 cm air gap. The increase in spot size due to the large air gap and range shifter will result in widening of the lateral penumbrae, which could spread out the dose distribution to the OARs adjacent to the target volume. Kraan et al. [15] have shown that the treatment plan with a small-spot machine results in sharper dose gradients, and this could reduce the dose to the organs at risk.

Previous studies [9, 14] were primarily focused on investigating the accuracy of the RS-PB and RS-MC in predicting the dose, range, distal-fall-off, spread-out Bragg Peak, and uniformity. The spot size is one of the fundamental parameters in PBS proton therapy. The accuracy of spot size calculation by proton dose calculation algorithms becomes very critical since the spot size can have an impact on several dosimetric parameters such as spot spacing, dose ripples, dose distributions within the target volume, and lateral penumbra. Hence, in addition to experimental measurements of the spot sizes, the current study was undertaken to evaluate the accuracy of spot size prediction by the RS-PB and RS-MC.

One of the requirements for the RS TPS commissioning is to measure the in-air spot profiles at the isocenter, and the same spot profiles can be used for both the algorithms (RS-PB and RS-MC). Also, our current version of the RS TPS does not require separate spot profile data for the range shifter. The results from the current study demonstrate that both the RS-PB and RS-MC agreed (± 0.1 mm) well with the measurements for the 0 cm air gap. However, for the larger air gaps (≥ 10 cm), the difference in spot sizes between the RS-PB and measurements was larger

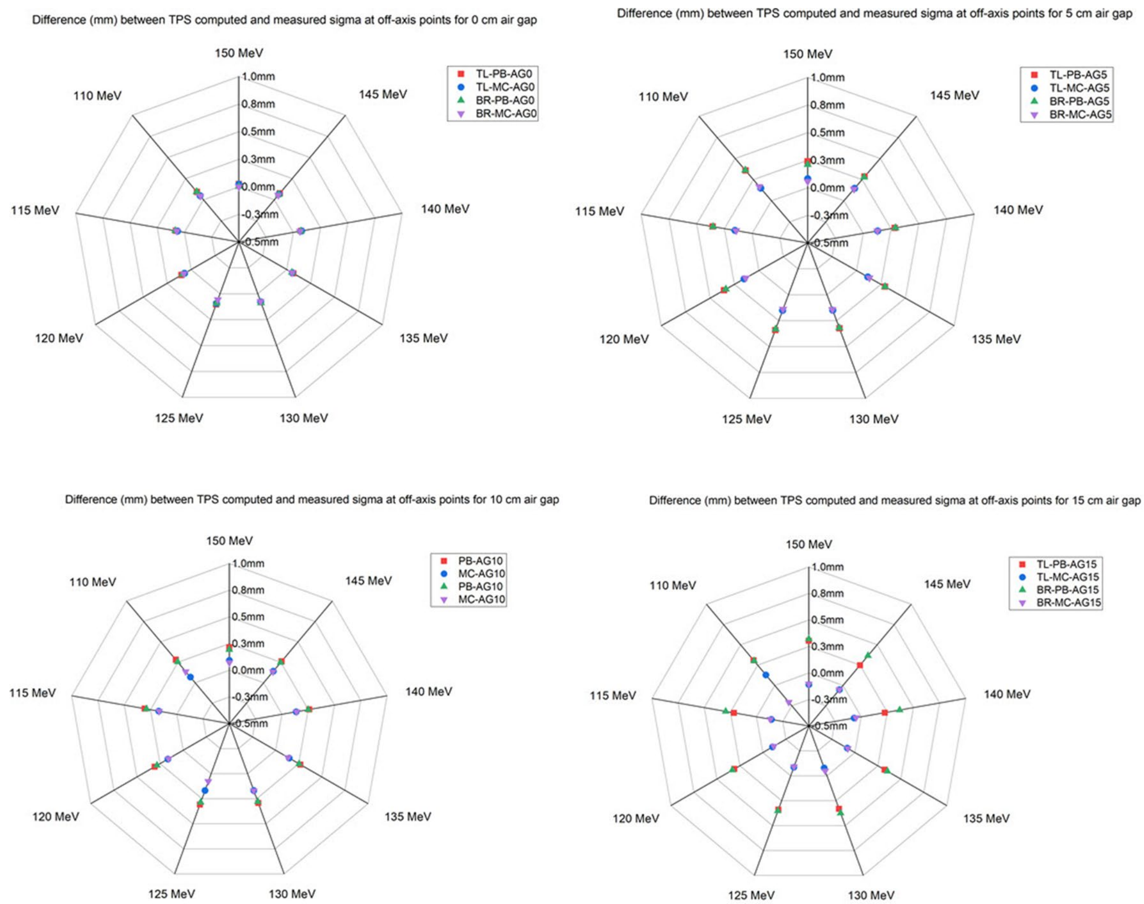

Fig. 10 The difference (mm) in spot size between the TPS (RS-PB and RS-MC) and measurements at off-axis points top-left (TL) and bottom-right (BR) for energies 110–150 MeV on a ProteusPLUS PBS dedicated nozzle. The results shown are for air gaps of 0–15 cm air gap in conjunction with 7.5 cm WET range shifter. [AG = Air Gap, TL = Top Left, BR = Bottom Right, MEAS = Measurement, RS-PB = RayStation Pencil Beam Algorithm, RS-MC = RayStation Monte Carlo Algorithm]

when compared to the ones between the RS-MC and measurements. The current study also demonstrated that, for the air gaps that are ≥ 5 cm, the spot sizes calculated by the RS-PB is always larger than the RS-MC calculated spot sizes and measurements. Overall, in comparison to the measurements (isocenter and off-axis points), the overestimation of spot size by the RS-PB was found to be up to 0.8 mm, whereas the RS-MC predicted the spot sizes within ± 0.3 mm.

The TPS results from the current study agree with the previous studies [9, 14] such that the RS-MC is more accurate than the RS-PB in predicting spot size at the phantom surface as a single pencil proton beam traverses through the range shifter followed by the air gaps (≥ 5 cm) and then finally reaching the phantom surface. In this scenario, a proton beam creates secondary protons in the range shifter. A larger discrepancy between the RS-PB and measurements is attributed to the lack of proper modeling within the RS-PB in accounting transport of secondary protons over the air gap on the phantom/patient surface and into the patient [9, 14].

Although it is a common practice in the proton center to minimize the air gap between the range shifter and patient surface, the air gap is dependent on the patient anatomy, selection of beam angles, external contour encompassing immobilization devices, and geometric safe limit of the machine without any collision. The air gap can be up to 35 cm for some clinical cases. Grassberger et al. [16] have demonstrated that lung plans generated by a larger spot machine were more found to be more robust than the ones generated by a smaller spot machine. For a mobile target, an interplay and plan robustness are a major concern, especially for a smaller spot machine. Currently, ProteusPLUS system at our center produces a smaller spot (i.e., about 3 mm for the highest energy (226.5 MeV) at the isocenter when no range shifter is involved in the proton beam path). Other proton centers may also have a similar limitation of not having small and large spot sizes at the same energy. Hence, it would be interesting to investigate the interplay effect using different spot sizes that are produced by the combination of range shifter and various air gaps.

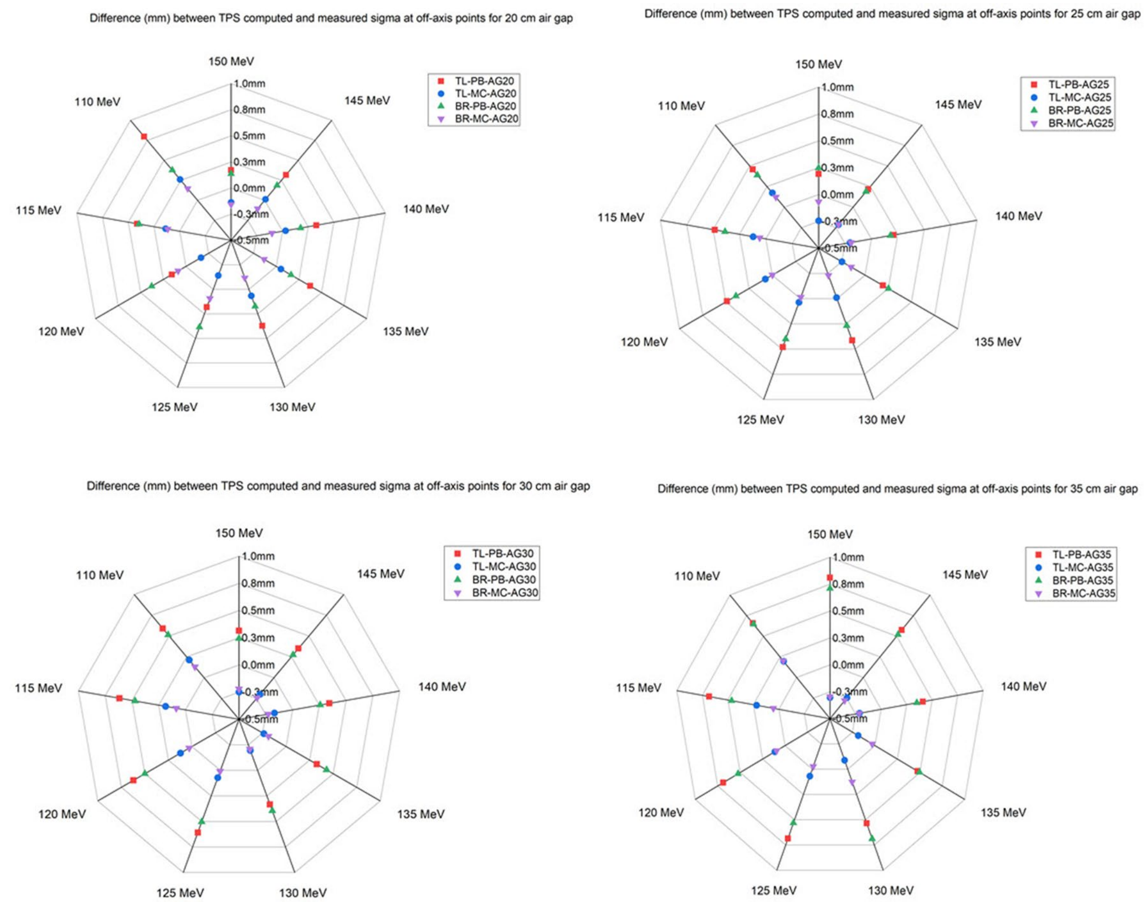

Fig. 11 The difference (mm) in spot size between the TPS (RS-PB and RS-MC) and measurements at off-axis points top-left (TL) and bottom-right (BR) for energies 110–150 MeV on a ProteusPLUS PBS dedicated nozzle. The results shown are for air gaps of 20–35 cm air gap in conjunction with 7.5 cm WET range shifter. [AG = Air Gap, TL = Top-Left, BR = Bottom-Right, MEAS = Measurement, RS-PB = RayStation Pencil Beam Algorithm, RS-MC = RayStation Monte Carlo Algorithm]

Several limitations exist in the current study. First, the spot size measurements and calculations were performed in-air at the isocenter and two off-axis locations, which were placed at the surface of the phantom. In a real clinical scenario, an isocenter would be typically placed inside the patient, and the spot size calculations inside patient/phantom would provide additional information on the behavior of the RS-PB and RS-MC. Second, our study does not involve wide varieties of inhomogeneities that are often encountered in treating clinical cases. A follow-up study on how low- and high-density media will impact on the spot size prediction accuracy of the RS-PB and RS-MC will be conducted in the near future. Despite these limitations, we believe that the current study provides valuable comprehensive spot size results for a modern ProteusPLUS PBS dedicated proton therapy machine as well as further validates that the RS-MC is more accurate than the RS-PB for proton dose calculations.

Conclusion

For a given energy at the end of the nozzle exit, the increase in in-air spot size due to range shifter and air gap is more pronounced at lower energies for all air gaps, but the largest air gap (35 cm) showed the highest increment in in-air spot size by up to a factor of 2.6 and 2.0 at energies of 110 MeV and 225 MeV, respectively, when compared to the air gap of 0 cm. The comparison between the TPS calculated and measured spot sizes demonstrate that the RS-MC is more accurate (within ± 0.3 mm), whereas the RS-PB overpredicted (up to 0.8 mm) the spot sizes when a range shifter (7.5 cm WET) and large air gaps are encountered in the proton beam path.

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Compliance with ethical standards

Conflict of interest Suresh Rana and E. James Jebaseelan Samuel declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

References

1. Pidikiti R, Patel BC, Maynard MR, Dugas JP, Syh J, Sahoo N, Wu HT, Rosen LR (2018) Commissioning of the world's first compact pencil-beam scanning proton therapy system. J Appl Clin Med Phys. 19(1):94–105
2. Saini J et al (2016) Clinical commissioning of a pencil beam scanning treatment planning system for proton therapy. Int J Part Ther. 3:51–60
3. Lin L, Huang S, Kang M, Hiltunen P, Vanderstraeten R, Lindberg J et al (2017) A benchmarking method to evaluate the accuracy of a commercial proton monte carlo pencil beam scanning treatment planning system. J Appl Clin Med Phys. 18(2):44–49
4. Langner UW, Eley JG, Dong L, Langen K (2017) Comparison of multi-institutional Varian ProBeam pencil beam scanning proton beam commissioning data. J Appl Clin Med Phys. 18(3):96–107
5. Gillin MT, Sahoo N, Bues M, Ciangaru G, Sawakuchi G, Poenisch F, Arjomandy B, Martin C, Titt U, Suzuki K, Smith AR, Zhu XR (2017) Commissioning of the discrete spot scanning proton beam delivery system at the University of Texas M.D. Anderson Cancer Center, Proton Therapy Center, Houston. Med Phys 37(1):154–163.
6. Sawakuchi GO, Titt U, Mirkovic D, Mohan R (2008) Density heterogeneities and the influence of multiple Coulomb and nuclear scatterings on the Bragg peak distal edge of proton therapy beams. Phys Med Biol. 53(17):4605–4619
7. Titt U, Mirkovic D, Sawakuchi GO, Perles LA, Newhauser WD, Taddei PJ, Mohan R (2010) Adjustment of the lateral and longitudinal size of scanned proton beam spots using a pre-absorber to optimize penumbrae and delivery efficiency. Phys Med Biol. 55(23):7097–7106
8. Gottschalk B, Koehler AM et al (1993) Multiple Coulomb scattering of 160 MeV protons. Nucl Instrum Methods Phys Res, Sect B 74(4):467–490
9. Shirey RJ, Wu HT (2018) Quantifying the effect of air gap, depth, and range shifter thickness on TPS dosimetric accuracy in superficial PBS proton therapy. J Appl Clin Med Phys. 19(1):164–173
10. Both S, Shen J, Kirk M, Lin L, Tang S, Alonso-Basanta M, Lustig R, Lin H, Deville C, Hill-Kayser C, Tochner Z, McDonough J (2014) Development and clinical implementation of a universal bolus to maintain spot size during delivery of base of skull pencil beam scanning proton therapy. Int J Radiat Oncol Biol Phys. 90(1):79–84
11. Lin L, Ainsley CG, Solberg TD, McDonough JE (2014) Experimental characterization of two-dimensional spot profiles for two proton pencil beam scanning nozzles. Phys Med Biol. 59(2):493–504
12. Rana S, Bennouna J et al (2019) Development and long-term stability of a comprehensive daily QA program for a modern pencil beam scanning (PBS) proton therapy delivery system. J Appl Clin Med Phys. 20(4):29–44
13. Saini J, Traneus E, Maes D, Regmi R, Bowen SR, Bloch C, Wong T (2018) Advanced Proton Beam Dosimetry Part I: review and performance evaluation of dose calculation algorithms. Transl Lung Cancer Res. 7(2):171–179
14. Russo S, Mirandola A, Molinelli S, Mastella E, Vai A, Magro G, Mairani A, Boi D, Donetti M, Ciocca M (2017) Characterization of a commercial scintillation detector for 2-D dosimetry in scanned proton and carbon ion beams. Phys Med. 34:48–54
15. Kraan AC, Depauw N, Clasie B, Giunta M, Madden T, Kooy HM (2018) Effects of spot parameters in pencil beam scanning treatment planning. Med Phys. 45(1):60–73
16. Grassberger C, Dowdell S, Lomax A, Sharp G, Shackleford J, Choi N, Willers H, Paganetti H (2013) Motion interplay as a function of patient parameters and spot size in spot scanning proton therapy for lung cancer. Int J Radiat Oncol Biol Phys. 86(2):380–386