Implication of spot position error on plan quality and patient safety in pencil-beam-scanning proton therapy

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Purpose: To quantitatively and systematically assess dosimetric effects induced by spot positioning error as a function of spot spacing (SS) on intensity-modulated proton therapy (IMPT) plan quality and to facilitate evaluation of safety tolerance limits on spot position.

Methods: Spot position errors (PE) ranging from 1 to 2 mm were simulated. Simple plans were created on a water phantom, and IMPT plans were calculated on two pediatric patients with a brain tumor of 28 and 3 cc, respectively, using a commercial planning system. For the phantom, a uniform dose was delivered to targets located at different depths from 10 to 20 cm with various field sizes from 2² to 15² cm². Two nominal spot sizes, 4.0 and 6.6 mm of 1σ in water at isocenter, were used for treatment planning. The SS ranged from 0.5σ to 1.5σ, which is 2–6 mm for the small spot size and 3.3–9.9 mm for the large spot size. Various perturbation scenarios of a single spot error and systematic and random multiple spot errors were studied. To quantify the dosimetric effects, percent dose error (PDE) depth profiles and the value of percent dose error at the maximum dose difference (PDE[ΔDmax]) were used for evaluation.

Results: A pair of hot and cold spots was created per spot shift. PDE[ΔDmax] is found to be a complex function of PE, SS, spot size, depth, and global spot distribution that can be well defined in simple models. For volumetric targets, the PDE[ΔDmax] is not noticeably affected by the change of field size or target volume within the studied ranges. In general, reducing SS decreased the dose error. For the facility studied, given a single spot error with a PE of 1.2 mm and for both spot sizes, a SS of 1σ resulted in a 2% maximum dose error; a SS larger than 1.25σ substantially increased the dose error and its sensitivity to PE. A similar trend was observed in multiple spot errors (both systematic and random errors). Systematic PE can lead to noticeable hot spots along the field edges, which may be near critical structures. However, random PE showed minimal dose error.

Conclusions: Dose error dependence for PE was quantitatively and systematically characterized and an analytic tool was built to simulate systematic and random errors for patient-specific IMPT. This information facilitates the determination of facility specific spot position error thresholds. © 2014 Author(s). All article content, except where otherwise noted, is licensed under a Creative Commons Attribution 3.0 Unported License. [http://dx.doi.org/10.1118/1.4885956]

Key words: proton therapy, spot spacing, IMPT

NOMENCLATURE

Δmax largest dose difference
DICOM Digital Imaging and Communication in Medicine
dose-volume histogram
IMPT intensity-modulated proton therapy
MU monitor unit
PDE percent dose error
PDE[ΔDmax] percent dose error at the maximum dose difference
PE position error
PTV planning target volume
SS spot spacing
SVol in the brain case study this refers to the target volume of 3 cc
TVol in the brain case study this refers to the target volume of 28 cc

1. INTRODUCTION

To date, scattering and scanning are the two major delivery approaches for proton therapy, although scanning systems have recently drawn more attention. Scanning systems can deliver a highly conformal dose in all directions (i.e., distal, proximal, and lateral) without collimation and compensation. In the plane transverse to the beam, the two-dimensional spot distribution is arranged on the basis of the shape of the target cross-section so that the conformal dose is delivered in this plane without the need for any collimation. Along the beam direction, the dose range can be controlled by changing the beam energy and intensity so that the thickness
and depth of the spread-out Bragg Peak can be controlled to conform to the distal and proximal boundaries of the target at any point.

The advantage of delivering a conformal dose in all directions without using a collimator or compensator is because the beam location, energy, and intensity can be controlled at each spot location. However, this freedom is sensitive to uncertainty of the delivered spot location. This uncertainty is present in any spot-scanning system and directly affects treatment plan quality and patient safety. The accuracy of the spot location, spot range, and dose delivered per spot all contribute to the accuracy of the delivery system.

Most proton therapy systems under construction or consideration at this time are designed (either mostly or exclusively) for scanning beam proton therapy. For our facility, the delivery system consists of a synchrotron accelerator and scanning nozzle. After the protons are accelerated by the synchrotron, the beam is transported through the beam line to one of several treatment rooms, and then it traverses the beam optics of the gantry and enters the scanning nozzle. Within the nozzle, two sets of steering magnets are used to set the spot location perpendicular to the beam direction. Misalignment of the beam before it enters the scanning nozzle, as well as fluctuation in the steering magnetic fields, can cause a position error (PE). Particularly, the displacement caused by uncertainties of steering magnetic fields (∆B/B) could be large although our specification for ∆B/B is ±0.1%. As a safety measure, a spot position monitor measures the actual spot locations downstream of the nozzle. If the spot position deviates from the expected position and exceeds a tolerance limit, the treatment will be terminated by the system. Recent reports have described how independent measurements on the delivered spot position agreed with the planned position to within 1 mm for a beam line similar to the one studied here.

Because of the complex relationship among factors such as spot size, spot dose, spot spacing (SS), and beam energy, the induced dosimetric error is not determined by PE alone. The SS, treatment depth, and global spot distribution are defined by the treatment plan, and spot size and dose per monitor unit (MU) are dependent on beam energy and are intrinsic to the facility. Therefore, understanding dose error dependence and sensitivity to each variable is necessary for understanding the overall impact of PE in a treatment delivery. Because of this complexity, defining a tolerance limit with a single PE value is not a trivial task.

In this study, a simulation method was used to study the dosimetric effects caused by PEs, with the intent of defining a safety threshold for clinical use of a spot-scanning beam. The study was designed to disentangle contributions to dose error from multiple variables so that the correlation of dose error with a single variable (spot position) could be evaluated. For example, the derived function of dose error in the space of PE and SS can be used to determine a single value of PE as the tolerance limit, given a user-defined SS. Single spot errors were designed to occur in targets located at various depths from 10 to 20 cm, which correspond to the range commonly encountered clinically. To explore dose impact extremes in the context of patient safety, systematic errors involving multiple spot clustering were simulated. Systematic and quantitative analysis was performed in a water phantom simulation study. Subsequently, the clinically relevant impact of PEs on the quality of intensity-modulated proton therapy (IMPT) plans was investigated for a specific clinical treatment (pediatric brain tumor).

2. MATERIALS AND METHODS

Spot PEs perpendicular to the beam direction were simulated by shifting spots away from their planned locations using a custom-built script that modifies the Digital Imaging and Communication in Medicine (DICOM) plan file. Plan optimization and dose distribution were calculated using Eclipse v10 treatment planning system (Varian Medical Systems, Palo Alto, CA). The treatment planning system was commissioned based on detailed Monte Carlo simulations of our nozzle. Based on different nozzle configurations the option of a small and large spot are available. The nominal spot size in σ, defined to be at isocenter at 10 cm depth in water (~110 MeV), is 4.0 and 6.6 mm, respectively. At the shallowest depth of 4 cm (70 MeV), the spot sizes are 5.5 and 9.3 mm for the small and large spot, and at the deepest depth of 32 cm (230 MeV), the spot sizes are 6.4 and 7.0 mm, respectively. After a treatment plan was generated, the DICOM RT Plan file was exported into Matlab software (version R2011b, MathWorks, Natick, MA). Custom-built code was used to choose the spots and shift their locations to mimic PE. The displacement was created by replacing original coordinates calculated by the treatment planning system with the shifted coordinates. The modified RT Plan DICOM file was then imported into the treatment planning system to calculate the resulting dose.

To assess the resulting dosimetric effects, the dose distribution of the shifted plan was compared with the original plan to calculate the percent dose error (PDE). PDE was defined as the ratio of dose difference (the dose of the shifted plan minus the dose of the original plan) to the original dose. The PDE has a three-dimensional distribution, so to perform quantitative evaluations, two metrics were defined: (1) the PDE depth profiles along the axis containing the largest dose differences (∆Dmax); and (2) the PDE value at the maximum absolute dose difference (PDE [∆Dmax]).

2.A. Water phantom study

The water phantom study represented the simplest situation, in which a single field delivered a uniform dose to a regularly shaped target volume. Multiple variables such as PEs, SS, treatment depth, and global spot distribution were changed systematically (as defined below) to evaluate the impact of spot PE.

2.A.1. Dose error dependence on multiple variables

PEs from 1 to 2 mm were simulated. Two spot sizes (4.0 and 6.6 mm in water at isocenter) were used for treatment planning and were abbreviated as SSpot and LSpot in the following discussion. SS similar to the spot size is typically used
Dosimetric effects on planar and linear target geometries were studied to evaluate the sensitivity of the dose error to dosimetric effects on planar and linear target geometries were studied to evaluate the sensitivity of the dose error to the plan. The plans were designed in this way to minimize any correlation of dose error with dose per spot and spot location. For these plans, the largest MUs were delivered in the deepest layer, so the shifted spot was chosen to be located in the middle of the deepest layer to evaluate the maximum potential dose impact. The single spot errors were studied with both LSpot and SSpot.

The steering magnetic field may have periodic fluctuation that could lead to multiple spots clustering together (e.g., magnitudes of magnetic fields were systematically lower than the programmed values, allowing spots to be positioned closer to the center than planned). To evaluate this condition, multiple spot clustering errors were simulated. Again, spots in the deepest layer were shifted toward the center of the spot matrix. In addition, PE at a fixed location, regardless of beam energy, was also simulated. For the multiple spot errors only SSpot was studied. The three types of clustering error studies can be summarized as follows:

1. The same PE occurred at the same location for all energy layers.
2. Spots in a row moved toward the center (linear clustering) in the deepest layer.
3. Adjacent spots moved toward the center (planar clustering) in the deepest layer.

### 2.B. Patient brain plan study

Two pediatric brain tumor treatments, one with a 28 cc target volume (abbrev., LVol) and the other with a 3 cc target volume (abbrev., SVol) were used to evaluate the impact of spot PE on clinical cases. Both targets were located at similar locations around the pituitary gland. This anatomic site was chosen because of the compact configuration and the small volumes of critical structures such as the optical pathway, which could receive an unplanned dose from spot misplacement.

#### 2.B.1. Treatment plan and simulated perturbations

For each target volume, both LSpot and SSpot were used for treatment plan calculations. The field setup consisted of two lateral fields and a multiple field algorithm was used for plan optimization. The studied SS was set to be 1 σ, i.e., 4 mm for SSpot and for 6.6 mm for LSpot. Based on the manufacturer’s recommendation and the results from the water phantom study, the maximum allowable PE for our system would be approximately 1.2 mm. The PE was therefore set to 1 mm. The resulting four plans with the configurations of LVol-SSpot, SVol-SSpot, SVol-LSpot, and LVol-LSpot, were normalized to have 100% prescribed dose covering 95% of the target volume, and the prescribed dose was 54 Gy.

The single spot error was simulated by identifying the spot with the largest MU in each of the two fields and applying a shift toward and away from the target along the x or y axis. This meant for each of the four plans, there were 16 shifted plans resulting from different combinations of the shift directions in the two fields. The PDE [ΔDmax] were compared among the four groups of shifted plans. The PDE depth profiles and the locations of PDE [ΔDmax] were summarized for one of the total 64 shifted plans, because this shifted plan...
generated the largest dose error and it was located near a critical structure.

As in the water phantom case, multiple spot error was simulated. Based on the manufacturer’s spot position specification, 5% of the total spots of a plan were programmed to be shifted. For planar systematic spot clustering error (abbr. planar systematic errors), the spots were grouped around and included the maximum MU spot in a layer; spots were shifted toward the center of this group by 1 mm. This planar clustering occurred in all layers. Finally, to demonstrate the effect in a more realistic clinical situation, random error was simulated by shifting randomly selected spots in random directions. The PDE [$\Delta D_{\text{max}}$] of planar systematic errors was calculated for $L_{\text{Vol-SSpot}}$ and the PDE [$\Delta D_{\text{max}}$] of random errors was calculated for all four configurations ($L_{\text{Vol-SSpot}}, S_{\text{Vol-SSpot}}, S_{\text{Vol-LSpot}}$). All plans were calculated with SS 0.5, 0.75, 1, 1.25, and 1.5 $\sigma$, which correspond to SS of 2, 3, 4, 5, and 6 mm for the SSpot, and 3.3, 5.0, 6.6, 8.3, and 9.9 mm for the LSpot. The PDE between the planar systematic errors and random errors for a given target volume and spot size were compared. In addition, the PDE of random errors between two target volumes and two spot sizes were compared. The dose volume statistics were used for evaluation.

3. RESULTS

3.A. Water phantom studies

3.A.1. Single spot error

The shift of spot location created a pair of hot and cold spots adjacent to the location of the shifted spot. Figure 1(b) shows the longitudinal view of the hot and cold spots in the cube-like target, and Fig. 1(c) shows the corresponding dose-difference plots.

Figure 1(d) shows an example of the defined PDE depth profile and PDE [$\Delta D_{\text{max}}$] value. The $\Delta D_{\text{max}}$ occurred (red dashed line) at almost the same location for all cases, near 90% of the distal edge. Beyond this point, substantial peaks and valleys appear in the PDE profile because of the sensitivity of the normalization to the steep dose gradient. Therefore, the data analysis excluded the PDE beyond this point.

For the plans calculated with the SSpot, linear correlations were observed between PDE [$\Delta D_{\text{max}}$] and PE. Figure 2(a) shows the PDE [$\Delta D_{\text{max}}$] against PE up to 2 mm for a given SS at a depth of 10 cm for cube 10. The solid lines represent linear fits ($R^2 > 0.98$). Larger SS yielded larger PDE for a given PE; further, as SS increased, the slopes of PDE (PE) became steeper. For example, for the plans with SS of 3 mm, the PDE increased at a rate 0.7% per mm of PE. However, if the plan was calculated with a 6-mm SS, the PDE increased at the rate of 3.1% per mm.

The correlation of PDE [$\Delta D_{\text{max}}$] with SS for a given PE followed a linear relationship as well [Fig. 2(b)]. Based on these partial correlations, the function of PDE [$\Delta D_{\text{max}}$] in the space of PE and SS can be well defined by a three-dimensional quadratic surface [Eq. (1)], where, PE and SS are in absolute unit of mm, and for cube 10, $a = -1.71 \pm 0.15$ and $b = 0.80 \pm 0.03$. Figure 2(c) shows the planar iso-PDE lines at 10 cm depth in the studied PE and SS ranges

$$\text{PDE} [\Delta D_{\text{max}}] = a' \text{PE} + b' \text{PE}^2 \text{SS}. \quad (1)$$

When the treated volume moved to greater depths, the slope of the PDE (PE, SS) surface became less steep [Fig. 2(d)]. Fit parameters in Eq. (1) were as follows: for cube15, $a = -1.39 \pm 0.16$ and $b = 0.64 \pm 0.03$; for cube20, $a = -0.97 \pm 0.08$ and $b = 0.48 \pm 0.02$.

When the LSpot was used, similar results as described above were found. Figure 2(e) compares the planar iso-PDE lines of the SSpot (solid black line) with the iso-PDE lines of the LSpot (dashed pink line). The unit of SS was converted to $\sigma$. Though PDE (PE, SS) functions were similar for both spot sizes, the PDE [$\Delta D_{\text{max}}$] of LSpot was slightly smaller over
most of the studied range. The differences became larger with increase of SS and PE. When SS was below approximately 0.7 \( \sigma \) or PE was below approximately 1 mm, the PDE of both spot sizes became almost identical. The green line in Fig. 2(e) represents the studied range in the patient cases. With the unit of SS and PE both normalized to \( \sigma \), the PDE [\( \Delta \text{Dmax} \)] of LS for PE was larger than that of SS for a given SS and PE. Figure 2(f) shows the 3D quadratic surface of LS of \( [0.5, 1.5, 2] \) and PE of \([0, 0.5, 1] \), the PDE surface of LS was above that of SS.

The derived PDE (PE, SS) functions can be expressed by Eq. (2) when PE and SS are presented in units of \( \sigma \) (indicated as PE’ and SS’ in the equation)

\[
PDE[\Delta \text{Dmax}] = a \sigma^2 \text{PE’} + b \sigma \text{PE’} \times \text{SS’},
\]

where \( a = -1.54 \pm 0.13, b = 0.44 \pm 0.01 \) for the LS on the cube 10 target at the depth of 10 cm. The reduction of the target dimension increased the dose error for a given PE and SS. For example, when the cubic target became a thin layer [Fig. 1(a)], the PDE [\( \Delta \text{Dmax} \)] increased by a factor of \( \sim 1.2 \) (SS = 4 mm; PE = 1 mm), and when the target was further reduced to a line, the PDE [\( \Delta \text{Dmax} \)] increased by a factor of \( \sim 3.3 \) over the volumetric target. Therefore, extra caution should be taken if the target is planar-like. On the other hand, the variation of field size had little effect on the PDE for volumetric targets (the largest SD of PDE [\( \Delta \text{Dmax} \)] among four studied field sizes for a SS was 0.14). This is probably because for a given location of PE spots located more than 3 \( \sigma \) away will have a negligible impact on the local dose error.

### 3.A.2. Multiple spot error

Figures 3(a)–3(c) show the misplaced spot arrangements and the dose difference distribution in the transverse plane for the three types of systematic PEs.

The impact of spot PE in the volume, planar, and linear systematic errors can be compared by determining the minimum number of shifted spots required to generate a given magnitude of PDE [\( \Delta \text{Dmax} \)]. In this example (SS = 5 mm; PE = 1 mm; SSpot), a hot spot of about 5.9% was generated. In the first scenario, 41 layers (i.e., 41 spots) were shifted. To generate the same magnitude hot spot in the second scenario (linear clustering), at least six clustered spots were necessary; in the third scenario (planar clustering), only four clustered spots were required.

As the number of misplaced spots increased, the magnitude of PDE initially increased and then saturated. For example, Fig. 3(d) shows the PDE depth profiles in the planar clustering scenario for different numbers of shifted spots. When the number of clustered spots increased from 4 to 16, the PDE increased substantially, but from 16 to 36, the PDE increased minimally. From 36 to 400, which was the total number of spots in that layer, the PDE profiles were nearly constant.

### 3.B. Patient brain plan study

#### 3.B.1. Single spot error

For PE of 1 mm and SS of 1 \( \sigma \), the mean values and the ranges of the PDE [\( \Delta \text{Dmax} \)] for the 16 shifted plans for each of four configurations (LVol-SSpot, SVol-SSpot, SVol-LSpot, and LVol-LSpot) (2.8 (1.4, 7.2), 2.7 (1.4, 5.5), 2.2 (0.7, 4.5), and 2.1 (0.8, 4.3), respectively. The PDE [\( \Delta \text{Dmax} \)] are comparable for all four configurations. For the same spot size, the PDE [\( \Delta \text{Dmax} \)] was almost the same for target volume of 28 vs 3 cc and the values of LS for SSpot were slightly smaller than those of SSSpot.

Figure 4(a) shows the PDE depth profiles for each of the two lateral fields for the shifted plan which generated the largest dose error. Because of normalization, the PDE appeared largest around the entrance, where there was no overlap of the two fields. The peak values of each field (PDE [\( \Delta \text{Dmax} \)]) were 2.7% and 7.2%, respectively. Figure 4(b) shows the absolute dose-error depth profiles for each field, with peak values of 152 cGy. Figure 4(c) shows the field setup.

In this plan, the PE in field 2 occurred near the right optic nerve. Figure 4(d) shows the sagittal image of the dose difference for this plan, where the outline of target volume is in red and the right optic nerve is in black. The inset of Fig. 4(d) shows the spot arrangement in the layer where the PE occurred. The spot brightness represents the value of MU. The largest MU spot is the brightest spot. It was shifted away from the target and toward the right optic nerve as indicated by a red arrow. Consequently, a hot spot was generated near the right optic nerve. Notice that another pair of hot and cold spot is also seen posterior to the target, which is from the PE from field 1. This pair of hot and cold spots appeared less obvious because the PE of field 1 occurred at the different sagittal location.

#### 3.B.2. Multiple spot error

Figure 5(a) shows the sagittal view of dose difference for the plan, calculated with SSpot and SS of 1 \( \sigma \) (4 mm) for
the planar systematic errors. An inner ring of hot spots surrounded by an outer ring of cold spots appears around the target volume as planar clustering propagates throughout the volume. This ring of hot and cold spots appears to varying degrees in all plans with planar systematic errors calculated with various SS (not shown). In contrast, the regular ring-shaped hot-and-cold zone was not formed when the PEs were randomized [Fig. 5(b)].

For the planar systematic errors, the dose-volume histogram (DVH) analysis shows differences for the target volume and several adjacent critical structures. For random errors, however, because the hot and cold spots were distributed throughout the target volume, no visible differences in the DVHs were observed.

Figure 5(c) compares data from the original plan with data from the shifted plan for the planar systematic errors calculated with SSpot and SS of 1 σ. Hot spots were generated in the structures near the PTV. For example, the maximum dose and mean dose to the planning target volume (PTV) were increased from 60.3 to 61.5 Gy and from 55.8 to 56.3 Gy, respectively. Maximum dose and mean dose to the left optic nerve were increased from 55.5 to 56.9 Gy and from 27.7 to 27.9 Gy, respectively. For the brain stem, however, the maximum dose increased from 60.0 to 61.1 Gy but the mean dose was reduced from 20.5 to 20.0 Gy due to the generation of cold spots.

Table I lists the values of maximum PDE [ΔDmax] for plans calculated with different SS ranging from 0.5 to 1.5 σ. For the LVol-SSpot, planar systematic error and random error are listed. For the other three configurations, the random errors are listed. Because multiple hot and cold spots were observed, the listed values correspond to the PDE [ΔDmax] of the hottest spot.

It can be seen that for the same amount of absolute PE of 1 mm and a given SS normalized by σ, the dose errors of random position error were slightly smaller for LSpot. When the SS was below 1.25 σ, the dose errors were less than approximately 2% across the board and the decrease of SS did not reduce dose errors noticeably. When the SS was above 1.25 σ, however, dose error of both random error and systematic error increased considerably. For the planar systematic errors, the dose error was 2–3 times larger than the random errors.

| Spot spacing, σ | LVol-SSpot Planar systematic error | Random error | LVol-SSpot Random error | LVol-LSpot Random error | LVol-LSpot Random error |
|-----------------|----------------------------------|--------------|------------------------|------------------------|------------------------|
| 0.5             | 2.0                              | 1.1          | 1.7                    | 1.5                    | 0.4                    |
| 0.75            | 3.3                              | 0.9          | 1.1                    | 1.0                    | 0.5                    |
| 1               | 5.4                              | 2.2          | 1.4                    | 2.2                    | 0.7                    |
| 1.25            | 5.9                              | 2.1          | 1.2                    | 0.9                    | 0.9                    |
| 1.5             | 6.4                              | 3.2          | 3.4                    | 2.5                    | 2.1                    |
4. DISCUSSION

4.A. Water phantom study

4.A.1. Single spot error

In order to have clinically relevant observations, the three cubic target geometries represent commonly treated target depths. For example, the cube10 target resembles the clinical configuration in a brain tumor treatment.

Because an appropriate SS used for planning is comparable to spot size, the range of SS studied was chosen to be between 0.5 and 1.5 $\sigma$ for both SSpot and LSpot. The studied PE ranged from 0 to 2 mm, which corresponds to the maximum value of PE of 0.5 $\sigma$ for SSpot and 0.3 $\sigma$ for LSpot. In theory, the spot can be shifted any distance and potentially beyond an adjacent spot. When PE increases to one SS or larger, the PDE [$\Delta_{\text{Dmax}}$] may not be linearly proportional to PE. Therefore, the derived PDE (SS, PE) correlations may only be accurate within the studied ranges, PE $\in [0, 0.5 \sigma]$.

The 3D quadratic surface of PDE (SS, PE) provides a guide for the safety threshold with a single value of PE. For example, if 2% is the maximum acceptable dose error, then for a given SS, the maximum allowable PE can be determined quickly by referring to the iso-PDE line [Fig. 2(c) or 2(e)] or to Eq. (1) or (2).

When the PDE for different spot sizes are compared, attention should be paid to whether the values of SS and PE are absolute or relative to the spot size. If SS is presented in the unit of $\sigma$ but PE is absolute, for the same PE and SS the PDE of LSpot is smaller, and an intersection of PDE of LSpot and SSpot can occur at the low SS or PE region [Fig. 2(e)]; if both SS and PE are normalized by $\sigma$, however, the PDE of LSpot is larger [Fig. 2(f)].

This suggests that planning with smaller SS, a larger number of spots, and smaller spot sizes would make the plan quality more robust to PE. If a single absolute value of PE is considered as a universal threshold for different spot sizes, the PDE of the smallest spot size of the system should be used for setting up the threshold, because the perturbation would be lessened with larger spot sizes if everything else such as the relative SS is kept the same. However, in practice, spot size is limited by the capability of the delivery system, and using SS that is too small would encounter other practical considerations such as spot size and treatment planning system. In Peterson’s work, the spot size was about 9 mm. Different SS ranged from 16 mm (1.8 $\sigma$) in the center to 13 mm (1.4 $\sigma$) on the edge of the target volume and varying spot MU in a layer were used for planning. The resulting PDE [$\Delta_{\text{Dmax}}$] for a PE of 1 mm was about 8%. In the current study, a constant SS was used for a given plan and the spot MU was kept the same in a layer. Considering the differences in the treatment planning and beam spot characteristics, for the largest spot size studied here (6.6 mm), the PDE [$\Delta_{\text{Dmax}}$] would be approximately 4% for a PE of 1 mm with a constant SS of 1.8 $\sigma$.

4.A.2. Multiple spot error

When clustering PE occurs, the magnitude of PDE saturates as the number of misplaced spots increases [Fig. 3(d)]. This is because the dose profile of a single spot perpendicular to the beam direction is approximately Gaussian-shaped and any effect beyond 3 $\sigma$ is negligible. The minimum number of shifted spots needed to cause dose error saturation can be estimated by the values of $\sigma$ and SS. For example, the plan shown in Fig. 3(c) had a $\sigma$ of ~4.7 mm, which means that for a SS of 5 mm at least three spots are needed to cover the distance of 3 $\sigma$ along one direction. This suggests that six shifted spots on one side (and 36 shifted spots in the plane) are necessary to saturate the dose error. The same concept applies to random multiple spot errors. The saturation of multiple spot errors means that for the worst-case scenario (i.e., PEs occurring at every spot), the induced dose error would reach a maximum limit, regardless of whether it was due to systematic or random errors.

4.B. Patient head CT study

4.B.1. Single spot error

The mean values of PDE [$\Delta_{\text{Dmax}}$] in the patient study were between 2% and 3% for all four configurations, which is higher than the water phantom case. Given the same PE of 1 mm and SS of 1 $\sigma$, PDE [$\Delta_{\text{Dmax}}$] of water phantom study would be 1.5% and 1.4% for SSpot and LSpot, respectively. In general, this difference may be attributable to spot dose modulation and the use of multiple fields in IMPT plans. The first factor increases PDE, whereas the latter decreases PDE where multiple fields overlapped. The mean values of PDE [$\Delta_{\text{Dmax}}$] were almost the same when the target volume changed from 28 to 3 cc (e.g., SSpot-LVol vs SSpot-SVol), which is consistent with field size independence observed in the water phantom study. Also, using LSpot generated lower PDE than using SSpot for a given absolute PE (e.g., SSpot-LVol vs LSpot-LVol), which agreed with the results of water phantom study [Fig. 2(e)]. Though the mean values of PDE [$\Delta_{\text{Dmax}}$] for each of the shifted plans were about 2%, the PDE [$\Delta_{\text{Dmax}}$] of a shifted plan can be much higher (7.2% in this example). This is because the shifted spot may locate where few adjacent spots are and the shifted spot has much larger MU than the rest of spots. The shift of such a heavy and semi-isolated spot would generate large dosimetric impact.

4.B.2. Multiple spot error

For a given SS, the variations of PDE [$\Delta_{\text{Dmax}}$] with two different target volumes and two spot sizes showed a similar trend as the single spot error case, which is also consistent.
with the water phantom study. In addition, the values of PDE [$\Delta D_{\text{max}}$] for random errors were similar to or less than those of a single spot error in the water phantom study. This may be because even though 5% of spots were shifted, the addition of the dose errors from multiple PEs to a local dose could be negligible since the locations of PEs were random throughout the volume and the distance between any two PEs was likely larger than 3 $\sigma$.

With planar systematic errors, a ring-shaped hot-cold zone formed directly adjacent to the target volume. This was because the spots with maximum MU are often located at the field edges, and spot clustering creates hot spots inside and cold spots outside the perturbation zone. By extension, if the spots moved systematically apart, rather than together, the inner ring would be cold and outer ring would be hot, which could also lead to notable hot spots in adjacent critical structures. Even with random errors, hot or cold spots are potentially created at the field edges, although the magnitude is much smaller.

When SS increases, whether errors were systematic or random, there was no additional advantage (reduction of dose error) when the SS was below 1.25 $\sigma$. However, the dose error increased rapidly when SS was greater than 1.25 $\sigma$. Therefore, considering system limitations, a SS of $\sim 1$ $\sigma$ appears optimal for both spot sizes of the beam line studied here, and is consistent with results from the single spot error analysis of water phantom study.

In summary, the PDE [$\Delta D_{\text{max}}$] calculated from the PDE (PE, SS) functions which are derived from the water phantom study provides a reasonable estimation for the PDE [$\Delta D_{\text{max}}$] in patients IMPT plans, but caution should be taken for the cases where spot dose modulation and spot location can result in larger PDE [$\Delta D_{\text{max}}$] at an undesired location. Therefore, the PDE (PE, SS) functions can be used for determining a universal absolute PE as a practical value for the safety threshold, but patient-specific evaluation should be considered especially for highly modulated plans and complex target geometry.

Based on this work, a spot position error threshold of 1.2 mm will be used in our facility. This value maintains a dose delivery error below 2% for the random and worst case single spot errors studied here, keeping patient-specific considerations in mind. It will be possible to reconstruct the actual delivered dose based on spot position log files. If actual dose error due to PE is deemed too large, reduction of the threshold may be considered. Conversely, if a large number of interlocks are triggered due to PE but the reconstructed delivered dose error is negligible, a larger threshold may be considered.

5. CONCLUSION

Spot positioning uncertainties are inherent in spot scanning proton therapy and will directly affect the quality of plan delivery and patient safety. An analytic tool has been developed to simulate both systematic and random spot PEs so that patient-specific evaluation can be readily accomplished and a facility-specific safety threshold for spot PE can be determined. The resulting dose errors from PEs are affected by SS, spot size, treatment depth, and surrounding spot arrangements. These variables were evaluated systematically, and the derived PDE functions provided a guide to determine a safety threshold for spot PE in routine clinical operation.

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