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Multi-Field Optimization Intensity-Modulated Proton Therapy (MFO-IMPT) for Prostate Cancer: Robustness Analysis through Simulation of Rotational and Translational Alignment Errors

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Abstract

Purpose—To evaluate the dosimetric consequences of rotational and translational alignment errors in patients receiving intensity-modulated proton therapy with multi-field optimization (MFO-IMPT) for prostate cancer.

Materials and Methods—Ten control patients with localized prostate cancer underwent treatment planning for MFO-IMPT. Rotational and translation errors were simulated along each of three axes: anterior–posterior (A-P), superior–inferior (S-I), and left–right.

Results—Clinical target volume (CTV) coverage remained high with all alignment errors simulated. Rotational errors did not result in significant rectum or bladder dose perturbations. Translational errors resulted in larger dose perturbations to the bladder and rectum. Perturbations in rectum and bladder doses were minimal for rotational errors and larger for translational errors. Rectum V45 and V70 increased most with A-P misalignment, whereas bladder V45 and V70 changed most with S-I misalignment. The bladder and rectum V45 and V70 remained acceptable even with extreme alignment errors. Even with S-I and A-P translational errors of up to 5 mm, the dosimetric profile of MFO-IMPT remained favorable.

Conclusions—MFO-IMPT for localized prostate cancer results in robust coverage of the CTV without clinically meaningful dose perturbations to normal tissue despite extreme rotational and translational alignment errors.

Keywords

proton therapy; prostate cancer; IMPT; robustness

Introduction

In spot scanning proton therapy, magnetic beam scanning technology is used to individually place monoenergetic Bragg peaks within a three-dimensional target; allowing for intensity-modulated proton therapy (IMPT) [1]. IMPT offers the promise of conformal target coverage

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by optimizing the energy fluence of spot scanning proton beams by differentiating incident proton beam energy in layers at different depths. This approach exploits the beneficial physical properties of proton beams at both the proximal and distal margins of a target, producing a highly conformal dose distribution [2]. For the treatment of prostate cancer, recent comparative dose modeling studies have demonstrated superior dose distribution to non-target tissue in the low-, medium-, and high-dose ranges with IMPT compared with intensity-modulated radiation therapy (IMRT) and passive scattering proton therapy [3–5].

When multiple beam angles are used to deliver IMPT, spot optimization can be performed for each proton beam angle independently or for all beam angles simultaneously. In IMPT using single-field optimization (SFO-IMPT), each beam is optimized individually to deliver the prescribed dose to the target while respecting the dose tolerances of normal tissue [6]. In IMPT with multi-field optimization (MFO-IMPT), all spots from all fields are optimized simultaneously. MFO-IMPT allows for superior dose distributions compared with either passively scattered proton therapy or SFO-IMPT. MFO-IMPT is also the most complex form of IMPT, where a homogenous dose distribution can be achieved within diverse geometric targets while limiting the radiation dose to normal structures near the target.

Treatment planning for proton beam therapy must consider potential sources of error inherent in all forms of external beam radiation therapy (ie. daily patient positioning reproducibility, inter-fractional anatomic changes, intra-fractional organ motion) as well as proton specific uncertainties such as intrinsic proton range uncertainty, Hounsfield unit stopping power conversions, and range degradation along the beam path. Dense tissues (i.e., bone) scatter protons more than less dense tissues[7]. All of these factors in combination create uncertainty about the actual point of dose falloff at the distal edge of a proton beam. When ultra-conformal radiation such as IMPT is used to treat prostate cancer, the combination of dose distribution uncertainty in the pelvis with a relatively steep dose gradient around the target volume underscores the importance of developing a treatment planning technique that preserves target volume coverage and normal tissue sparing despite the potential for patient misalignment. We previously described the use of a scanning target volume for SFO-IMPT treatment planning and reported on the dosimetric consequences of rotational and translational errors using this planning technique [6]. In this study, we apply this planning technique to MFO-IMPT and evaluate the fidelity of this treatment planning technique by simulating rotational and translational alignment errors.

Materials and Methods

Institutional review board (IRB) approval was waived for this dosimetric analysis.

Treatment planning technique

Ten control patients with localized prostate cancer underwent treatment planning for MFO-IMPT. For all patients, two carbon-coated zirconium dioxide fiducial markers were placed within the prostate under ultrasound guidance before computed tomography (CT) simulation. Patients were instructed to have a comfortably full bladder and all patients underwent an enema before the simulation. Bladder filling was quantified and recorded using a portable ultrasound bladder scanner (Verathon, Bothell, WA). A gas-release endorectal balloon (RadiaDyne, Houston, TX) was inflated with 60–100 mL of water to standardize rectal filling and immobilize the prostate. The patient was in the supine position, and the thighs and legs were immobilized in a leg and foot cradle. Initial scout films were obtained in the anterior–posterior and lateral directions to confirm symmetric alignment of the pelvic bones. Once the treating physician verified optimal positioning, 2.5-mm-thick CT images with three-dimensional reconstruction were obtained from L4 through the mid-femur. The entire set-up and imaging process was repeated to confirm setup reproducibility.

The acquired study sets were uploaded to the Eclipse (Varian Medical Systems, Palo Alto, CA) treatment planning system for target volume delineation, identification of organs at risk, and MFO-IMPT treatment planning.

The clinical target volume (CTV), bladder, rectum (with balloon), femoral heads, and fiducial markers were contoured by a single physician. The CTV was defined as the prostate and caudal seminal vesicle (proximal 1 cm). The rectum was defined from the ischial tuberosities to the sigmoid flexure. Gas cavities in the rectum were identified and assigned water density. A scanning target volume (STV) was generated as an expansion around the CTV as follows: 12 mm lateral, 6 mm anterior–superior–inferior, and 5 mm posterior accounting for proton range uncertainty along the proximal and distal margin of the CTV and patient set-up error. The concept of STV-based treatment planning has been empirically validated for spot-scanning proton beams and has been described previously^[6] and is consistent with IMPT treatment planning methodology described by Liu et al.^[8], Plugfelder et al.^[9], and Fredriksson et al.^[10] where proton range uncertainty and intra-fractional motion considerations are factored into the CTV expansion.

Intensity-Modulated Proton Therapy Treatment Planning

The spot scanning proton beam plans were optimized using MFO, where all spots from all fields were optimized simultaneously. Each plan consisted of opposed right and left lateral beams (gantry angles of 270° and 90°, respectively) with incident proton beam energies typically from approximately 150–200 MeV. Both fields were treated daily, with equal beam weighting. The total prescribed dose was 75.6 Gy (RBE), delivered in 42 equivalent fractions. The relative biological effectiveness (RBE) correction factor for physical to biological dose was 1.1. Treatment was designed to cover 100% of the CTV and >95% of the STV. For simplicity, the treatment planning algorithm was solely optimized for target coverage without avoidance structure inclusion. Dose distributions were calculated using a pencil beam convolution algorithm for proton beam therapy. The spot spacing was set to 0.65 times the full width at half-maximum of the spot in air at the isocenter for the maximum energy used for each lateral field. Typical spot spacing was 7 mm. Each spot position was visited once if the maximum optimized raw monitor unit for the position was <0.04. The spot was revisited if the maximum raw monitor unit was >0.04.

Simulation of setup errors

Rotational alignment errors were simulated using $\pm 3^\circ$ and $\pm 5^\circ$ symmetric rotations of each lateral beam about the original treatment axis. To simulate a $+5^\circ$ rotational setup error, the right and left lateral beam gantries were set at 275° and 95°, respectively. This process was repeated for -5° (gantry positions of 265° and 85°) and for $\pm 3^\circ$. Yaw alignment errors were simulated through table rotations of $\pm 3^\circ$ and $\pm 5^\circ$. Translational alignment errors were simulated through bidirectional 3-mm and 5-mm isocenter displacements along each of three axes: anterior–posterior (A-P), superior–inferior (S-I), and left–right (L-R). Thus, a total of 20 alignment errors were simulated for each patient. After misalignment simulation, the dose distribution of each MFO-IMPT plan was re-calculated using the control case spot delivery pattern without re-optimization. The simulated setup errors were assumed to be present for each individual fraction over the duration of the prescribed therapy.

Absolute and volumetric dose assessments for all contoured structures were recorded for the control plans and for each alignment error simulated. CTV coverage was determined by modeling the minimum CTV dose (CTV min), the maximum CTV dose (CTV max), the mean CTV dose (CTV mean), and the percentage of the CTV receiving at least the prescription dose of 75.6 Gy (RBE) (CTV V75.6). The minimum, maximum, and mean dose to the bladder and rectum were recorded, as were the percentages of each structure receiving

at least 45 Gy (RBE) (V45) and 70 Gy (RBE) (V70). Finally, the maximum dose to the femoral heads was recorded.

Statistical analysis

For each measured value, the mean and standard deviation (SD) of the percentage differences between control cases and test cases were calculated. A corrected *t*-test using Dunnett's correction for multiple comparisons was used to evaluate for statistical significance, which was defined as $p < 0.05$.

Results

Characteristics of control cases

Spot scanning proton beam parameters for MFO-IMPT delivery for the 10 control cases are listed in Table 1. The resultant dosimetric characteristics of the control cases are shown in Table 2. An example of dose modeling for a control case is shown in Figure 1.

Effect of rotational errors

CTV—Acceptable CTV coverage was maintained with all rotational misalignments simulated. There were no significant differences in dose delivery for CTV max, CTV mean, or CTV V75.6. CTV min was modestly affected by rotational setup errors; the mean percentage difference between control and test cases for all rotational errors was -0.8 (range, -1.10 to -0.44 , SD, 0.47). All CTV comparisons are shown in Table 3.

Rectum—Rotational errors of up to 5° resulted in no significant dose perturbations to rectum V70 or V45. The maximum rectum dose increased with all rotational setup errors. The mean rectum dose increased with -5° rotational error. The magnitude of the dose perturbation was small for each of these parameters. For example, with a -5° rotational error, the mean percentage difference in maximum dose to the rectum was 1.39 [absolute mean rectum maximum dose, 80.1 Gy (RBE)] and the mean percentage difference in mean rectum dose was 1.52 [absolute mean rectum mean dose, 22.2 Gy (RBE)]. All rectum comparisons are shown in Table 4.

Bladder—Dose metrics to the bladder were not significantly affected by rotational errors. The absolute value of the mean of the mean percentage differences was <1 for the bladder mean, maximum, V45, and V70. All bladder comparisons are shown in Table 5.

Femoral head—Rotational errors resulted in no significant perturbations to the maximum dose to the femoral heads. The mean maximum dose was consistently 38 Gy (RBE) with all rotational errors. No test case resulted in a maximum femoral head dose of >46 Gy (RBE).

Effect of yaw errors

CTV—CTV coverage was maintained with all yaw misalignments simulated. There were no significant differences in dose delivery for CTV max, CTV mean or CTV V75.6. CTV min was modestly affected by rotational setup errors; the mean percentage difference was -0.6 (SD, 0.34). See Table 3 for all CTV comparisons.

Rectum—Yaw errors resulted in no significant dose perturbations to rectum V70, rectum V45, or mean rectum dose. The maximum rectum dose increased with $\pm 5^\circ$ yaw error. The magnitude of the dose perturbation was small. The absolute values of the mean percentage differences for $\pm 5^\circ$ yaw error were all <1 . See Table 4 for all rectum comparisons.

Bladder—Yaw setup errors had no significant effect on bladder mean dose, maximum dose, V45, or V70. The mean bladder V70 was 6.6% (range, 2.5–11.2%) for all simulated yaw errors. See Table 5 for all bladder comparisons.

Femoral head—For all yaw errors simulated, the mean percentage difference between control and test cases in the maximum dose to the femoral heads was not significant. The mean maximum dose was consistently 38 Gy (RBE) with all yaw errors. No test case resulted in a maximum femoral head dose of >46 Gy (RBE).

Effect of translational errors

CTV—CTV dose distribution was modestly affected by translational errors of up to 5 mm. Translational errors of 3 mm did not significantly affect any CTV parameter. Translational errors of 5 mm reduced CTV V75.6 in each of the three axes evaluated. The magnitude of this reduction was minimal; no translational error produced a mean CTV V75.6 of <99%. There were no significant differences in dose delivery for CTV mean or CTV max. CTV min was reduced by 5-mm translational errors in each of the three axes analyzed. The means of the mean CTV min in absolute dose were as follows: L-R, 76.6 Gy (RBE) [range, 75.8–77.7 Gy (RBE)]; S-I, 75.8 Gy (RBE) [range, 71.2–77.6 Gy (RBE)]; and A-P, 74.7 Gy (RBE) [range, 70.9–77.4 Gy (RBE)]. A-P errors resulted in a mean percentage reduction in CTV min of up to 5.15%, although no measured CTV min value was <70 Gy (RBE) and CTV min below the prescribed dose was rare. See Table 3 for all CTV comparisons.

Rectum—As expected with an opposed lateral beam arrangement, A-P and S-I translational errors significantly affected rectal dosimetry. For example, the mean percentage difference in rectum V70 between control cases and a 5-mm posterior (–5 mm) setup error was 91.91 (SD, 9.47). A 5-mm anterior (+5 mm) setup error resulted in a mean percentage difference of –70.40 (SD, 5.63) in rectum V70. Even with a 5-mm posterior translational error, the mean rectum V70 and V45 remained acceptable, at 18.6% and 32.8%, respectively. L-R translational errors did not significantly affect rectum dosimetry. See Table 4 for all rectum comparisons. Figure 2 shows box-plot representations of the spread of data for rectum dosimetry with S-I and A-P misalignments.

Bladder—Bladder dosimetry was similarly affected by A-P and S-I translational errors. S-I misalignment produced the greatest bladder dose perturbation. For example, the mean percentage difference in bladder V70 between control cases and a 5-mm superior (+5 mm) setup error was 66.03 (SD, 14.00). A 5-mm inferior (–5 mm) setup error resulted in a mean percentage difference of –57.64 (SD, 8.49) in bladder V70. Even with a 5-mm superior translational error, the mean bladder V70 and V45 remained acceptable, at 10.9% and 18.9%, respectively. L-R translational errors did not significantly affect bladder dosimetry. See Table 5 for all bladder comparisons. Figure 3 shows box-plot representations of the spread of data for bladder dosimetry with S-I and A-P misalignments.

Femoral head—For all translational errors simulated, the mean percentage difference between test and control cases in the maximum dose to the femoral heads was not significant. The mean maximum dose was consistently 38 Gy (RBE) with all translational errors. No test case resulted in a maximum femoral head dose of >46 Gy (RBE).

Discussion

The MFO-IMPT treatment planning technique used in this study resulted in robust prescription dose coverage of the CTV even with rotational errors of up to 5° and translational errors of up to 5 mm. In this analysis of 210 MFO-IMPT treatment plans,

rotational misalignments did not result in meaningful dose perturbations to the rectum, bladder, or CTV. Translational misalignments resulted in larger dose perturbations to the bladder and rectum, an expected finding considering the opposed lateral beam arrangement. Primarily because of favorable rectum and bladder dosimetry in the control cases using MFO-IMPT, the absolute and volumetric dose profile for the rectum and bladder remained favorable even though the perturbations increased with extreme translational misalignment.

Using spot scanning proton beam technology to deliver IMPT confers certain dosimetric advantages over IMRT and passively scattered proton therapy [4,5,11,12]. IMPT improves proximal target dose conformity and enhances targeting of complex geometric targets compared with passively scattered proton therapy. Furthermore, the ability to omit patient-specific beam apertures and compensators may also confer operational advantages over passively scattered proton therapy. Although ultra-conformal treatments such as IMPT are highly attractive delivery techniques, there are legitimate concerns about the robustness of IMPT to errors in patient positioning [13–15].

In a similar analysis, we previously demonstrated SFO-IMPT treatment planning to be a robust method of IMPT delivery [6]. Although the current study was not designed to allow for direct dosimetric comparisons between SFO-IMPT and MFO-IMPT plans, the rectum and bladder dosimetry appears favorable using MFO-IMPT, with a lower bladder and rectum V45 and V70 in control cases compared with SFO-IMPT in identical targets. This would be the expected benefit of using MFO-IMPT. Similar to our original analysis of SFO-IMPT, translational errors along the A-P and S-I axes significantly affected rectum and bladder dosimetry for MFO-IMPT. This finding underscores the importance of accurate treatment verification using daily image guidance with fiducial markers and other mechanisms of reducing patient positioning to minimize the likelihood and magnitude of translational errors along these axes. The clinical significance of a consistent translational error of up to 5 mm is likely to be trivial because bladder and rectum dosimetry with MFO-IMPT remained favorable even with these translational errors. Because simultaneous field optimization might result in greater sensitivity of treatment plans to patient positioning errors along the L-R axis, we included simulated misalignment here. Misalignments of up to 5 mm along the L-R axis had no meaningful impact on dosimetry, suggesting that the currently applied lateral STV expansion is sufficient.

This study has a few limitations. We used a single planning study for each control patient to simulate each alignment error. Therefore, internal organ motion or density alterations along the beam path resulting from inter-fraction rectal gas were not accounted for as potential variables. Soukup *et al.* analyzed the sensitivity of MFO-IMPT and IMRT treatment plans to internal organ movement in four patients who underwent multiple on-treatment CT verification imaging [11]. Those authors demonstrated the complexities of IMPT treatment planning and the necessity of accounting for the possibility of tissue inhomogeneity. After reviewing a mean of 16 CT data sets per patient, with and without water equivalent density overwrite of rectal gas cavities, Soukup *et al.* observed unacceptably low total doses in the target volume for patients with rectal gas on the planning CT image. However, they observed an improvement in total equivalent uniform dose using MFO-IMPT compared with IMRT when tissue inhomogeneity overwrite was performed [11]. In our study, routine strategies such as the use of a gas-release, water-filled endorectal balloon with water equivalent density overwrite of rectal gas cavities were part of the treatment planning process to protect against the effects of such errors. Therefore, the impact of internal organ motion on tissue inhomogeneity could be considered inconsequential with respect to our results.

In conclusion, the approach to spot scanning MFO-IMPT treatment planning for localized prostate cancer used in this study results in robust coverage of the CTV without clinically meaningful dose perturbations to normal tissue even with extreme rotational or translational errors. Efforts should be made to consistently verify patient positioning when delivering MFO-IMPT to minimize dose delivery discordant with the treatment plan; most notably, A-P and S-I misalignments should be minimized when using an opposed lateral beam arrangement.

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References

1. Gillin, MT.; Sahoo, N.; Bues, M., et al. Med Phys. Vol. 37. Anderson Cancer Center, Proton Therapy Center; Houston: 2010. Commissioning of the discrete spot scanning proton beam delivery system at the University of Texas M.D.; p. 154-163.
2. Lomax AJ, Boehringer T, Coray A, et al. Intensity modulated proton therapy: a clinical example. Med Phys. 2001; 28(3):317-324. [PubMed: 11318312]
3. Dowdell SJ, Metcalfe PE, Morales JE, Jackson M, Rosenfeld AB. A comparison of proton therapy and IMRT treatment plans for prostate radiotherapy. Australas Phys Eng Sci Med. 2008; 31(4):325-331. [PubMed: 19239059]
4. Widesott L, Pierelli A, Fiorino C, et al. Helical tomotherapy vs. intensity-modulated proton therapy for whole pelvis irradiation in high-risk prostate cancer patients: dosimetric, normal tissue complication probability, and generalized equivalent uniform dose analysis. Int. J. Radiat. Oncol. Biol. Phys. 2011; 80(5):1589-1600. [PubMed: 21167651]
5. Choi S, Amin M, Palmer M, et al. Comparison of Intensity Modulated Proton Therapy (IMPT) to Passively Scattered Proton Therapy (PSPT) in the Treatment of Prostate Cancer. International Journal of Radiation Oncology*Biophysics. 2011; 81:S154-S155.
6. Meyer J, Bluett J, Amos R, et al. Spot scanning proton beam therapy for prostate cancer: treatment planning technique and analysis of consequences of rotational and translational alignment errors. Int. J. Radiat. Oncol. Biol. Phys. 2010; 78(2):428-434. [PubMed: 20100641]
7. Weber U, Kraft G. Comparison of carbon ions versus protons. Cancer J. 2009; 15(4):325-332. [PubMed: 19672150]
8. Liu W, Zhang X, Li Y, Mohan R. Robust optimization of intensity modulated proton therapy. Med Phys. 2012; 39(2):1079-1091. [PubMed: 22320818]
9. Pflugfelder D, Wilkens JJ, Oelfke U. Worst case optimization: a method to account for uncertainties in the optimization of intensity modulated proton therapy. Phys Med Biol. 2008; 53(6):1689-1700. [PubMed: 18367797]
10. Fredriksson A, Forsgren A, Hårdemark B. Minimax optimization for handling range and setup uncertainties in proton therapy. Med Phys. 2011; 38(3):1672-1684. [PubMed: 21520880]
11. Soukup M, Söhn M, Yan D, Liang J, Alber M. Study of robustness of IMPT and IMRT for prostate cancer against organ movement. Int. J. Radiat. Oncol. Biol. Phys. 2009; 75(3):941-949. [PubMed: 19801105]
12. Schwarz M, Pierelli A, Fiorino C, et al. Helical tomotherapy and intensity modulated proton therapy in the treatment of early stage prostate cancer: a treatment planning comparison. Radiother Oncol. 2011; 98(1):74-80. [PubMed: 21176983]
13. Miralbell R, Taussky D, Rinaldi O, et al. Influence of rectal volume changes during radiotherapy for prostate cancer: a predictive model for mild-to-moderate late rectal toxicity. Int. J. Radiat. Oncol. Biol. Phys. 2003; 57(5):1280-1284. [PubMed: 14630262]
14. Cella L, Lomax A, Miralbell R. Potential role of intensity modulated proton beams in prostate cancer radiotherapy. Int. J. Radiat. Oncol. Biol. Phys. 2001; 49(1):217-223. [PubMed: 11163518]

15. Albertini F, Casiraghi M, Lorentini S, Rombi B, Lomax AJ. Experimental verification of IMPT treatment plans in an anthropomorphic phantom in the presence of delivery uncertainties. *Phys Med Biol*. 2011; 56(14):4415–4431. [PubMed: 21709345]

Fig. 1.
Example of the dosimetry for a control case in sagittal and axial planes.

Fig. 2. Box-plot representation of percentage differences between control and test cases for the rectum V45 and V70 for simulated translational errors. The centerline in the box represents the median value. The top and bottom edges of the box represent the 25th and 75th percentile. The whiskers represent the range.

Fig. 3. Box-plot representation of percentage differences between control and test cases for the bladder V45 and V70 for simulated translational errors. The centerline in the box represents the median value. The top and bottom edges of the box represent the 25th and 75th percentile. The whiskers represent the range.

Table 1

Baseline beam characteristics for the 10 control cases

Characteristic	Mean value (range)
CTV, cm ³	78 (48–113)
STV, cm ³	179 (128–238)
Right beam maximum nominal energy, MeV	199 (188–209)
Right beam layers	23 (21–24)
Right beam spots	2047 (1529–2616)
Left beam maximum nominal energy, MeV	201 (196–209)
Left beam layers	22 (21–24)
Left beam spots	2023 (1520–2559)

Abbreviations: CTV = clinical target volume; STV = scanning target volume

Table 2

Baseline dosimetric characteristics for the 10 control cases

Characteristic	Mean value (range)
CTV	
Minimum, Gy(RBE)	76.6 (75.8–77.6)
Maximum, Gy(RBE)	81.0 (79.3–84.5)
Mean, Gy(RBE)	78.1 (77.5–79.1)
V75.6, %	100 (100)
Rectum	
Maximum, Gy(RBE)	79.0 (78.2–82.5)
V45, %	22.1 (16.8–27.3)
V70, %	9.7 (7.7–11.9)
Bladder	
Maximum, Gy(RBE)	80.4 (79.0–83.4)
V45, %	13.7 (6.3–19.7)
V70, %	6.7 (2.5–11.2)
Femoral head	
Maximum, Gy(RBE)	38.1 (35.7–44.5)

Abbreviations: CTV = clinical target volume; RBE = relative biological effectiveness; V_x = percentage of structure receiving x Gy(RBE).

Table 3

Effect of misalignment errors on CTV coverage

Shift	Mean percentage difference between control and test cases (SD)			
	CTV minimum	CTV maximum	CTV mean	CTV V75.6
Rotation				
+3°	-0.44 (0.47)	0.00 (0.92)	0.02 (0.08)	0.00 (0.00)
+5°	-1.00 (0.59) *	0.73 (1.2)	0.04 (0.14)	-0.14 (0.30)
-3°	-0.76 (0.29) *	0.73 (1.24)	0.01 (0.07)	-0.03 (0.09)
-5°	-1.10 (0.54) *	1.20 (1.67)	0.04 (0.13)	-0.36 (0.78)
Yaw				
+3°	-0.44 (0.39) *	0.09 (0.35)	0.00 (0.00)	-0.01 (0.03)
+5°	-0.79 (0.38) *	0.36 (0.53)	0.02 (0.06)	-0.03 (0.09)
-3°	-0.34 (0.21)	-0.02 (0.39)	0.00 (0.00)	0.00 (0.00)
-5°	-0.75 (0.37) *	0.33 (0.80)	0.02 (0.06)	-0.01 (0.03)
A-P				
+3 mm	-0.72 (0.75)	0.04 (0.39)	0.00 (0.05)	-0.01 (0.03)
+5 mm	-5.15 (1.70) *	0.13 (0.68)	-0.09 (0.06)	-0.84 (1.14) *
-3 mm	-0.19 (0.77)	0.04 (1.07)	-0.23 (0.73)	0.00 (0.00)
-5 mm	-3.89 (2.09) *	-0.11 (1.57)	-0.01 (0.10)	-0.22 (0.23)
S-I				
+3 mm	-0.11 (0.26)	-0.47 (0.93)	0.01 (0.03)	0.00 (0.00)
+5 mm	-1.36 (0.80) *	-0.56 (1.62)	0.04 (0.07)	-0.01 (0.03) *
-3 mm	-0.26 (0.28)	0.10 (0.78)	0.03 (0.05)	-0.01 (0.03)
-5 mm	-2.75 (1.71) *	0.09 (1.38)	0.01 (0.07)	-0.16 (0.18)
L-R				
+3 mm	-0.11 (0.26)	-0.47 (0.93)	0.01 (0.03)	0.00 (0.00)
+5 mm	-1.36 (0.80) *	-0.56 (1.62)	0.04 (0.07)	-0.01 (0.03)
-3 mm	-0.26 (0.28)	0.10 (0.78)	0.03 (0.05)	-0.01 (0.03)
-5 mm	-2.75 (1.71) *	0.09 (1.38)	0.01 (0.07)	-0.16 (0.18) *

Abbreviations: CTV = clinical target volume; A-P = anterior-posterior; S-I = superior-inferior; L-R = left-right; Vx = percentage of structure receiving x Gy(RBE).

* $p < 0.05$

Table 4

Effect of misalignment errors on rectum dosimetry

Shift	Mean percentage difference between control and test cases (SD)			
	Rectum mean	Rectum maximum	Rectum V45	Rectum V70
Rotation				
+3°	−0.14 (0.48)	0.70 (0.44) *	−0.33 (0.59)	−0.69 (1.70)
+5°	0.06 (0.86)	1.25 (0.63) *	−0.33 (0.96)	−0.82 (3.00)
−3°	0.70 (0.53)	1.02 (0.42) *	0.85 (0.76)	0.64 (2.18)
−5°	1.52 (0.97) *	1.39 (0.61) *	1.48 (1.13)	2.76 (4.07)
Yaw				
+3°	0.10 (0.39)	0.37 (0.79)	−0.03 (0.40)	−0.19 (1.23)
+5°	0.24 (0.68)	0.63 (0.82) *	0.10 (0.67)	−0.63 (1.95)
−3°	0.03 (0.34)	0.30 (0.82)	0.04 (0.51)	−0.27 (0.85)
−5°	0.07 (0.59)	0.18 (1.38) *	0.08 (0.59)	−0.66 (1.63)
A-P				
+3 mm	−20.26 (2.19) *	−1.14 (0.70) *	−25.77 (2.68) *	−44.78 (5.05) *
+5 mm	−33.30 (2.45) *	−2.18 (1.17) *	−42.23 (2.98) *	−70.40 (5.63) *
−3 mm	22.31 (1.83) *	1.58 (0.47) *	28.56 (2.58) *	53.26 (4.68) *
−5 mm	37.62 (3.13) *	2.36 (0.61) *	48.35 (4.22) *	91.91 (9.47) *
S-I				
+3 mm	−0.53 (1.61)	0.12 (0.45)	−1.07 (2.01)	−3.40 (3.73)
+5 mm	−1.17 (2.69)	0.41 (0.62)	−2.07 (3.51)	−5.79 (6.32) *
−3 mm	0.08 (1.52)	0.42 (0.28)	0.75 (1.75)	3.02 (3.34)
−5 mm	−0.13 (2.51)	0.78 (0.41) *	1.11 (3.02)	4.40 (5.72)
L-R				
+3 mm	0.00 (0.00)	0.00 (0.05)	0.00 (0.00)	0.00 (0.00)
+5 mm	0.00 (0.00)	−0.03 (0.07)	0.00 (0.00)	−0.08 (0.25)
−3 mm	0.00 (0.00)	0.02 (0.04)	−0.04 (0.13)	0.02 (0.43)
−5 mm	0.00 (0.00)	0.03 (0.05)	−0.04 (0.13)	0.02 (0.43)

Abbreviations: A-P = anterior–posterior; S-I = superior–inferior; L-R = left–right; Vx = percentage of structure receiving x Gy(RBE).

*
 $p < 0.05$

Table 5

Effect of misalignment errors on bladder dosimetry

Shift	Mean percentage difference between control and test cases (SD)			
	Bladder mean	Bladder maximum	Bladder V45	Bladder V70
Rotation				
+3°	0.07 (0.23)	0.51 (0.89)	−0.03 (0.50)	0.09 (0.93)
+5°	0.13 (0.49)	1.13 (1.40)	0.13 (0.85)	0.50 (1.54)
−3°	−0.11 (0.32)	0.61 (0.89)	−0.03 (0.33)	0.22 (1.42)
−5°	−0.12 (0.66)	1.02 (1.31)	−0.30 (0.83)	−0.29 (2.27)
Yaw				
+3°	0.23 (0.69)	0.37 (0.79)	0.18 (0.73)	−0.38 (2.67)
+5°	0.50 (1.20)	0.63 (0.82)	0.35 (1.40)	−0.66 (4.08)
−3°	−0.28 (0.64)	0.30 (0.82)	−0.39 (0.70)	−0.71 (2.29)
−5°	−0.44 (1.16)	0.18 (1.38)	−0.66 (1.26)	−1.65 (4.23)
A-P				
+3 mm	8.65 (1.52) *	0.39 (0.68)	10.51 (1.92) *	17.40 (4.64) *
+5 mm	14.35 (2.79) *	0.75 (1.14)	17.24 (3.52) *	28.70 (7.62) *
−3 mm	−9.67 (2.18) *	0.13 (0.67)	−11.48 (2.83) *	−18.32 (4.69) *
−5 mm	−16.37 (3.51) *	0.11 (1.11)	−19.57 (4.46) *	−31.39 (8.22) *
S-I				
+3 mm	18.89 (2.74) *	0.31 (0.42)	23.35 (3.60) *	39.00 (8.16) *
+5 mm	32.01 (4.70) *	0.70 (0.79)	39.67 (6.18) *	66.03 (14.00) *
−3 mm	−18.81 (2.85) *	−0.84 (1.37)	−22.95 (3.89) *	−36.11 (6.22) *
−5 mm	−30.43 (3.80) *	−1.22 (1.76) *	−36.98 (5.19) *	−57.64 (8.49) *
L-R				
+3 mm	0.00 (0.00)	0.01 (0.09)	0.00 (0.00)	0.00 (0.00)
+5 mm	0.00 (0.00)	0.00 (0.11)	0.07 (0.22)	−0.12 (0.38)
−3 mm	0.00 (0.00)	0.05 (0.05)	0.07 (0.22)	0.00 (0.00)
−5 mm	0.00 (0.00)	−0.11 (0.39)	0.07 (0.22)	0.10 (0.32)

Abbreviations: A-P = anterior–posterior; S-I = superior–inferior; L-R = left–right; Vx = percentage of structure receiving x Gy(RBE).

*
p < 0.05