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Original Article

Interfractional Seminal Vesicle Motion Relative to the Prostate Gland for Image-guided Radiotherapy for Prostate Cancer with/without Androgen Deprivation Therapy: A Retrospective Cohort Study

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We investigated differences in seminal vesicle (SV) length and interfractional SV motion relative to the prostate gland in prostate cancer patients. We compared 32 patients who received androgen deprivation therapy (ADT) before radiotherapy with 12 patients receiving radiotherapy alone at Okayama University Hospital in August 2008-July 2011. We examined the right and left SVs' length and motion by computed tomography (CT) to determine the ADT's effects and analyzed 347 CT scans in a multiple linear regression model. The ADT patients' SV length was significantly shorter than the non-ADT patients'. The differences in right and left SV lengths between the ADT and non-ADT patients were 6.8 mm (95% CI 2.0-11.7 mm) and 7.2 mm (95% CI 3.1-11.3 mm) respectively in an adjusted regression model. SV motion did not differ between the ADT and non-ADT patients in terms of interfractional motion of the SV tips and the SVs' center relative to the prostate gland. The ADT patients had significantly shorter SVs compared to the non-ADT patients, but no difference in SV motion was observed. SV interfractional motion should thus be compensated using the same planning margins, regardless of whether ADT is used.

Key words: prostate cancer, androgen deprivation therapy, seminal vesicle length, seminal vesicle motion, image-guided radiotherapy

Due to the advances in the biochemical detection of early prostate cancer by a simple laboratory test using prostate-specific antigen (PSA), prostate cancer is now the most commonly diagnosed cancer among men in the U.S., and likely in Europe and Japan as well [1]. In recent years, a marked increase in the number of patients with prostate cancer, especially among the elderly, has been noted [2]. Considering the increasing number of elderly patients with prostate cancer, radiotherapy (RT) has become one of the major treatment modalities.

It is well known that the volume of the otherwise untreated prostate gland shrinks during the course of androgen deprivation therapy (ADT). After 3 months of ADT, the volume of the prostate is reduced by 20-50% [3-9], and it continues to shrink up to 12 months after the beginning of ADT, albeit at a slower rate [10-15]. Therefore, the irradiated volume needed during RT and the associated side effects could be

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reduced; some authors have reported a reduction in the frequency of acute urinary and late gastrointestinal (GI) toxicities when ADT is used [16, 17].

The development and clinical introduction of image-guided RT (IGRT) has resulted in more accurate treatments of prostate cancer [18], and the risk of toxicity can thus be further reduced [19]. Many different imaging techniques can be used for prostate cancer, such as ultrasonography, portal imaging, megavolt computed tomography (CT), in-room CT, cone beam CT, in-room magnetic resonance imaging (MRI), and four-dimensional marker-based localization systems such as Calypso [18]. For prostate localization, registration techniques can be based on the registration of implanted fiducial markers, delineations, or soft tissue [20-22].

For patients with intermediate- and high-risk prostate cancer, the seminal vesicles (SVs) are usually involved and are included in the clinical target volume [23]. Irradiation of the SVs has been shown to improve the overall and biochemical survival for these groups of patients [24]. However, for prostate treatment that includes the SVs, margin reduction is limited to a large extent by the mobility of the SVs, as they may become deformed and/or move to a certain extent relative to the prostate gland. Several reports showed interfractional motion characteristics of the SV relative to the prostate [20, 25-27]. To our knowledge, there has been no report on the differences in SV motion relative to the prostate gland during RT with or without ADT. In addition, although there are a few reports that the SV volume is reduced by ADT [28, 29], there has been no report on changes in SV length. If the SV length can be shortened by ADT, the mobility of the SV may also decrease, thus potentially leading to reductions in the irradiated volume and side effects.

In the present retrospective analysis, we investigated differences in SV length and SV interfractional motion relative to the prostate gland in prostate cancer patients who have undergone RT with or without ADT.

Materials and Methods

Patients. The cases of 44 consecutive patients who met our inclusion criteria and who underwent 3D-conformal RT or intensity-modulated radiotherapy (IMRT) at the Department of Radiology, Okayama University Hospital between August 2008 and July 2011 were retrospectively analyzed in this study. The inclusion criteria were: (1) no previous surgery or trans-urethral resection of the prostate, (2) the availability of clinical information concerning ADT, and (3) the presence of at least one calcified nodule in the prostate gland. All patients had biopsy-proven prostate carcinoma (T1c-3b) and underwent 3D-conformal RT or inversely planned "step-and-shoot" IMRT at 10 MeV photon energy. The median total doses were 72 Gy in 36 fractions.

Our study's protocol was approved by the Ethics Committee and Institutional Review Board of Okayama University Hospital (ID no. 1738). All patients were informed about the risks and benefits of treatment, agreed to have their cases analyzed, and provided written informed consent.

Androgen deprivation therapy. In this study, we compared a group of 32 patients who underwent ADT to reduce the prostate size prior to RT with a group of 12 patients who underwent RT alone. The ADT group was treated primarily with a luteinizing hormone-releasing agonist plus an anti-androgen agent. ADT was administered for a mean of 12.2 months (range 4.9-47.2 months) before the RT.

Data acquisition. All of the patients underwent a simulation CT scan in the supine position for treatment planning 1-1.5hr after urination to ensure a distended bladder during simulation, but no instructions were given on bowel emptying, diet, or laxative use. The patients were immobilized using a HIP-FIX system (CIVCO Medical Solutions, Orange City, IA, USA).

A pelvic simulation CT scan was performed without the use of oral or intravenous contrast material, so that the planning scan could be directly compared with the non-contrast CT scans performed during the treatment course. All patients were treated using a commercially available integrated CT-LINAC system (FOCAL unit, Toshiba Medical Systems, Tokyo, Japan), which allowed for convenient CT imaging during the daily RT session with the patient immobilized in the treatment position. Before each CT scan, the patient was aligned using skin marks drawn during the simulation, and the CT scans were always performed just before the daily treatments throughout the RT course. All CT scans (including the planning CT scan) were performed without contrast using 1-mm axial slices throughout the imaged area (Asteion Super 4 Edition, Toshiba Medical Systems). To minimize daily variations in bladder dis-

tension, the simulated conditions were maintained.

The acquired CT scans were imported into the Pinnacle^3 treatment planning system (Philips Medical Systems, Andover, MA, USA). Seven to eight time points were chosen for each patient (planning CT and CT during treatment on days 5, 10, 15, 20, 25, 30, and 35; total, 347 CT scans). There was no primary time point of interest. Among the total of 347 CT scans, 253 CT scans were in the ADT group and 94 CT scans were in the non-ADT group.

The prostate gland, bilateral SVs, bladder, and rectum were manually contoured on the axial images for CT scans from the slice level of 1.5 cm above the SV tip to the slice level 1.5 cm below the prostate apex or anal verge. Points of interest were set manually at the seminal base and bilateral SV tips. The center of the SV was determined as the center of 3 slices volume in the cranio-caudal direction in the middle of the SV [26]. We calculated the average rectal and bladder cross-sectional areas (CSAs) by dividing the total rectal and bladder volume by the rectal and bladder length. We calculated the length of each right and left SV by summing the distance from the seminal base to the center of the SV and the distance from the center of the SV to the SV tip.

Organ motion. We measured the SV motion by first identifying a calcified nodule in the prostate gland on the planning CT. The calcified nodule on the planning CT was then jointly registered to the calcified nodule at the same position in the daily CT scan, based on chamfer matching, by obtaining translations in three dimensions. For this study, the registrations were limited to translations only, because we simulated only the standard couch shift to correct the interfractional motions.

To quantify the positional shift for each point (bilateral SV tips and bilateral SV centers) during treatment, we calculated the change in the position of each point relative to those on the planning CT in each direction (x-axis: lateral; y-axis: anterioposterior; z-axis: superio-inferior). We defined the anterior shifts, inferior shifts, and left displacements as positive values, and we defined the posterior shifts, superior shifts, and right displacements as negative values.

Statistical analysis. We first examined the patients' clinical characteristics based on their ADT status. The variables were compared using an unpaired *t*-test for continuous variables and the chi-squared test for categorical variables. We also examined the effect of ADT on the length and motion of the bilateral SVs. The SV lengths were examined separately for the left and right sides. The motions of the bilateral SV tips and bilateral SV centers were examined based on the x-axis (left), y-axis (left), z-axis (left), and the x-axis (right), y-axis (right), and z-axis (right). The motion values were transformed to absolute values because we examined the magnitude of motion. We then employed a multiple linear regression analysis to examine the effect of ADT. After establishing a crude model, we adjusted for potentially confounding factors, as follows: bladder volume (per 10 cm^3), rectum volume (per 10 cm^3), average bladder CSA (per 10 cm^3), average rectum CSA (per 10 cm^3), T factor ($<$3a or $>$3b), and age (per decade).

We used generalized estimating equations (GEEs) to evaluate potential correlations between intra-patient measurements. By using GEEs, we investigate whether the results can be adapted to each patient. We used a measurement as a unit of analysis in the GEE analysis. The GEE models were estimated using an exchangeable correlation matrix with robust standard errors [30], and the correlation (ρ) in each model was calculated. We estimated coefficients and 95% confidence intervals (CIs). Statistical significance was set at $p < 0.05$ (two-sided). All analyses were conducted using the statistical software package Stata12 (StataCorp, College Station, TX, USA).

Results

Patient characteristic. The background comparisons were made based on the ADT status. Significant findings were higher T stage, lower bladder volume, and wider average rectum CSA in the ADT compared to the non-ADT group (Table 1).

SV length. Table 2 shows the results for the length of the right and left SVs. The SV length was significantly shorter in the patients who received ADT. There were no significant differences between the two patient groups for the other factors. High correlations in the total series of patients were observed ($\rho = 0.9/0.8$ in right/left SV lengths, respectively).

Interfractional variability in SV position relative to the prostate gland. Tables 3 and 4 show the results of our analysis of the motion of the bilateral SV tips. No significant differences were found between the ADT and

Table 1 Patient characteristics, Okayama, Japan (2008–2011)

	ADT (+)[1] n = 32		ADT (−)[2] n = 12		*p*-value
	n	%	n	%	
Measured 7 times	3	9.4	1	8.3	0.91
Measured 8 times	29	90.6	11	91.7	
T factor					
1c	1	3.1	5	41.7	<0.01
2a	4	12.5	4	33.3	
2b	3	9.4	1	8.3	
2c	7	21.9	2	16.7	
3a	12	37.5	0	0.0	
3b	5	15.6	0	0.0	
	Mean	SD	Mean	SD	*p*-value
Age (years)	71.1	6.2	67.8	6.9	0.13
Bladder volume (cm^3)	124.4	46.5	138.1	51.6	0.02
Rectum volume (cm^3)	51.4	20.8	48.1	20.8	0.20
Average bladder CSA (cm^2)	29.9	9.3	30.4	10.4	0.72
Average rectum CSA (cm^2)	6.2	2.6	5.3	2.2	<0.01
Radiotherapy duration (days)	53.3	2.1	53.8	2.4	0.56
ADT duration (months)	12.2	8.6	−	−	

ADT, androgen deprivation therapy; SD, standard deviation; CSA, cross-sectional area.
[1]Patients who received androgen deprivation therapy prior to radiotherapy. [2]Patients who received radiotherapy alone.
ADT group: 253 measurements ($3 \times 7 + 29 \times 8 = 253$). Non-ADT group: 94 measurements ($1 \times 7 + 11 \times 8 = 94$).
Chi-squared tests were used for the analysis of the categorical variable. Unpaired *t*-tests were used for the analysis of the continuous variable.

Table 2 Regression analysis results for the difference in length of the right and left seminal vesicles, Okayama, Japan (2008–2011)

	Right			
	Crude model		Adjusted model	
	Estimate (mm)	95% CI	Estimate (mm)	95% CI
ADT (non-ADT as reference)	−6.1	−10.1 to −2.1*	−6.8	−11.7 to −1.9*
Bladder volume (per 10 cm^3)			0.1	−0.2 to 0.4
Rectum volume (per 10 cm^3)			0.4	−0.8 to 1.6
Average bladder CSA (per 10 cm^2)			−0.1	−1.4 to 1.3
Average rectum CSA (per 10 cm^2)			−2.3	−14.1 to 9.5
Severe T factor (< 3a/> 3b)			0.7	−3.4 to 4.8
Age (per decade)			1.6	−1.3 to 4.4
ρ (rho)		0.9		0.9

	Left			
	Crude model		Adjusted model	
	Estimate	95% CI	Estimate	95% CI
ADT (non-ADT as reference)	−5.7	−9.1 to −2.4*	−7.2	−11.3 to −3.1*
Bladder volume (per 10 cm^3)			0.0	−0.3 to 0.3
Rectum volume (per 10 cm^3)			−0.1	−2.1 to 1.8
Average bladder CSA (per 10 cm^2)			0.7	−0.7 to 2.1
Average rectum CSA (per 10 cm^2)			3.7	−15.0 to 22.3
Severe T factor (< 3a/> 3b)			2.2	−1.2 to 5.6
Age (per decade)			0.3	−2.2 to 2.7
ρ (rho)		0.8		0.8

ADT, androgen deprivation therapy; CI, confidence interval; CSA, cross-sectional area.
*Statistically significant ($p < 0.05$)

Table 3 Regression analysis results for the motion of the right seminal vesicle tip, Okayama, Japan (2008–2011)

	Crude model		Adjusted model	
	Estimate (mm)	95% CI	Estimate (mm)	95% CI
X-axis				
ADT (non-ADT as reference)	−1.4	−3.7 to 0.9	−1.7	−4.3 to 0.9
Bladder volume (per 10 cm^3)			0.1	−0.1 to 0.4
Rectum volume (per 10 cm^3)			−0.6	−2.2 to 1.0
Average bladder CSA (per 10 cm^2)			−0.6	−1.7 to 0.6
Average rectum CSA (per 10 cm^2)			6.6	−7.0 to 20.3
Severe T factor (< 3a/> 3b)			0.1	−0.8 to 1.0
Age (per decade)			0.3	−0.5 to 1.1
ρ (rho)	0.6		0.6	
Y-axis				
ADT (non-ADT as reference)	0.3	−2.3 to 2.8	1.4	−0.7 to 3.6
Bladder volume (per 10 cm^3)			0.0	−0.4 to 0.5
Rectum volume (per 10 cm^3)			1.0	−0.7 to 2.7
Average bladder CSA (per 10 cm^2)			−0.7	−2.6 to 1.2
Average rectum CSA (per 10 cm^2)			−5.8	−19.9 to 8.4
Severe T factor (< 3a/> 3b)			−1.2	−2.9 to 0.5
Age (per decade)			−1.0	−2.9 to 0.9
ρ (rho)	0.6		0.6	
Z-axis				
ADT (non-ADT as reference)	−0.3	−1.2 to 0.6	−0.3	−1.2 to 0.6
Bladder volume (per 10 cm^3)			−0.1	−0.2 to 0.1
Rectum volume (per 10 cm^3)			0.1	−0.6 to 0.7
Average bladder CSA (per 10 cm^2)			0.1	−0.6 to 0.9
Average rectum CSA (per 10 cm^2)			0.4	−5.0 to 5.9
Severe T factor (< 3a/> 3b)			0.0	−0.9 to 0.9
Age (per decade)			−0.3	−1.1 to 0.4
ρ (rho)	0.3		0.3	

ADT, androgen deprivation therapy; CI, confidence interval; CSA, cross-sectional area.

non-ADT groups in the motion of the right and left SV tips in any axis, in either the crude or the adjusted model. A not-very high correlation in the total series of patients was observed (ρ = 0.3-0.6/0.3-0.5 in right/left SV tips motion, respectively).

Tables 5 and 6 show the results of the analysis of motion of the center of bilateral SVs. No significant differences were found in the motion of the center of the right or left SVs in any axis in the crude model. In the adjusted model, the correlation between the rectum volume and the motion of the center of the right SV (y-axis) and the correlation between the rectum volume/average CSA and the motion of the center of the left SV (x-axis). A not-very high correlation in the total series of patients was observed (ρ = 0.2-0.6/0.3-0.5 in the center of the right/left SV motions, respectively).

Discussion

We analyzed the differences in the length of the SVs in patients who underwent RT with or without ADT using in-room CT, and our findings revealed that the patients who underwent ADT had significantly shorter SVs compared to those who underwent ADT. The shorter SVs can contribute to a decrease in irradiation volume, especially for locally advanced prostate cancer patients, and they may contribute to the reduction of harmful side effects caused by the irradiation.

To our knowledge, there has been no report on the differences in SV motion relative to the prostate gland during RT with or without ADT. We thus analyzed the differences in SV movement in patients who did or did not undergo ADT, using in-room CT, based on the hypothesis that shorter SVs have less mobility. We found that SV mobility was not different between the ADT and non-ADT groups, but the mobility was affected by the rectum change, which is consistent with a previous report [27].

With regard to changes in the SVs, to our knowledge, there have been only two reports stating that

Table 4 Regression analysis results for the motion of the left seminal vesicle tip, Okayama, Japan (2008–2011)

	Crude model		Adjusted model	
	Estimate (mm)	95% CI	Estimate (mm)	95% CI
X-axis				
ADT (non-ADT as reference)	−0.9	−2.3 to 0.4	−1.2	−2.7 to 0.4
Bladder volume (per 10 cm^3)			0.1	−0.2 to 0.5
Rectum volume (per 10 cm^3)			−0.7	−1.9 to 0.6
Average bladder CSA (per 10 cm^2)			−0.5	−2.1 to 1.2
Average rectum CSA (per 10 cm^2)			4.3	−7.4 to 16.0
Severe T factor (< 3a/> 3b)			2.6	−1.1 to 1.6
Age (per decade)			0.3	−0.6 to 1.3
ρ (rho)	0.5		0.5	
Y-axis				
ADT (non-ADT as reference)	0.2	−1.4 to 1.9	0.9	−0.7 to 2.5
Bladder volume (per 10 cm^3)			0.1	−0.2 to 0.4
Rectum volume (per 10 cm^3)			−0.1	−1.4 to 1.3
Average bladder CSA (per 10 cm^2)			−0.6	−2.0 to 0.8
Average rectum CSA (per 10 cm^2)			1.2	−10.0 to 12.4
Severe T factor (< 3a/> 3b)			−0.8	−2.2 to 0.6
Age (per decade)			−0.7	−1.9 to 0.5
ρ (rho)	0.3		0.3	
Z-axis				
ADT (non-ADT as reference)	−0.1	−1.6 to 1.3	−0.4	−1.9 to 1.1
Bladder volume (per 10 cm^3)			−0.1	−0.3 to 0.1
Rectum volume (per 10 cm^3)			−0.2	−1.2 to 0.7
Average bladder CSA (per 10 cm^2)			0.3	−0.7 to 1.3
Average rectum CSA (per 10 cm^2)			3.2	−5.9 to 12.2
Severe T factor (< 3a/> 3b)			0.0	−1.4 to 1.4
Age (per decade)			−0.1	−1.2 to 1.1
ρ (rho)	0.6		0.5	

ADT, androgen deprivation therapy; CI, confidence interval; CSA, cross-sectional area.

human SVs shrink with androgen ablation [28, 29], and there has been no report on the change in SV length. Terasaki *et al.* showed that the decrease in the mean maximum horizontal area was 36% at 4 months and that it changed in parallel with the serum testosterone level [28]. Furuya *et al.* showed through transrectal ultrasonography that the reduction in SV volume was 32.4% between the baseline values and 3-6 months after ADT [29].

Several reports have described the interfractional motion characteristics of the SVs relative to the prostate. Frank *et al.* observed that the variability in SV displacement appeared to be greater than the variability in prostate displacement with respect to bony anatomy [27]. van der Wielen *et al.* found that the deformation of the seminal vesicles relative to intraprostatic markers was significant (SD ≤ 3 mm). Consequently, the effect on treatment planning margins for prostate rotation corrections was small [20].

Jian *et al.* reported that the SVs can move independently from the prostate, and the motion magnitude is larger in the anterioposterior direction. A minimum margin of 4.5 mm to the SV was recommended for IMRT with prostate-only guidance [25]. Smitsmans *et al.* demonstrated that residual SV displacement that was not captured by the marker position is quite large (2-3 mm) in the anterioposterior direction in marker-based IGRT. Therefore, correcting for rotations is not advisable when the SVs are part of the target volume, and the margin design for SVs should take these uncertainties into account [26].

Several authors have already reported that ADT reduces the rate of harmful side effects by decreasing the irradiation volume needed for RT for prostate cancer patients [16, 17]. In fact, it is the reduction in prostatic volume caused by ADT that enables the reduced irradiation volume. The results of the present study clearly demonstrated that the patients who were treated with ADT had significantly shorter SVs compared to those who did not undergo ADT. A high correlation

Table 5 Regression analysis results for the motion of the center of the right seminal vesicle, Okayama, Japan (2008–2011)

	Crude model		Adjusted model	
	Estimate (mm)	95% CI	Estimate (mm)	95% CI
X-axis				
ADT (non-ADT as reference)	−0.1	−0.9 to 0.6	−0.6	−1.4 to 0.2
Bladder volume (per 10 cm^3)			0.0	−0.1 to 0.1
Rectum volume (per 10 cm^3)			−0.3	−0.7 to 0.1
Average bladder CSA (per 10 cm^2)			0.0	−0.8 to 0.7
Average rectum CSA (per 10 cm^2)			3.0	−0.7 to 6.7
Severe T factor (< 3a/> 3b)			0.3	−0.5 to 1.1
Age (per decade)			0.5	0.0 to 1.0
ρ (rho)	0.5		0.5	
Y-axis				
ADT (non-ADT as reference)	−0.1	−2.1 to 2.0	0.4	−1.4 to 2.2
Bladder volume (per 10 cm^3)			−0.1	−0.3 to 0.2
Rectum volume (per 10 cm^3)			1.2	0.1 to 2.2*
Average bladder CSA (per 10 cm^2)			0.1	−1.0 to 1.2
Average rectum CSA (per 10 cm^2)			−6.6	−15.9 to 2.7
Severe T factor (< 3a/> 3b)			−0.5	−1.8 to 0.9
Age (per decade)			−0.4	−2.0 to 1.2
ρ (rho)	0.6		0.6	
Z-axis				
ADT (non-ADT as reference)	−0.4	−0.9 to 0.1	−0.5	−1.0 to 0.0
Bladder volume (per 10 cm^3)			0.0	−0.1 to 0.0
Rectum volume (per 10 cm^3)			0.2	−0.1 to 0.6
Average bladder CSA (per 10 cm^2)			0.1	−0.2 to 0.5
Average rectum CSA (per 10 cm^2)			−1.7	−4.3 to 1.0
Severe T factor (< 3a/> 3b)			0.2	−0.2 to 0.6
Age (per decade)			−0.1	−0.5 to 0.2
ρ (rho)	0.2		0.2	

ADT, androgen deprivation therapy; CI, confidence interval; CSA, cross-sectional area.

regarding the bilateral SV length was observed, which is not unexpected because the SV length should not change at each measurement point in each patient. This shortening would lead to a reduced irradiation volume for RT in prostate cancer cases that include a seminal vesicle in the irradiation range, such as in cases of locally advanced prostate cancer.

On the other hand, according to previous reports, it is necessary to consider the SV mobility relative to the prostate when setting the irradiation volume in IGRT [20,25-27]. We hypothesized that the SV movement would be reduced if the SV was shortened by ADT; however, we observed no difference in SV movement, and the SV movement was affected further by factors such as the state of the rectum. A not-very strong correlation was observed regarding SV motion, which indicated that the trend of SV motion was not constant in each patient. We therefore recommend that the interfractional motion of SVs should be compensated for by using the same planning margins whether or not ADT is used when determining the irradiation volume.

One of the limitations of our study is that one or more other unmeasured/unknown confounders (*i.e.*, body mass index [BMI] and abdominal circumference [31]) between the ADT and non-ADT groups may have influenced the length and mobility of the SVs. We did not collect the patients' BMI or abdominal circumference data, due to a loss of data. Another limitation is that the SV length and extent of motion were measured based on CT images. Studies based on MRI in which the anatomic structure contrast is high are more precise. In addition, the registrations were performed using a calcified nodule in the prostate gland, likely by employing implanted fiducial markers; however, the registrations were limited to translations only because we simulated only the standard couch shift to correct interfractional motions. With this method, the deformation and rotation of the prostate during daily treatment is not considered. The analyzed data were taken from patients who visited the university hospital, and

Table 6 Regression analysis results for the motion of the center of the left seminal vesicle, Okayama, Japan (2008–2011)

	Crude model		Adjusted model	
	Estimate (mm)	95% CI	Estimate(mm)	95% CI
X-axis				
ADT (non-ADT as reference)	0.5	0.0 to 1.0	0.5	−0.3 to 1.3
Bladder volume (per 10 cm^3)			0.1	0.0 to 0.2
Rectum volume (per 10 cm^3)			−0.5	−0.9 to −0.1*
Average bladder CSA (per 10 cm^2)			−0.4	−1.0 to 0.1
Average rectum CSA (per 10 cm^2)			4.3	0.8 to 7.8*
Severe T factor (< 3a/> 3b)			−0.2	−0.9 to 0.5
Age (per decade)			−0.1	−0.4 to 0.3
ρ (rho)	0.3		0.3	
Y-axis				
ADT (non-ADT as reference)	−0.6	−2.2 to 1.0	−0.3	−1.6 to 1.0
Bladder volume (per 10 cm^3)			−0.1	−0.3 to 0.2
Rectum volume (per 10 cm^3)			0.3	−0.7 to 1.4
Average bladder CSA (per 10 cm^2)			0.0	−1.2 to 1.1
Average rectum CSA (per 10 cm^2)			−0.6	−9.8 to 8.6
Severe T factor (< 3a/> 3b)			−0.4	−1.5 to 0.6
Age (per decade)			−0.6	−1.7 to 0.5
ρ (rho)	0.5		0.5	
Z-axis				
ADT (non-ADT as reference)	0.0	−0.6 to 0.6	−0.4	−1.1 to 0.3
Bladder volume (per 10 cm^3)			−0.1	−0.1 to 0.0
Rectum volume (per 10 cm^3)			0.0	−0.4 to 0.4
Average bladder CSA (per 10 cm^2)			0.2	−0.2 to 0.7
Average rectum CSA (per 10 cm^2)			0.8	−3.2 to 4.8
Severe T factor (< 3a/> 3b)			0.4	−0.3 to 1.0
Age (per decade)			0.2	−0.3 to 0.7
ρ (rho)	0.5		0.4	

ADT, androgen deprivation therapy; CI, confidence interval; CSA, cross-sectional area.

thus the possibility remains that the backgrounds of the patients were different from those of the patients who visited general hospitals. It may thus be questionable to interpret our results as generalized. These limitations should be addressed in future studies. It is difficult to perform a randomized controlled study from the ethical point of view, because ADT reduces the rate of harmful side effects for prostate cancer patients. A propensity score analysis in which the confounding factors evaluated in this study, BMI, and abdominal circumference are well adjusted should thus be performed.

In conclusion, the patients who underwent ADT had significantly shorter SVs compared to the patients who did not undergo ADT. No differences in SV movement were observed between these groups. Compensation for the interfractional motion of SVs should thus use the same planning margins whether or not ADT is used with RT.

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