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Scientific Article

Factors Affecting Prostate Displacement During Volumetric Modulated Arc Therapy in Prone Position After High-Dose-Rate Brachytherapy for Prostate Cancer

Takayuki Sakurai, MD, PhD,[a,]* Shigeyuki Takamatsu, MD, PhD,[a] Satoshi Shibata, MD, PhD,[a] Risako Minamikawa, MD,[a] Masahiro Yamazaki, MD,[a] Hironori Kojima, PhD,[b] Kimiya Noto, PhD,[b] Tomoyuki Makino, MD, PhD,[c] Shohei Kawaguchi, MD, PhD,[c] Takahiro Nohara, MD, PhD,[c] Atsushi Mizokami, MD, PhD,[c] and Toshifumi Gabata, MD, PhD[a]

[a]*Department of Radiology, Graduate School of Medicine, Kanazawa University, Kanazawa, Ishikawa, Japan;* [b]*Department of Radiology, Kanazawa University Hospital, Kanazawa, Ishikawa, Japan; and* [c]*Department of Integrative Cancer Therapy and Urology, Graduate School of Medicine, Kanazawa University, Kanazawa, Ishikawa, Japan*

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Purpose: In irradiating the prostate and pelvic lymph node regions, registration based on bony structures matches the pelvic lymph node regions but not necessarily the prostate position, and it is important to identify factors that influence prostate displacement. Therefore, we investigated factors influencing prostate displacement during volumetric modulated arc therapy after single-fraction high-dose-rate brachytherapy (HDR-BT) for prostate cancer and the trends in displacement for each fraction.

Methods and Materials: Seventy patients who underwent pelvic volumetric modulated arc therapy of 46 Gy in the prone position 15 days after 13 Gy HDR-BT were included. Prostate displacement relative to bony structures was calculated using cone beam computed tomography. Systematic error (SE) and random error (RE) were evaluated in the right-left (RL), craniocaudal (CC), and anteroposterior (AP) directions. The association with clinical and anatomic factors on the planning computed tomography or magnetic resonance imaging was analyzed. Prostate volume change (PVC) was defined as the volume change at 2 days after HDR-BT. Displacement trends were individually examined from the first to 23rd fractions.

Results: The mean SE in the RL, CC, and AP directions was −0.01 mm, −2.34 mm, and −0.47 mm, respectively. The root mean square of the RE in the RL, CC, and AP directions was 0.44 mm, 1.14 mm, and 1.10 mm, respectively. SE in the CC direction was independently associated with bladder volume ($P = .021$, t statistic = 2.352) and PVC ($P < .001$, t statistic = −8.526). SE in the AP direction was independently associated with bladder volume ($P = .013$, t statistic = −2.553), PVC ($P < .001$, t statistic = 5.477), and rectal mean area ($P = .008$, t statistic = 2.743). RE in the CC direction was independently associated with smoking ($P = .035$). RE in the AP direction was associated with PVC ($P = .043$). Gradual displacement caudally and posteriorly occurred during the irradiation period.

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*Corresponding author: Takayuki Sakurai, MD, PhD; E-mail: tkyk81@gmail.com

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Conclusions: Anatomic characteristics of the bladder, rectum, and prostate predict SE. Smoking and PVC predict RE. In particular, whether PVC is ≥140% affects setting internal margins.

Introduction

Brachytherapy combined with external beam radiation therapy (EBRT), recommended by the National Comprehensive Cancer Network guidelines (version 4.2022) for high-risk and very-high-risk prostate cancer, is a treatment modality that has better biochemical control than other radiation therapy modalities.[1] EBRT to the pelvic lymph node regions (PLNs) should be considered in high-risk and very-high-risk disease and administered in regional-risk disease.[1] Intensity modulated radiation therapy (IMRT) techniques have improved pelvic EBRT by reducing the dose to organs at risk (OAR) without compromising the dose to the targets and by reducing toxicity.[2-5] In pelvic EBRT using IMRT, registration based on the bony structure by image guided radiation therapy (IGRT) is preferred to match the PLNs and reduce the dose to the small intestine.[6] However, the interfractional organ motion of the prostate and that of the PLNs are not correlated.[7] In particular, registration based on bony structures will match the PLNs but not necessarily the prostate position. Therefore, achieving a high degree of reproducibility in the relative positioning of the prostate to bony structures and understanding prostate displacement and its associated factors to establish optimal internal margins for the prostate are important.

Various studies[8-12] have reported anatomic changes in the bladder and/or rectum during the irradiation period as factors influencing prostate displacement. However, these factors cannot be evaluated before initiating EBRT. Factors that can be evaluated before initiating EBRT include the body mass index (BMI) as a clinical factor and the rectal volume or area on the planning computed tomography (CT) as an anatomic characteristic.[13-17] Higher BMI may decrease prostate displacement,[13,15,17] possibly because visceral fat compresses and immobilizes the prostate to the pelvic floor. Large rectal volume on the planning CT affects prostate displacement toward the rectal side during the irradiation period,[16] and a larger rectal mean area on the planning CT requires a larger margin on the rectal side of the prostate.[15] Rectal volume on the planning CT can predict changes in rectal volume and prostate displacement during the irradiation period.[14] However, previous studies report findings obtained with patients in the supine position. EBRT administered with the patient in the prone position is useful for rectal sparing and reducing the rectal dose.[2,18,19] Furthermore, it has been reported that the use of a belly board can suppress respiratory motion,[20] which is a problem in the prone position, and improve reproducibility and reduce the dose to OAR.[2,21] In the prone position, rectal and bladder volume changes during the irradiation period are factors of prostate displacement.[9,22] However, these factors cannot be evaluated before initiating EBRT. No study has investigated the influence of clinical factors and anatomic characteristics on prostate displacement in the prone position that can be evaluated on the planning CT before EBRT. Furthermore, these factors in EBRT after brachytherapy have not been reported. Factors affecting prostate displacement in prone-position EBRT after brachytherapy that can be evaluated before EBRT are still unknown and require clarification.

We have performed 13-Gy single-fraction high-dose-rate brachytherapy (HDR-BT), followed by pelvic EBRT of 46 Gy in 23 fractions, with patients in the prone position using the volumetric modulated arc radiation therapy (VMAT) technique for high-risk or higher-risk prostate cancer. This protocol has good biochemical progression-free survival and safety.[23-25] The aim of this study was to investigate the clinical factors and anatomic characteristics of the planning CT or magnetic resonance imaging (MRI) that influence prostate displacement and assess the prostate displacement trends for each fraction from the first to 23rd fractions.

Methods and Materials

Study design and patients

This retrospective study was approved by the appropriate institutional review board (approval No. 2022-003 [113989]) and was conducted according to the tenets of the Declaration of Helsinki. Patients with prostate cancer who underwent 13-Gy single-fraction HDR-BT with iridium 192 between January 2019 and May 2022 were included in the analysis. Patients who received EBRT at other institutions after HDR-BT or who received EBRT in the supine position at our institution were excluded. Finally, 70 patients were included in the analysis.

Radiation therapy protocol

Day 0

Single-fraction HDR-BT of 13 Gy was administered, as previously reported.[24] Three fiducial markers (diameter × length: 0.9 × 3.0 mm; CIVCO Radiotherapy, Coralville, IA), used as indicators of the prostate position, were implanted in the prostate (2 implants in the base and 1 implant in the posterior apex).

Day 3

Planning CT images (Aquilion LB scanner; Canon Medical Systems, Otawara, Japan) of 2-mm slice thickness were obtained. The contouring method used was previously reported.[24] The prostate plus 3 mm and the seminal vesicle comprised the clinical target volume (CTV), and the planning target volume (PTV) margin was 8 mm (5 mm only on the rectal side). The PLNs were also a CTV, and the PTV margin for the PLNs was 5 mm.

Day 15

VMAT of 46 Gy in 23 fractions was started. The linear accelerator was the Elekta Infinity scanner (Elekta AB, Stockholm, Sweden).

To ensure the reproducibility of the bladder and rectal contents, patients were instructed to defecate and urinate and to drink 200 mL of water 30 minutes before the planning CT and irradiation. After July 2021, patients were premedicated with the herbal medicine, Daikenchuto (5 g/d), a few days before the planning CT to prevent the retention of rectal contents.[26] Patients were immobilized in the prone position with a vacuum bag (Engineering System Co, Matsumoto, Nagano, Japan). To reduce respiratory-induced prostate motion and the dose to the small intestine, the vacuum bag had a quadrangular opening in the center with longitudinal and transverse dimensions of 25 cm, like a belly board, and was applied to allow the abdomen to extend into its aperture (Fig. E1).

IGRT protocol and evaluation of interfractional internal prostate motion

Initial patient setup was performed by using Sentinel/Catalyst (C-Rad, Uppsala, Sweden), monitoring the patient's surface optically, and comparing it to the planned reference surface. Thereafter, 110 kV cone beam CT (CBCT) images (360° full-scan; slice thickness, 1 mm) were obtained for IGRT. Registrations were performed using a dual registration tool (DRT) (Elekta XVI system, version 5.0.4; Elekta AB). The DRT involves 2 steps (Fig. E2). In the first step, the Chamfer match algorithm,[27] called "Bone (T+R)," was used and included the automatic bony structure registration in the following 6 directions: right-left (RL), craniocaudal (CC), anteroposterior (AP), roll, pitch, and yaw. In the second step, the 3 fiducial markers on the CBCT were registered to match those on the planning CT by using a Chamfer matching method, called "Seed (T)," in 3 directions (3D): RL, CC, and AP.

After the second step, relative displacements between the fiducial markers and the bony anatomy were quantified in 3D and were defined as interfractional internal prostate motion. Rotational displacement of the fiducial markers was not considered. For recording and analysis, anterior, cranial, and right-sided displacements were coded as positive displacements, whereas posterior, caudal, and left-sided displacements were coded as negative displacements. Given the prone position, the anterior side was the rectal side, and the posterior side was the pubic bone side. Systematic error (SE; ie, the mean prostate displacement) and random error (RE; ie, the standard deviation of prostate displacement) in each patient were statistically examined.[28] The displacement trend during the irradiation period was also evaluated. The actual irradiation was not performed in the second step, but rather only in the first step (ie, bony registration). If the relative displacement of the fiducial markers in the second step was >5 mm in 3D, manual adjustments were performed to ensure that the displacement of the fiducial markers was <5 mm, while ensuring that PLNs were well contained within the PTV. The patient position correction system used was the HexaPOD evo RT system with iGUIDE 2.2 (Elekta AB).

Evaluation of clinical factors and anatomic characteristics

Clinical factors evaluated were age; BMI; number of applicators; presence of premedication, smoking, or diabetes; and history of pelvic surgery. The anatomic characteristics were rectal volume, rectal mean area, bladder volume, and prostate volume change. Radiation oncologists performed the contouring of all organs by using Maestro (version 7.0.3; MIM Software Inc, Cleveland, OH). Anatomic characteristics of the rectum and bladder were evaluated with the planning CT. The rectum was delineated from 20 mm above the prostate to 20 mm below the prostate. The rectal mean area was calculated as rectal volume divided by its length in the CC direction. Prostate volumes were assessed using T2-weighted MRI for planning HDR-BT or VMAT. Prostate volume change was calculated by dividing the prostate volume 2 days after HDR-BT by the prostate volume within 4 weeks before HDR-BT.

Clinical and anatomic characteristics of the patients

The clinical and anatomic characteristics of the patients are shown in Table 1. All patients had high-risk or higher-risk prostate cancer, and 73.4% had very high-risk or regional-risk prostate cancer. After HDR-BT, the prostate volume increased in most patients (median, 134.6%; range, 99.9%-181.3%), especially toward the cranial and rectal sides (Fig. E3).

Table 1 Patient clinical and anatomic characteristics (N = 70)

	Value	(Range or %)
Age (y)	71	(55-81)
Body mass index (kg/m^2)	24.4	(18.1-32.5)
Number of applicators	17	(11-17)
Premedication, no. (%)		
Yes	21	(30)
No	49	(70)
Smoking, no. (%)		
Current	8	(11.4)
Never or former	62	(88.6)
Diabetes, no. (%)		
Yes	21	(30)
No	49	(70)
History of pelvic surgery, no. (%)		
Yes	3	(4.3)
No	67	(95.7)
Clinical T stage (UICC 8th), no. (%)		
≤T2c	17	(24.3)
T3a	22	(31.4)
T3b	20	(28.6)
T4	11	(15.7)
NCCN risk classification, no. (%)		
High	18	(25.7)
Very high	36	(51.4)
Regional	16	(22.9)
Prostate volume before HDR-BT	16.7	(7.4-53.3)
Prostate volume after HDR-BT	23.3	(10.7-71.3)
Prostate volume change (%)	134.6	(99.9-181.3)
Rectal volume (cm^3)	58.5	(36.4-115.2)
Rectal mean area (cm^2)	7.6	(4.7-14.2)
Bladder volume (cm^3)	95.1	(49.1-391.4)

Values are presented as median (range) unless otherwise noted. Bladder and rectal volumes were evaluated with the planning computed tomography images, and prostate volume, with T2-weighted magnetic resonance imaging.
Abbreviations: HDR-BT = high-dose-rate brachytherapy; NCCN = National Comprehensive Cancer Network; UICC = Union for International Cancer Control.

Statistical analysis

The mean SE and root mean square (RMS) of the RE were calculated. Associations between the patients' clinical factors or anatomic characteristics described previously and SEs or REs of the prostate in each patient were evaluated using the Student *t* test or linear regression analysis, when appropriate. The significance level in univariate analysis (UVA) was set at $P < .1$. All significant variables in the UVA ($P < .1$) were included in the multivariate analysis (MVA), performed with multiple linear regression analysis. The significance level in MVA was set at $P < .05$. To evaluate the displacement trend during the irradiation period, the mean prostate displacement was calculated for each fraction from the first to 23rd fractions. We compared the displacement of the first fraction to each subsequent fraction using the paired *t* test. All statistical analyses were conducted using EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan).[29]

Results

Analysis of interfractional internal prostate motion

In total, 1598 CBCT image sets acquired from the 70 patients were analyzed. In 2 patients, CBCT images were not taken because of a malfunction in 6 irradiation, and the ExacTrac system (BrainLAB AG, Munich, Germany) was used for IGRT. Table 2 shows the SEs and REs in each patient. The mean SE in the RL, CC, and AP directions were −0.01 mm, −2.34 mm, and −0.47 mm, respectively, with a particularly noticeable displacement toward the caudal side and posterior (ie, pubic bone) side. The RMS of RE in the RL, CC, and AP directions was 0.44 mm, 1.14 mm, and 1.10 mm, respectively.

Relationship between SE or RE and patient characteristics

The statistical association of SE and RE with patient clinical and anatomic characteristics is shown in Table 3.

Table 2 Systematic error and random error

Systematic error (mm)*	Mean	Range
Right-left	−0.01	(−1.46, 1.82)
Craniocaudal	−2.34	(−7.45, 1.23)
Anteroposterior	−0.47	(−4.99, 4.03)
Random error (mm)†	RMS	Range
Right-left	0.39	(0.16, 1.40)
Craniocaudal	1.07	(0.25, 2.14)
Anteroposterior	1.04	(0.36, 2.05)

Abbreviation: RMS = root mean square.
* Systematic error was calculated as the mean of prostate displacement in each patient.
† Random error was calculated as the standard deviation of prostate displacement in each patient.

Table 3 Statistical association of systematic error and random error with clinical and anatomic characteristics

	Univariate analysis			Multivariate analysis			
Characteristic	Right-left	Craniocaudal	Anteroposterior	Craniocaudal		Anteroposterior	
Analysis of systematic error							
Age	.309	.924	.371				
Body mass index	.893	.818	.702				
Number of applicators	.366	.402	.873				
Premedication	.321	.757	.464				
Smoking (current or not)	.704	.171	.616				
Diabetes	.304	.818	.731				
History of pelvic surgery	.541	.268	.169		Adjusted r^2		Adjusted r^2
Prostate volume change	.293	**<.001***	**<.001***	**<.001†** (***t*** **= −8.526)**	**0.534**	**<.001†** (***t*** **= 5.477)**	**0.378**
Rectal volume	.658	.869	**.053***			Excluded‡	
Rectal mean area	.507	.698	**.044***			**.008†** (***t*** **= 2.743)**	
Bladder volume	.513	**.048***	**.019***	**.021†** (***t*** **= 2.352)**		**.013†** (***t*** **= −2.553)**	
Analysis of random error							
Age	.670	.234	.714				
Body mass index	.970	.771	.577				
Number of applicators	.711	.680	.663				
Premedication	.095	.627	.588		Adjusted r^2		
Smoking (current or not)	.992	**.037***	.308	**.035†** (***t*** **= 2.155)**	**0.08**		
Diabetes	.573	.327	.213				
History of pelvic surgery	.085	.833	.564				
Prostate volume change	.475	**.079***	**.043***	.073 (*t* = 1.821)			
Rectal volume	.739	.604	.938				
Rectal mean area	.867	.691	.934				
Bladder volume	.671	.834	.887				

* Statistically significant in univariate analysis ($P < .1$).
† Statistically significant in multiple regression analysis ($P < .05$).
‡ Because rectal volume and rectal mean area had variance inflation factors greater than 10 in the multiple regression analysis, rectal volume was excluded in the multiple regression analysis of the anteroposterior direction.
Data are *P* values, with *t* statistics in parentheses, unless otherwise noted.

For SE, MVA revealed that SE in the CC direction was associated with bladder volume (P = .021, t statistic = 2.352) and prostate volume change (P < .001, t statistic = −8.526) (adjusted r^2 = 0.534) (Fig. 1A, 1B), whereas SE in the AP direction was associated with bladder volume (P = .013, t statistic = −2.553), prostate volume change (P < .001, t statistic = 5.477), and rectal mean area (P = .008, t statistic = 2.743) (adjusted r^2 = 0.378) (Fig. 1C-E).

For RE, MVA revealed that the mean RE in the CC direction was significantly higher in the current smoker group than in the never or former smoker group (1.35 mm vs 1.03 mm; P = .035) (Fig. 2A). The mean RE in the CC direction is shown for all 3 smoking groups (never, former, and current) in Fig. E4 (UVA: never vs former, P = .628; former vs current, P = .088; never vs current, P = .032). In UVA, the RE in the AP direction was associated with prostate volume change (adjusted r^2 = 0.045, P = .043) (Fig. 2B). However, MVA was not conducted in the analysis of RE in the AP direction, because only 1 factor differed significantly in the UVA.

Prostate volume change had the strongest effect on SE in the CC and AP directions. The most significant between-group difference occurred when the prostate volume change was ≥140% for SE in the CC direction (data not shown). In patients with a prostate volume change of more than 140%, the SEs in the CC and AP directions were −3.45 mm (95% confidence interval [CI], −4.57 to −3.31) and 0.62 mm (95% CI, −0.03 to 1.27), respectively. In contrast, in patients with less than 140% prostate volume change, SEs in the CC and AP directions were −1.06 mm (95% CI, −1.52 to −0.60) and −1.33 mm (95% CI, −1.84 to −0.82), respectively.

Prostate displacement trends for each fraction

The prostate displacement trends in each fraction, from the first to the 23rd fraction, are shown in Fig. 3A and 3B. The tendency for these fiducial markers to be displaced caudally and posteriorly (ie, pubic bone side) occurred gradually from the first to 23rd fractions. Compared with the first fraction, significant displacement was observed especially after the 18th fraction (except for the 19th and 23rd fraction) in the CC direction (P < .05) and after the second fraction in the AP direction (P < .05). In the AP direction, strong significant differences were observed after the eighth fraction (P < .001). Gradual displacements of the prostate were compared between groups based on whether the prostate volume change was ≥140% (Fig. 3C, 3D). During the irradiation period, prostate volume changes ≥140% were more likely to cause gradual caudal displacement than were volume changes <140% (Fig. 3C).

Discussion

In VMAT in the prone position after HDR-BT, anatomic and clinical factors were associated with SE and RE, respectively. A gradual caudal and posterior (ie, pubic bone side) displacement occurred during the irradiation period. To the best of our knowledge, this study is the first to report an association of clinical factors or anatomic characteristics on the planning images with prostate displacement in VMAT in the prone position after HDR-BT. Prostate volume change after HDR-BT had the greatest effect on the SE, which is particularly important to note. These findings will be useful in establishing optimal internal margins for the prostate for each patient receiving EBRT after brachytherapy. Internal margins for the prostate should be set to account for caudal (95% CI, 3.31-4.57 mm) and anterior (95% CI, −0.03 to 1.27 mm) displacement when the prostate volume change is greater than 140%, and to account for caudal (95% CI, 0.60-1.52 mm) and posterior (95% CI, 0.82-1.84 mm) displacement when the prostate volume change is less than 140%.

In this study, prostate volume change after HDR-BT had the greatest effect on displacement in the CC and AP directions. Prostate volume increase due to prostate edema after HDR-BT is well recognized.[30-34] On postoperative day 1, prostate volume increases by up to 1.72 times, with a gradual improvement thereafter.[35] The volume as well as the shape of the prostate changes dynamically.[36] We believe that the edema and shape changes affected displacement in the CC and AP directions. The smaller the prostate volume before HDR-BT, the greater the volume increase immediately after HDR-BT (Pearson's correlation coefficient = −0.266, P = .026). A previous study reported similar results.[35] Thus, a smaller prostate volume is associated with larger prostate volume change and SE in EBRT after HDR-BT. Additionally, Martinez et al reported on prostate volume changes during 4-fraction HDR-BT (9.5 Gy per fraction) and found greater prostate volume after the fourth fraction than immediately after implant.[33] Because the prostate volume was the largest after the fourth fraction, the SE of the prostate in EBRT after HDR-BT may be larger after fractional HDR-BT than after single-fractional HDR-BT.

With regard to gradual displacement, a study on the displacement of fiducial markers during EBRT alone reported gradual caudal and anterior (ie, pubic bone side) displacement.[37] A study evaluating seed displacement after permanent prostate brachytherapy reported that a seed in the base was more likely to be caudally displaced.[38] By contrast, a seed in the apex of the posterior prostate is more likely to be anteriorly displaced (ie, pubic bone side) as the postoperative edema improves.[38] Another study[39] reported that the seed in the posterior prostate migrated anteriorly (ie, pubic bone side) as the postoperative edema improved. In the current study, fiducial markers were

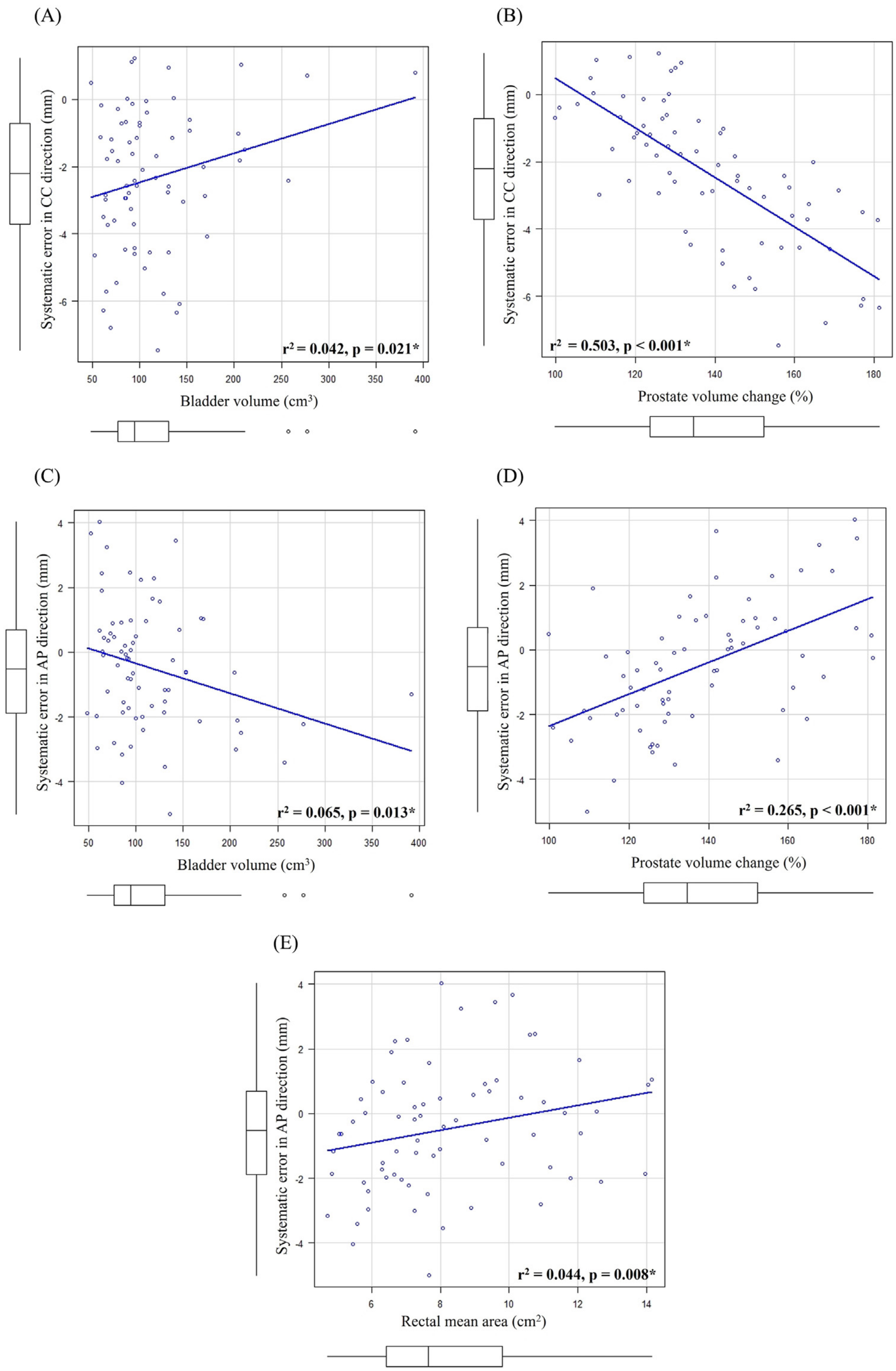

Figure 1 Scatter diagram of the systematic error in the CC direction and the anatomic characteristics. (A) Bladder volume. (B) Prostate volume change. Scatter diagram between systematic error in the AP direction and anatomic characteristics. (C) Bladder volume. (D) Prostate volume change. (E) Rectal mean area. The box indicates the interquartile range. The whiskers indicate Q1 to Q1.5 (IQR), Q3 + Q1.5 (IQR). The r^2 value is based on single regression analysis. *Significant difference in multiple regression analysis ($P < .05$). *Abbreviations:* AP = anteroposterior; CC = craniocaudal; IQR = interquartile range.

inserted at the aforementioned sites. A similar displacement of the fiducial markers may have occurred with edema improvement during the irradiation period. However, with regard to SE in the AP direction, the prostate tends to displace to the rectal side when the prostate volume change is large (Fig. 1D). In other words, in cases

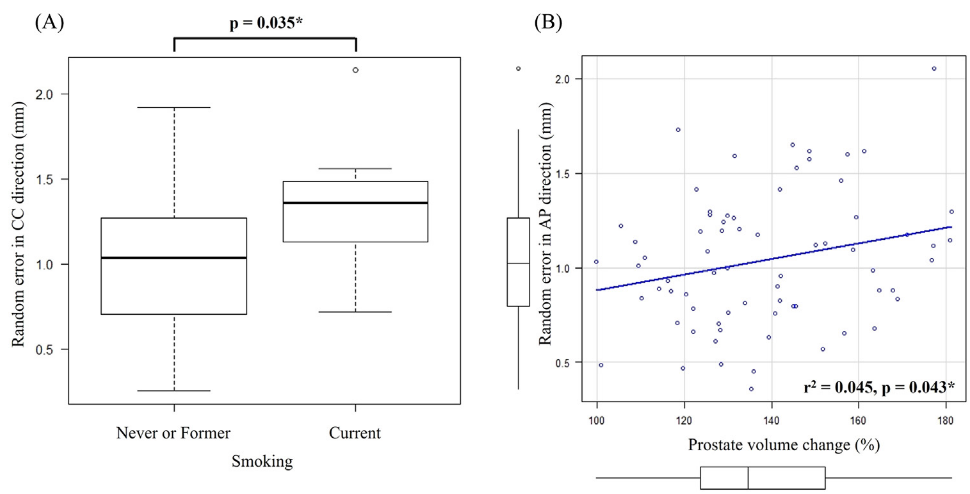

Figure 2 Random error findings. (A) Comparison of random errors in the CC direction between smokers and non-smokers. (B) Scatter diagram of the random error in the AP direction and prostate volume change. The box indicates the IQR. The whiskers indicate Q1 to Q1.5 (IQR), Q3 + Q1.5 (IQR). The r^2 value is based on single regression analysis. *Significant difference in (A) multiple regression analysis or (B) single regression analysis (P < .05). *Abbreviations:* AP = anteroposterior; CC = craniocaudal; IQR = interquartile range.

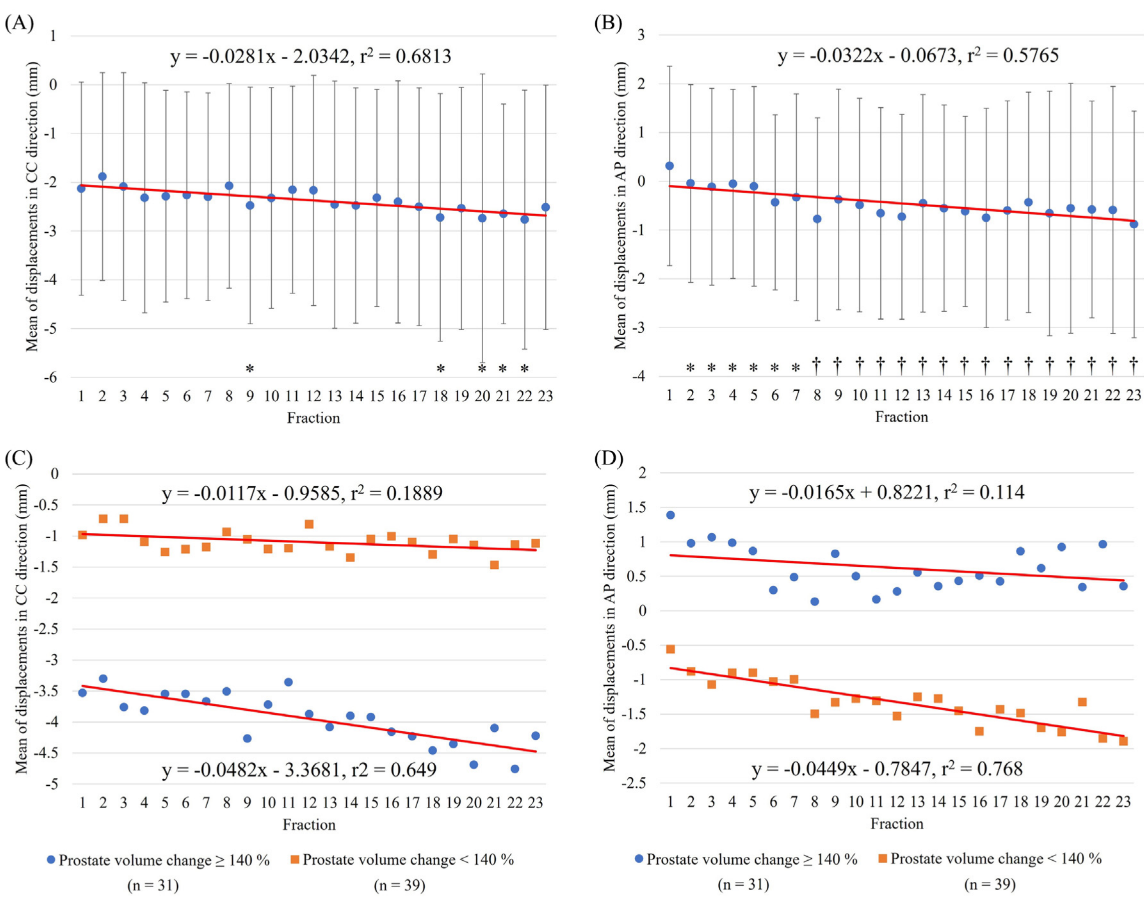

Figure 3 Mean prostate displacement from the first to 23rd fractions. (A) CC direction. (B) AP direction. Mean prostate volume changes of ≥140% or <140% are compared in the CC direction (C) and the AP direction (D). The scatter plots present the mean displacement value with standard deviation error bars. The straight line indicates the linear approximation. *Significant difference in paired t test (P < .05). †Significant difference in paired t test (P < .001). *Abbreviations:* AP = anteroposterior; CC = craniocaudal.

with a large prostate volume change, the prostate was displaced to the rectal side between days 3 and 13, followed by gradual displacement anteriorly (ie, pubic bone side) during the irradiation period. A study on EBRT alone reported that a fast increase in volume after implantation of the fiducial markers is followed by a reduction; upon EBRT initiation, the radiation causes prostate edema in the first days of treatment, but later, radiation therapy causes a reduction in volume.[37] The displacement observed in the present study is thought to have been caused by a complex combination of edema, shape changes, and volume loss in the prostate. In the CC direction, a mean displacement of −2.13 mm had already occurred at the first fraction (day 15), which we considered to be an effect of some improvement in edema from day 3 (day of the planning CT) to day 15. Based on these findings and those in a previous study,[31] we changed the timing of the planning CT from day 3 to day 7 to avoid the effects of prostate edema as much as possible.

With regard to the association between rectal volume and prostate displacement, the present study demonstrated that in the prone position, as in the supine position,[15,16] a large mean rectal area on the planning CT tended to displace the prostate toward the rectum (ie, anteriorly) during the irradiation period. This finding may be related to the fact that the prostate is less likely to displace to the rectal side if the rectum is collapsed on the planning CT. In addition, if much rectal content exists, the prostate is more likely to be displaced to the rectal side because of irradiation-related diarrhea.

In the supine position, previous reports[13,15,16] have ruled out bladder volume on the planning CT as a predictor of prostate displacement. In the current study, a larger bladder volume on the planning CT tended to displace the prostate posteriorly (ie, pubic bone side) and cranially. Furthermore, the bladder volume during the irradiation period could be predicted from the bladder volume on the planning CT (adjusted r^2 = 0.251, $P < .001$) (Fig. E5). With a larger bladder volume on the planning CT, the bladder volume decreased during the irradiation period, and with a smaller bladder volume, the bladder volume increased during the irradiation period (adjusted r^2 = 0.490, $P < .001$) (Fig. E6). In the prone position, other studies have reported that changes in bladder volume during the irradiation period can result in prostate displacement in the AP[9,19] or CC direction.[9] The influence of bladder volume may be greater in the prone position than in the supine position.[9] Especially in the prone position, confirming bladder volume with ultrasonography before irradiation may be useful.[40]

The current study demonstrated that smoking was associated with the RE in the CC direction. We have no findings that would explain this result. No study has reported an association between smoking and RE. We infer the following, based on the results of studies reported to date. In the prone position, displacement in the CC direction is more likely to occur because of changes in bladder volume.[9] Smoking is a factor that further exacerbates urinary tract symptoms.[41] It can also exacerbate genitourinary toxicity in patients undergoing radiation therapy for prostate cancer.[42,43] Urinary tract symptoms may be worse, and bladder volume fluctuations, greater, in patients who smoke than in other patients. It is necessary to further investigate the relationship between smoking and residual urine and bladder volumes during the irradiation period.

Several reports suggest that, in the supine position, a higher BMI decreases prostate displacement.[13,15,17] However, the present study found no association in the prone position. We believe that visceral fat falls within the aperture of the vacuum bag and that the visceral fat cannot compress the prostate in the prone position.

This study had some limitations. The present method could not distinguish between displacement of the prostate itself and displacement of fiducial markers due to improvement in edema. We did not directly study changes in the prostate or rectal volume that occurred during the irradiation period. Approximately 20% to 40% of patients treated with this protocol developed grade ≥1 acute diarrhea.[23-25] Given that diarrhea reduces rectal content, it may affect prostate displacement. Thus, similar results may not be obtained if PLNs are not irradiated. Rotational movement was also not analyzed in this study. MVA was additionally performed, with the exclusion of 3 patients whose bladder volume was >250 mL on the planning CT (Table E1). In this analysis, bladder volume was associated with SE in the AP direction but not in the CC direction. Accordingly, the association between SE and bladder volume in the CC direction may be due to an outlier effect.

Conclusion

In VMAT in the prone position after HDR-BT, anatomic characteristics of the bladder and rectum on the planning CT and prostate volume change on the planning MRI predicted SE, whereas smoking and prostate volume change on the planning MRI predicted RE. During the irradiation period after HDR-BT, fiducial markers tended to gradually displace caudally and posteriorly (ie, pubic bone side). These findings should be considered when determining treatment protocols. In particular, when setting the internal margins, the possibility of the aforementioned interfractional internal prostate motions should be taken into account. Furthermore, changing the timing of planning CT from day 3 to day 7 may reduce the effect of prostate volume change on SE.

Disclosures

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.adro.2023.101277.

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