Assessment of interfractional prostate motion in patients immobilized in the prone position using a thermoplastic shell

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The aim of this study was to evaluate the interfractional prostate motion of patients immobilized in the prone position using a thermoplastic shell. A total of 24 patients with prostate calcifications detectable using a kilovoltage X-ray image-guidance system (ExacTrac X-ray system) were examined. Daily displacements of the calcification within the prostate relative to pelvic bony structures were calculated by the ExacTrac X-ray system. The average displacement and standard deviation (SD) in each of the left–right (LR), anterior–posterior (AP), and superior–inferior (SI) directions were calculated for each patient. Based on the results of interfractional prostate motion, we also calculated planning target volume (PTV) margins using the van Herk formula and examined the validity of the PTV margin of our institute (a 9-mm margin everywhere except posteriorly, where a 6-mm margin was applied). In total, 899 data measurements from 24 patients were obtained. The average prostate displacements ± SD relative to bony structures were 2.8 ± 3.3, −2.0 ± 2.0 and 0.2 ± 0.4 mm, in the SI, AP and LR directions, respectively. The required PTV margins were 9.7, 6.1 and 1.4 mm in the SI, AP and LR directions, respectively. The clinical target volumes of 21 patients (87.5%) were located within the PTV for 90% or more of all treatment sessions. Interfractional prostate motion in the prone position with a thermoplastic shell was equivalent to that reported for the supine position. The PTV margin of our institute is considered appropriate for alignment, based on bony structures.

Keywords: intensity-modulated radiotherapy; interfractional prostate motion; prone position; prostate cancer; thermoplastic shell

INTRODUCTION

Several studies have been conducted to determine whether a supine or prone fixation position is superior for external beam radiotherapy (EBRT) in patients with prostate cancer [1–11]. However, the optimal treatment position for prostate EBRT remains controversial and inconclusive because each position has its own merits and demerits. The merit of the prone position is that the irradiation dose to the rectum is reduced because the seminal vesicles are pulled away from the rectum [1, 11]. It has also been reported that the geometric relationship between the prostate and pelvic bony anatomy is more consistent in the prone position [5], a finding that is very important for centers that use bony-structure-based positioning. Conversely, a demerit of the prone position is the greater prostate motion compared with the supine position [3, 4]. Additionally, the supine position is more comfortable for patients and more convenient for therapists than the prone position [3].

We have treated patients with localized prostate cancer using intensity-modulated radiotherapy (IMRT) in the prone position fixed with a thermoplastic shell since 2000. We adopted the prone position for two reasons. First, the rectal dose is reduced because we treat mainly locally advanced
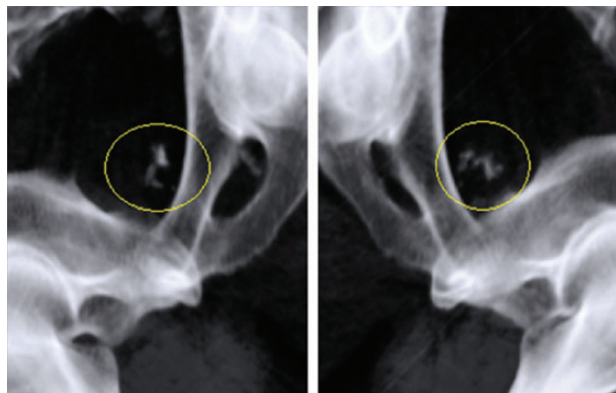
Fig. 1. Examples of ExacTrac X-ray images. Intra-prostatic calcifications were clearly detected (yellow circle).

prostate cancer patients in whom the seminal vesicles are included in the clinical target volume (CTV) [11]. Second, we applied bony-structure-based positioning because we had no soft-tissue-based image-guided radiotherapy (IGRT) options when we first began using IMRT for prostate cancer. To compensate for the expected large prostate motion in the prone position, we immobilized patients by using a thermoplastic shell.

To our knowledge, only three reports have examined interfractional prostate motion in the prone position when immobilized with a thermoplastic shell [3, 12, 13]. However, those reports did not document sufficient data with systematic and random errors to calculate the required planning target volume (PTV) margin because they examined only three additional computed tomography (CT) data measurements per patient or assessed the lateral portal image alone. Therefore, no report to date has determined the adequate PTV margin in the prone position while immobilized using a thermoplastic shell.

Beginning in 2007, we were able to use a dual-orthogonal kilo-voltage (kV) X-ray IGRT system (ExacTrac X-ray system; BrainLAB AG, Feldkirchen, Germany) for patient positioning. This system also allows detection of calcification within the prostate (Fig. 1). Because calcification in the prostate is a reliable marker of prostate position [14], using this IGRT system we are able to assess interfractional prostate motion in all fractions without the need for an invasive procedure, based on routinely acquired clinical data. The aim of the present study was to evaluate interfractional prostate motion in patients immobilized with a thermoplastic shell in the prone position. Additionally, we validated the adequacy of the PTV margin applied at our institute.

MATERIALS AND METHODS

Patients' characteristics
Between August 2007 and August 2010, 163 consecutive patients with localized prostate cancer (cT1c-T4N0M0) received IMRT using Novalis (BrainLAB AG) at our

Table 1. Patients' characteristics and treatment parameters

Age (years)	59–80 (median, 72)
T stage (UICC 2002)	
T1c–T2b	17
T2c	3
T3a	4
Gleason score	
≤6	7
7	8
≥8	9
Initial PSA value (ng/ml)	5.03–49.00 (median, 10.55)
NAHT period (months) (CAB)	4–21 (median, 7)
RT dose (Gy)	
70	3
74	12
78	9

UICC = classification of the International Union Against Cancer, NAHT = neoadjuvant hormonal therapy, CAB = combined androgen blockade, PSA = prostate-specific antigen, RT = radiotherapy.

institute. Of these, the ExacTrac X-ray system clearly detected calcification within the prostate in 24 patients. Since all of the system's image data for localization were stored and accessible, we included these 24 patients in the present analyses. The median age of the study population was 72 years (range, 59–80 years). T-stage was 17 with T1c–T2b, 3 with T2c, and 4 with T3a. The median prostate-specific antigen (PSA) and Gleason scores were 10.55 ng/ml and 7, respectively. Patients' characteristics are summarized in Table 1. Witten informed consent was obtained from the patients to use their clinical data for research purposes and for publication.

Radiation therapy
Each patient underwent pretreatment planning CT scans (LightSpeed RT; GE Healthcare, Waukesha, WI, USA) of 2.5-mm slice thickness. All patients were instructed to void the bladder and rectum about 1–1.5 h before the CT simulation, according to their individual urinary conditions. In actual treatments, patients were also required to void the bladder and rectum at exactly the same timing as set in the CT simulation. In addition, the treatment time was fixed by each patient to maintain patients' condition. Patients were immobilized in the prone position with a thermoplastic shell (Hip Fix system; CIVCO Medical Solutions, Kalona, IA, USA) that extended from the mid-thigh to the upper third of the leg, in combination with a vacuum pillow (Vac-Lok
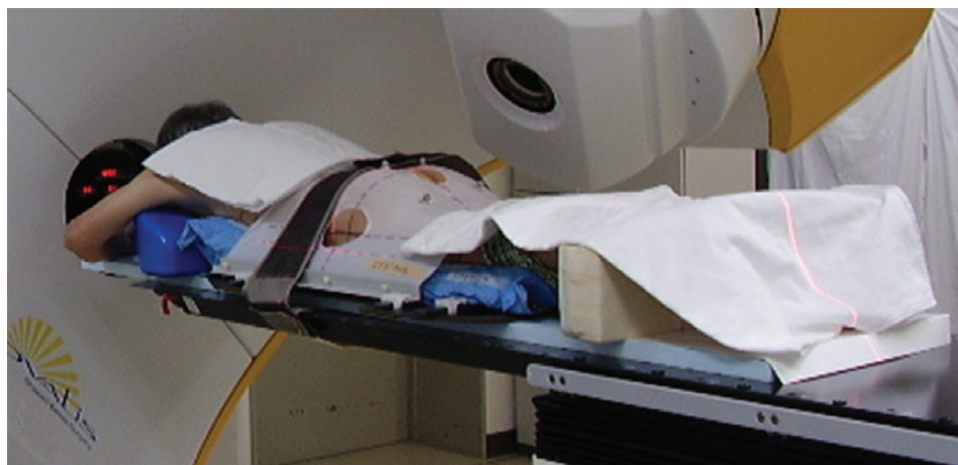
Fig. 2. Patient fixed in the prone position with the combination of a thermoplastic shell, a vacuum pillow and a leg support.

system; CIVCO Medical Solutions) and a leg support (Fig. 2). Details of our planning protocol have been reported previously [15, 16]. Briefly, the CTV consisted of the prostate and seminal vesicles (base to the whole depending on the clinical stage), not including the lymph node area. The PTV was the CTV plus a 9-mm margin everywhere except posteriorly, where a 6-mm margin was applied. The PTV was treated with a dose of between 70 Gy in 35 fractions and 78 Gy in 39 fractions (median, 74 Gy). Patients were positioned based on their pelvic bone structures using the ExacTrac X-ray system immediately before each treatment session.

Analysis of interfractional prostate motion

Displacement of the position of a calcification within the prostate between each daily session and the DRR image at the CT simulation was calculated based on the ExacTrac data. If more than one calcification was identified within the prostate, the largest one was used to calculate the position. The average displacement and the standard deviation (SD) in each of the left–right (LR), anterior–posterior (AP), and superior–inferior (SI) directions were calculated for each patient.

Calculation of the required PTV margin

The required PTV margins were generated using the van Herk formula ($2.5\Sigma + 0.7\sigma$) [17]. The Σ was calculated as the SD of the mean displacement for each individual patient. The σ was determined by computing the root mean square of the SD of an individual patient's displacements. This method is intended to guarantee that 90% of patients receive a minimum cumulative CTV dose of at least 95% of the prescribed dose.

Comparison of prostate motion with other reports and validation of the PTV margin

To validate the adequacy of the applied PTV margin, we calculated the required PTV margin using the van Herk formula to compare prostate motion with other reports, which often report Σ and σ values [8, 18–24], because we believe that the calculated PTV margin expresses the total possible variation of prostate motion simply.

In addition, we generated accumulated CTV dose reflecting interfractional prostate motion. This allowed estimation of actually delivered target dose and was generated as follows. First, isocenter-shifted plans, in which the isocenter was shifted to compensate for the corresponding positional error of the prostate by each fraction, were generated for every patient. Then, all plans of the individual patient were summed up on the Eclipse (ver. 8.6) treatment-planning system (Varian Medical Systems, Palo Alto, CA, USA), and the accumulated CTV dose was calculated. We assessed the dose–volume histogram (DVH) of this accumulated CTV dose. We also evaluated the probability of prostate motion coverage within our clinical PTV margin.

RESULTS

In total, 899 ExacTrac X-ray system data measurements from 24 patients were available for registration of bony structures and calcification. The average prostate displacements ± SD relative to the bony structure were -2.0 ± 2.0, 2.8 ± 3.3 and 0.2 ± 0.4 mm, in the AP, SI and LR directions, respectively. There was a tendency for a large shift in the SI direction, and displacement of more than 10 mm was observed only in the SI direction. The displacement in the LR direction was generally small.

Table 2 summarizes the means, SDs, ranges, Σ, σ and PTV margins of interfractional prostate displacement in the

Table 2. Interfractional prostate displacement

	AP (mm)	SI (mm)	LR (mm)
Mean	−2.0	2.8	0.2
Minimum	−9.6	−11.2	−3.4
Maximum	6.0	15.4	4.7
Σ	2.0	3.3	0.4
σ	1.6	2.2	0.6

LR = left–right, AP = anterior–posterior, SI = superior–inferior, + = motion to the right/posterior/superior directions about isocenter, Σ = the SD of the average displacement for each individual patient, σ = the root mean square of the individual SD.

AP, SI and LR directions. The Σ values of the AP, SI and LR directions were 2.0, 3.3 and 0.4 mm, respectively, and the σ values were 1.6, 2.2 and 0.7 mm, respectively. Both Σ and σ were also largest in the SI direction. The PTV margins calculated using the van Herk formula were 6.1, 9.7 and 1.4 mm in the AP, SI and LR directions, respectively. The prostate displacement of 21 patients (87.5%) was within the applied PTV margins (9-mm margin everywhere except posteriorly, where a 6-mm margin was applied) in 90% or more of all treatment sessions. With regard to the DVH of the accumulated CTV dose, the average mean dose ± SD and the dose at the 95% volume level of the cumulative DVH (D95) ± SD of the CTV were 100.7 ± 1.3% (range, 96.7–102.4%) and 96.2 ± 5.8% (range, 73.1–100.7%), respectively (Fig. 3).

DISCUSSION

Table 3 summarizes previously reported PTV margins for interfractional organ motion errors relative to a bony structure [8, 18–24]. The data include seven studies in the supine position without a thermoplastic shell, one in the supine position with a thermoplastic shell, and one prone position without a thermoplastic shell. Their calculated PTV margins were 4.7–10.5 mm (mean, 8.0 mm), 4.0–12.0 mm (mean, 8.5 mm) and 1.4–4.5 mm (mean, 3.2 mm) in the AP, SI and LR directions, respectively. Our results fall within the range of those reported previously, indicating that the prostate motion relative to the bony structure in individuals immobilized in the prone position using a thermoplastic shell is comparable to that in the supine position.

To our knowledge, only three publications have examined prostate motion in patients immobilized with a thermoplastic shell in the prone position. Takayama *et al*. [12] reported prostate motion using three additional CT scans in seven patients, with or without a double-balloon rectal catheter. The mean prostate displacements ± SD were 2.8 ± 1.8, 2.7 ± 1.8 and 1.3 ± 0.7 mm in the AP, SI and LR directions, respectively. Zelefsky *et al*. [13] also reported interfractional
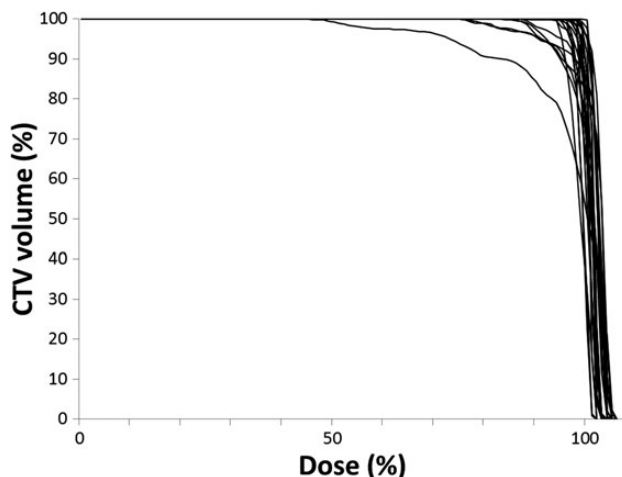
Fig. 3. Dose–volume histograms of the accumulated CTV dose for all patients. The acceptable CTV coverage of D95 ≥ 95% was achieved in about 80% of the patients (*n* = 19).

prostate motion in 50 patients, as determined by using three additional CT scans. The mean prostate displacements ± SD were − 1.2 ± 2.9, −0.5 ± 3.3 and −0.6 ± 0.8 mm in the AP, SI and LR directions, respectively. Bayley *et al*. [3] examined 20 patients randomized with regard to treatment when immobilized in the supine or prone position, and measured prostate motion using the daily lateral film to compare bony landmarks and fiducial marker positions. The mean prostate motions ± SD in the prone position were 0.7 ± 4.0 and 0.7 ± 3.7 mm in the AP and SI directions, respectively. Although these reports did not include Σ and σ data, which enable calculation of the required PTV margin, the SD results were similar to those we report here.

Compared with other reports fixed in the supine position without any fixation devices, our study resulted in smaller displacements in the AP direction and comparable displacements in other directions (Table 3). It is reported that the prone position without any fixation devices produced greater prostate motion than the supine position [3, 4]. We believe those results were mainly due to the respiratory motion of the chest and abdomen. That is, the respiratory motion easily affects the prostate position in the prone position because chest and abdomen are touching the couch. In contrast, application of a thermoplastic shell can contribute to restricting respiratory-related movement. In addition, prostate locations in the prone position are less influenced by rectal gas than those in the supine position, because the rectal gas tends to move and be stored in part of the rectosigmoid (Fig. 4). On the other hand, rectal gas can easily push the prostate upwards in the supine position, as indicated in Fig. 5. A smaller displacement in the AP direction was also reported by Khosa *et al.* but using the supine position and immobilization with a thermoplastic shell [20]. As indicated before, rectal gas in the supine position without fixation devices can greatly affect the prostate position in the AP direction

Table 3. Comparison of required PTV margins calculated from interfractional errors relative to a bony structure using the van Herk formula

Position	Thermoplastic shell	Method	No. of Patients	Method	No. of data	Margin (mm)		
						AP	SI	LR
Supine	–	Bylund *et al.* [19]	24	MVCT without M	972	7.0	4.0	3.1
		Tanyi *et al.* [24]	14	CBCT with M	546	10.2	8.9	1.6
		Nederveen *et al.* [21]	23	EPID with M	675	7.5	11.9	3.1
		Osei *et al.* [23]	20	EPID with M	642	6.6	7.4	4.4
		Alonso-Arrizabalaga *et al.* [18]	30	ExacTrac with M	1330	10.5	12.0	4.1
		O'Daniel *et al.* [22]	10	kV CT without M	243	10.4	8.6	2.8
		Stroom *et al.* [30]	15	kV CT without M	240	8.3	8.2	4.0
	+	Khosa *et al.* [20]	10	EPID with M	180	4.7	7.3	3.6
Prone	–	Stroom *et al.* [30]	15	kV CT without M	240	8.8	6.6	3.7
	+	This study	24	ExacTrac with calcification	899	6.1	9.7	1.4

CT = computed tomography, MVCT = megavoltage cone beam CT, M = fiducial marker, CBCT = cone beam CT, EPID = electronic portal imaging device, AP = anterior-posterior; SI = superior-inferior, LR = left-right, ExacTrac = ExacTrac X-ray system, kV = kilo-volt.
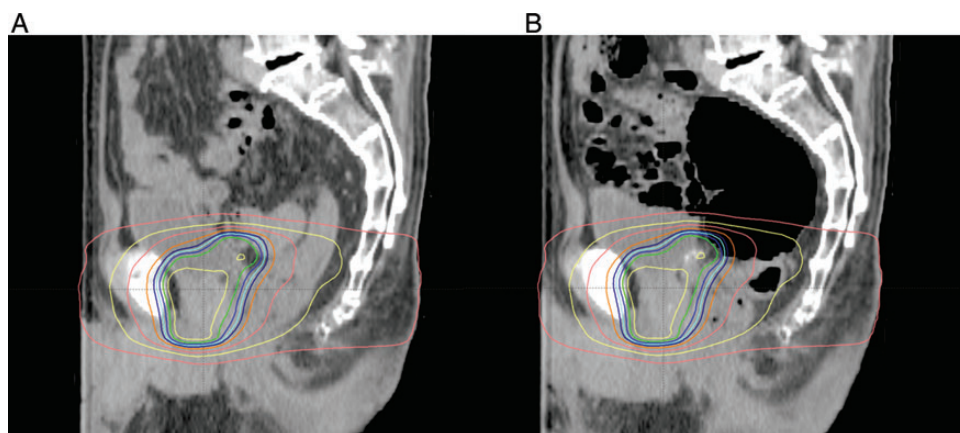

Fig. 4. An example of the impact of rectal gas on the prostate position in the prone fixation. (**A**) Sagittal view of simulation CT with dose distribution curves. (**B**) Sagittal view of follow-up CT superimposed on dose distribution curves at planning. Although a large amount of rectal gas exists, the prostate dose was maintained because most of the gas is located in the rectosigmoid region of the rectum.

(Fig. 5). It is believed that the use of a thermoplastic shell in the supine position can contribute to restriction of severe rectal dilatation by gas because of the increased abdominal pressure from the thermoplastic shell. To date and to our knowledge, no study has compared prostate motion in the same position with and without a thermoplastic shell. More detailed studies are necessary in the future, but the use of a thermoplastic shell probably reduces interfractional prostate movement in the AP direction.

Our required PTV margin using the van Herk formula (9.7, 6.1 and 1.4 mm in the SI, AP and LR directions, respectively) is similar to the PTV margin of our institute. Indeed, the CTV of 21 patients (87.5%) was within our PTV

margins for 90% or more of all treatment sessions. Additionally, for the DVH of the accumulated CTV dose, dose coverage of the CTV was almost satisfied. In fact, it was reported that a 1.5-cm PTV margin had no significant impact on the PSA control rate, but had a significantly negative impact on late rectal damage, compared with a 1.0-cm margin [25]. Therefore, our PTV margin may be relevant as far as fitting to the bony structure in the prone position in a patient immobilized with a thermoplastic shell. However, to prevent delivery of an insufficient dose to the CTV in patients with relatively large prostate movements, it will be necessary to shift to the prostate-based IGRT approach. Indeed, we began to use this prostate IMRT approach in 2010.
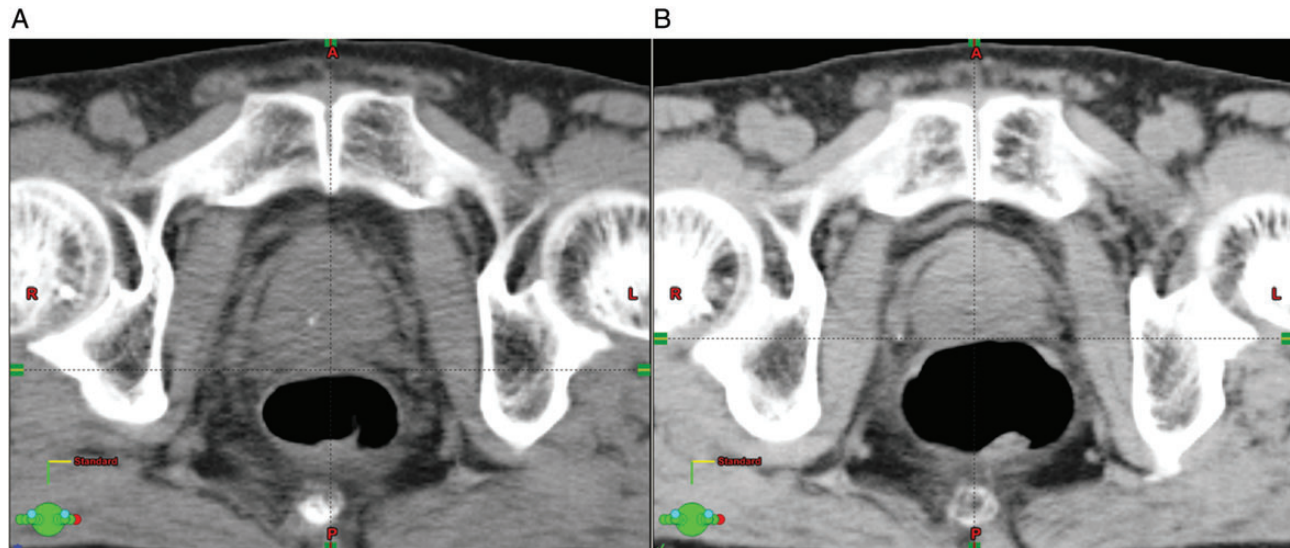
Fig. 5. An example of impact of rectal gas on the prostate position in the supine position. (**A**) Axial view of simulation CT; (**B**) Axial view of follow-up CT. The amount of the rectal gas directly affects the position of the prostate.

The present study has the limitation that using only the largest calcification within the prostate cannot account for prostate rotation. However, previous study has indicated that rotation errors are small, and rotation alignment offers only 1-2 mm advantage compared with translational shift alone [26]. Another limitation is that the intrafractional prostate motion was not considered. Several reports on intrafractional prostate motion have been published to date [4, 9, 10, 27–29]. However, intrafractional prostate motion in the prone position in those immobilized with a thermoplastic shell has not yet been assessed. We are currently investigating intrafractional prostate motion, and will report the data in the near future.

Compared with other reports, our results demonstrate that the effect of immobilization with a thermoplastic shell in the prone position is comparable to that in the supine position. The superiority of the geometric relationship between the prostate and pelvic bony anatomy in the prone position compared with that in the supine position [5] was not determined in the present study. However, if identical PTV margins are necessary in both positions, the prone position may be preferable due to the reduced irradiation dose to the rectum [11]. Interfractional prostate motion in those immobilized in the prone position using a thermoplastic shell is equivalent to that in the supine position reported elsewhere. The PTV margin of our institute is generally appropriate when aligned to the bony structure, although prostate-based positioning will be required for patients with a large prostate motion.

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