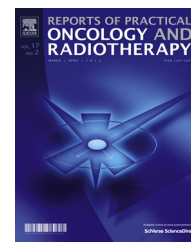


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Original research article

Does intensity-modulated radiation therapy (IMRT) alter prostate size? Magnetic resonance imaging evaluation of patients undergoing IMRT alone



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ABSTRACT

Aim: To assess the changes in prostate size in patients with prostate cancer undergoing intensity-modulated radiation therapy (IMRT).

Background: The effect of size change produced by IMRT is not well known.

Materials and methods: We enrolled 72 patients who received IMRT alone without androgen-deprivation therapy and underwent magnetic resonance imaging (MRI) examination before and after IMRT. The diameter of the entire prostate in the anterior–posterior (P-AP) and left–right (P-LR) directions was measured. The transitional zone diameter in the anterior–posterior (T-AP) and left–right (T-LR) directions was also measured.

Results: The average relative P-AP values at 3, 6, 12, 24, and 36 months after IMRT compared to the pre-IMRT value were 0.94, 0.90, 0.89, 0.89, and 0.90, respectively; the average relative P-LR values were 0.93, 0.92, 0.91, 0.91, and 0.90, respectively. The average P-AP and P-LR decreased by approximately 10% during the 12 months post-IMRT, and remained unchanged thereafter. The average relative T-AP values at 3, 6, 12, 24, and 36 months after IMRT compared to the pre-IMRT value were 0.93, 0.88, 0.91, 0.87, and 0.89, respectively; the average relative T-LR values were 0.96, 0.90, 0.91, 0.87, and 0.88, respectively. The average T-AP and T-LR also decreased by approximately 10% during the 12 months post-IMRT, and remained unchanged thereafter. At 12 months after IMRT, the average relative T-AP was significantly lower in patients with recurrence than in those without recurrence.

Conclusions: The average prostate diameter decreased by approximately 10% during the 12 months after IMRT; thereafter remained unchanged.

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1. Background

One of the optimal treatment options for prostate cancer is external beam radiotherapy.¹ Intensity-modulated radiation therapy (IMRT) has been widely used for external beam irradiation of localized prostate cancers. Several studies have revealed that IMRT is safer than three-dimensional conformal radiation therapy, especially in terms of gastrointestinal adverse events.^{2–5} The safety of IMRT also allows dose escalation, leading to better tumor control.^{6,7}

Androgen-deprivation therapy (ADT) is also used for prostate cancer depending on clinical stage.^{8,9} Nevertheless, ADT may decrease the size of the prostate.¹⁰ Furthermore, brachytherapy may change prostate size irrespective of the dose rate.^{11,12}

2. Aim

In this study, we assessed the changes in prostate size in patients with localized prostate cancer undergoing IMRT alone by using magnetic resonance imaging (MRI). We also analyzed the relationship between prostate size and prostate-specific antigen (PSA) levels.

3. Materials and methods

3.1. Patients

Between February 2006 and August 2010, 525 patients with localized prostate cancer received IMRT. Among them, patients who received IMRT alone without ADT and underwent MRI examination before and once or more after IMRT were enrolled in this study. ADT is usually performed for intermediate- and high-risk patients. In principle, ADT was commenced 3–6 months prior to radiotherapy for intermediate- and high-risk patients. Adjuvant ADT was performed for high-risk patients for up to 24 months. Some of the patients with intermediate- and high-risk prostate cancers refused ADT. Seventy-two patients met this criterion and were included in the study. The study was conducted with the approval of our institutional review board. Written informed consent was obtained from each patient before administering radiotherapy.

The patient characteristics are shown in Table 1. We used the risk classification for prostate cancer proposed by D'Amico.¹³

3.2. Treatment planning

Patients were instructed to empty their bladder 60 min prior to the treatment. Each patient was positioned supine on a couch within the immobilization devices and underwent computed tomography (CT). Axial CT images of 2.5-mm thickness were obtained from the superior border of the sacroiliac joint to 5 cm below the ischial tuberosity.

The IMRT and image-guided radiotherapy plans were created using the TomoTherapy Treatment Planning System (TomoTherapy Inc., Madison, WI, USA). The IMRT plans

Table 1 – Patient characteristics (N = 72).

Median age (range) (years)	70 (53–83)
Median initial PSA (range) (ng/ml)	6.7 (3.9–22.1)
Clinical stage	
T1c	32
T2a	32
T2b	1
T2c	7
Gleason's score	
4	2
6	36
7	32
8	2
Low risk	27
Intermediate risk	36
High risk	9

PSA: prostate-specific antigen.

involving helical tomotherapy (HT) were created using an inverse treatment planning system. The CT datasets with structures and contours in Pinnacle³ (Hitachi Medical Co., Tokyo) were transferred to the HT planning workstation. The clinical target volume (CTV) was defined as the prostate and the proximal portions of the seminal vesicles in patients with T1–T3a cancers. For patients with T3b cancers, the entire seminal vesicle was included in the CTV. The planning target volume (PTV) margin was set at 5 mm in all directions. For low- and intermediate-risk patients with biopsy-positive core rate $\leq 50\%$, prescribed dose was 74 Gy; for intermediate-risk patients with biopsy-positive core rate $> 50\%$, it was 76 Gy; and for high-risk patients, it was 78 Gy. The daily fraction dose was 2.0 Gy, 5 times a week. The dose constraints for PTV were as follows: the dose administered to 95% of the PTV was $> 90\%$ ($> 95\%$, is preferable), the volume of the PTV receiving at least 90% of the prescribed dose was $> 96\%$ (> 98 is preferable), and the maximum dose was $< 110\%$ of the prescribed dose. The rectum was delineated from 15 mm superior to 15 mm inferior to the PTV. Then, a rectal wall thickness of 3-mm was created. A bladder wall with a thickness of 3-mm was also created. The rectum and bladder were used for optimization. Because higher doses were received by rectal and bladder walls compared to doses received by corresponding solid organs, the rectum and bladder walls were used for evaluation of a dose-volume histogram.¹⁴ The dose constraints for the rectum were as follows: V40 $< 60\%$, V60 $< 30\%$, V70 $< 20\%$, and V78 $< 1\%$. The dose constraints for the bladder were as follows: V40 $< 60\%$ and V70 $< 35\%$. Vx is defined as the percentage of the volume of the structure receiving at least one dose of “x” Gy. Megavoltage CT image-guided verification was performed daily prior to each treatment. The photon energy used was 6 MV.

3.3. Evaluation

MRI was performed on a 1.5-T MR imager (Genesis Signa; GE Healthcare, WI, USA). The images used in this study were 3-mm axial T2-weighted fast spin-echo images (repetition time, 2400 ms; echo time, 99 ms). The diameter of the entire prostate in the anterior–posterior (P-AP) and left–right (P-LR) directions was measured for each patient on the image slice with maximum division surface. The diameter of the transitional zone

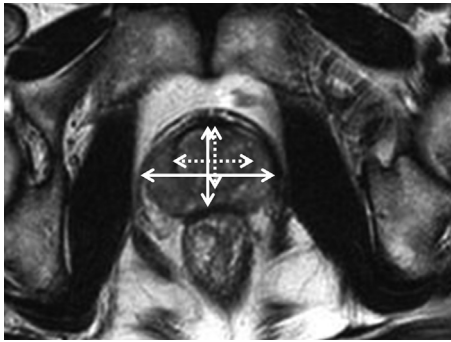


Fig. 1 – The diameter of the entire prostate (solid line) and the transitional zone (dashed line) in the anterior–posterior and left–right directions is measured.

in the anterior–posterior (T-AP) and left–right (T-LR) directions was also measured on the same slice (Fig. 1).

The differences in PSA levels at 1 year after IMRT were compared between groups with P-AP reduction rate $\geq 5\%$ and $<5\%$. In the same way, analysis was performed for P-LR, T-AP, and T-LR. The differences in the reduction rate in each direction were compared between patients with and without recurrence. The parameters were compared using the Mann–Whitney U test. A p value <0.05 was considered to indicate a significant difference.

4. Results

The median follow-up period was 74 months (range, 52–104 months). After IMRT, 212 follow-up MRI scans were performed (mean, 2.9 times/patient).

The transition of the P-AP and P-LR is shown in Fig. 2. The average relative P-AP values at 3, 6, 12, 24, and 36 months after IMRT compared to the pre-IMRT value (\pm standard deviation)

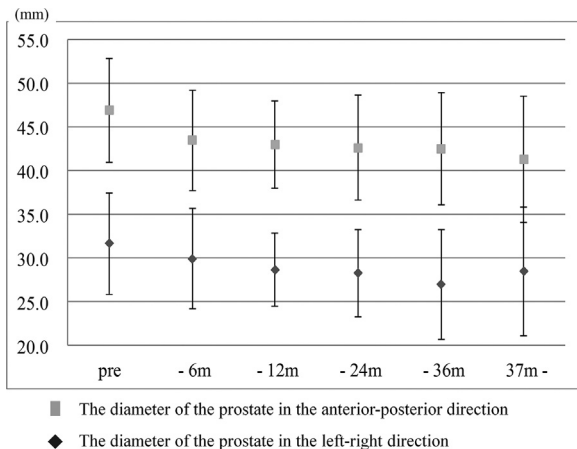


Fig. 2 – The transition of the diameter of the prostate in the anterior–posterior (P-AP) and left–right (P-LR) directions is shown. The average P-AP and P-LR decreased by approximately 10% during the 12 months after intensity-modulated radiation therapy (IMRT); thereafter, the diameters remained unchanged.

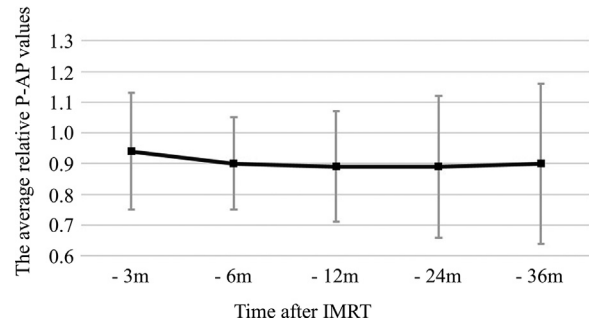


Fig. 3 – The average relative diameter of the prostate in the anterior–posterior directions (P-AP) values after intensity-modulated radiation therapy (IMRT) compared to the pre-IMRT.

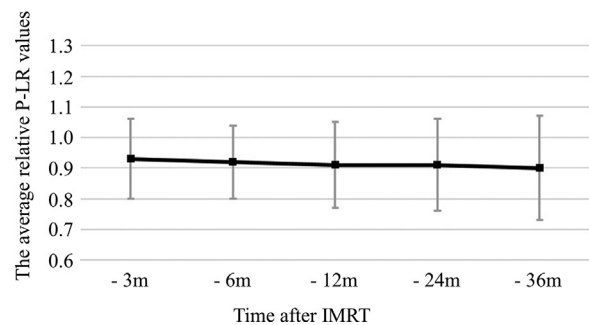


Fig. 4 – The average relative diameter of the prostate in the left–right directions (P-LR) values after intensity-modulated radiation therapy (IMRT) compared to the pre-IMRT.

(i.e. the ratios of the values at the post-IMRT time points with the pre-IMRT value) were 0.94 (± 0.19), 0.90 (± 0.15), 0.89 (± 0.18), 0.89 (± 0.23), and 0.90 (± 0.26), respectively (Fig. 3); the corresponding values (\pm standard deviation) for the average relative P-LR were 0.93 (± 0.13), 0.92 (± 0.12), 0.91 (± 0.14), 0.91 (± 0.15), and 0.90 (± 0.17), respectively (Fig. 4). The average P-AP and P-LR decreased by approximately 10% during the 12 months after IMRT, and remained unchanged thereafter. The average relative T-AP values at 3, 6, 12, 24, and 36 months after IMRT compared to the pre-IMRT value (\pm standard deviation) (i.e. the ratios of the values at the post-IMRT time points with the pre-IMRT value) were 0.93 (± 0.27), 0.88 (± 0.22), 0.91 (± 0.26), 0.87 (± 0.33), and 0.89 (± 0.32), respectively (Fig. 5); the corresponding values (\pm standard deviation) for the average relative T-LR were 0.96 (± 0.31), 0.90 (± 0.33), 0.91 (± 0.32), 0.87 (± 0.38), and 0.88 (± 0.43), respectively (Fig. 6). The average T-AP and T-LR also decreased by approximately 10% during the 12 months after IMRT, and remained unchanged thereafter (Fig. 7). The prostate size decreased in approximately 80% of the patients after IMRT. The percentage of patients with prostate size decrease $>5\%$ at 12 months after IMRT were 55%, 59%, 54%, and 58% in P-AP, P-LR, T-AP, and T-LR, respectively. There was no significant difference in PSA levels according to the change in the relative diameter of the P-AP, P-LR, T-AP, and T-LR at 12 months after IMRT (Table 2).

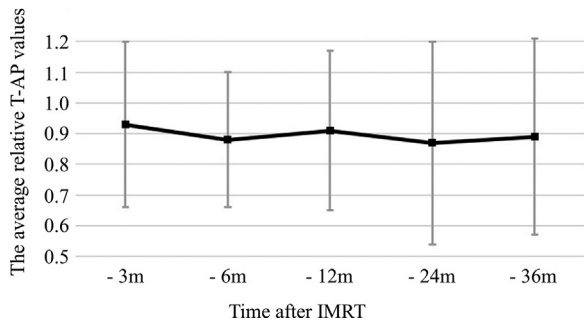


Fig. 5 – The average relative diameter of the transitional zone in the anterior–posterior directions (T-AP) values after intensity-modulated radiation therapy (IMRT) compared to the pre-IMRT.

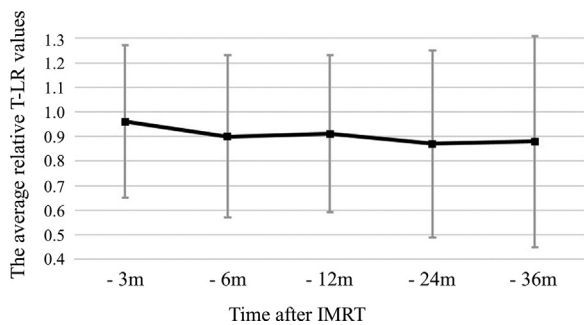


Fig. 6 – The average relative diameter of the transitional zone in the left–right directions (T-LR) values after intensity-modulated radiation therapy (IMRT) compared to the pre-IMRT.

Local recurrence was observed in 8 patients. At 12 months after IMRT, the average relative T-AP was significantly lower in patients with recurrence than in those without recurrence (Table 3.).

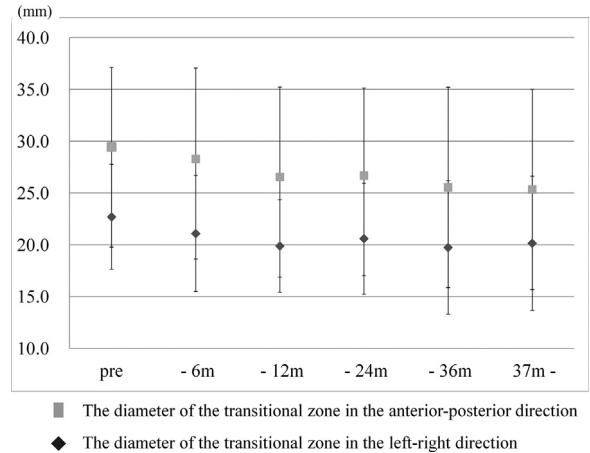


Fig. 7 – The transition of the diameter of the transitional zone in the anterior–posterior (T-AP) and left–right (T-LR) is shown. The average T-AP and T-LR decreased by approximately 10% during the 12 months after intensity-modulated radiation therapy (IMRT); thereafter, the diameters remained unchanged.

5. Discussion

The prostate is surrounded by several soft-tissue structures (the bladder, seminal vesicle, venous plexus, neurovascular bundles, muscles, rectum, etc.).^{15,16} Because of the small differences in density, the interfaces between the prostate and these structures are not well defined on CT. The fuzziness of the outline of the prostate on CT tends to result in an overestimation of prostate size. MRI has a better soft-tissue resolution and reveals the interfaces more clearly,^{17,18} thereby decreasing the risk of overestimation of prostate size.¹⁹⁻²¹ Therefore, patients who had not undergone MRI after IMRT were excluded from this study.

Table 2 – The average PSA levels at 12 months after IMRT in patients with diameter reduction rate $\geq 5\%$ and $<5\%$.

	PSA levels (ng/ml)							
	P-AP	p value	P-LR	p value	T-AP	p value	T-LR	p value
Reduction rate $\geq 5\%$	1.3	0.6005	1.2	0.1919	1.3	0.1361	1.2	0.2563
Reduction rate $< 5\%$	1.1		1.2		1.2		1.2	

PSA: prostate specific antigen; IMRT: intensity-modulated radiation therapy; P-AP and P-LR: the diameter of the prostate in the anterior–posterior and left–right directions, respectively; T-AP and T-LR: the diameter of the transitional zone in the anterior–posterior and left–right directions, respectively.

Table 3 – The average relative diameter at 12 months after IMRT in patients with and without recurrence.

	Reduction rate (%)							
	P-AP	p value	P-LR	p value	T-AP	p value	T-LR	p value
Recurrence (N = 8)	8	0.1118	8	0.2741	15	0.0409	5	0.6997
No recurrence (N = 64)	7		8		7		6	

IMRT: intensity-modulated radiation therapy; P-AP and P-LR: the diameter of the prostate in the anterior–posterior and left–right directions, respectively; T-AP and T-LR: the diameter of the transitional zone in the anterior–posterior and left–right directions, respectively.

ADT plays an important role in the treatment of prostate cancer. As hormonal therapy used for volume reduction before brachytherapy for prostate cancer, ADT may decrease prostate size. Studies have shown atrophy of the nonmalignant prostatic tissue after ADT.¹⁰ Tanaka et al. reported that patients who had received low-dose rate brachytherapy without ADT showed an approximately 20% decrease in prostate volume at 12 months after seed implantation.²² High-dose rate brachytherapy may also change prostate size.¹²

Although many patients have shown decreased prostate size after IMRT, some of them were treated with a combination of ADT. The hormonal therapy might mask the effect of size reduction by IMRT. Moreover, the effect of size change produced by external beam radiotherapy is not well known. This study revealed that prostate size decreased by approximately 10% after IMRT alone. This is the most important finding of this study.

There was no significant difference in PSA levels according to the change in relative diameter at 12 months after IMRT. However, the average relative T-AP was significantly lower in patients with recurrence than in those without recurrence. The reason for this result is not clear because only a small number of patients experienced recurrence. Studies with larger sample size are required to understand the reason behind this result.

Conflict of interest

None declared.

Financial disclosure

None declared.

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