

Dose–volume histogram comparison between static 5-field IMRT with 18-MV X-rays and helical tomotherapy with 6-MV X-rays

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We treated prostate cancer patients with static 5-field intensity-modulated radiation therapy (IMRT) using linac 18-MV X-rays or tomotherapy with 6-MV X-rays. As X-ray energies differ, we hypothesized that 18-MV photon IMRT may be better for large patients and tomotherapy may be more suitable for small patients. Thus, we compared dose–volume parameters for the planning target volume (PTV) and organs at risk (OARs) in 59 patients with T1–3 N0M0 prostate cancer who had been treated using 5-field IMRT. For these same patients, tomotherapy plans were also prepared for comparison. In addition, plans of 18 patients who were actually treated with tomotherapy were analyzed. The evaluated parameters were homogeneity indices and a conformity index for the PTVs, and D2 (dose received by 2% of the PTV in Gy), D98, Dmean and V_{10–70 Gy} (%) for OARs. To evaluate differences by body size, patients with a known body mass index were grouped by that index (<21; 21–25; and >25 kg/m²). For the PTV, all parameters were higher in the tomotherapy plans compared with the 5-field IMRT plans. For the rectum, V_{10 Gy} and V_{60 Gy} were higher, whereas V_{20 Gy} and V_{30 Gy} were lower in the tomotherapy plans. For the bladder, all parameters were higher in the tomotherapy plans. However, both plans were considered clinically acceptable. Similar trends were observed in 18 patients treated with tomotherapy. Obvious trends were not observed for body size. Tomotherapy provides equivalent dose distributions for PTVs and OARs compared with 18-MV 5-field IMRT. Tomotherapy could be used as a substitute for high-energy photon IMRT for prostate cancer regardless of body size.

Keywords: helical tomotherapy; IMRT; prostate cancer; dose–volume histogram; body size

INTRODUCTION

The role of intensity-modulated radiation therapy (IMRT) seems to have been established in the definitive treatment of localized prostate cancer [1–4]. By delivering ≥ 78 Gy in 2-Gy daily fractions or doses equivalent to or higher than this level, high local control rates (>80%) are obtained with acceptable complication rates [5–9]. For IMRT of prostate cancer, linac-based systems using a dynamic multileaf collimator (sliding window) or step-and-shoot mode have been commonly used worldwide. The treatment usually employs

coplanar 5–9 static ports of X-ray beams from various angles. Following the establishment of linac-based IMRT, helical tomotherapy-based IMRT using the TomoTherapy Hi-Art[®] system (Accuray Inc., Sunnyvale, CA, USA) has been introduced. The possible differences between linac-based and tomotherapy-based IMRT are discussed, and the respective advantages and disadvantages are pointed out for each modality [10–12].

In our institution, linac-based IMRT for prostate cancer was commenced in 2004, employing 18-MV X-rays from five static ports. The clinical outcomes of our treatment have

shown good tumor control and acceptable toxicities [13, 14]. Recently, a newer version of tomotherapy (TomoTherapy HD[®]) has been introduced into our institution and has become available for prostate cancer treatment. Tomotherapy treatment is usually delivered with a 360-degree rotation of a compact 6-MV linac gantry [15–17]. Since the X-ray energy and radiation delivery methods are quite different from those of linac-based IMRT, it was a concern that dose distributions may be somewhat different between the two modalities and that, as a result, clinical outcomes may be affected [18, 19]. Therefore, we planned this study to compare dose distributions between 18-MV linac-based IMRT and 6-MV tomotherapy. Owing to the depth–dose characteristics of the X-rays, we hypothesized that 18-MV linac-based IMRT might be better for large patients and tomotherapy more suitable for smaller patients. Planning studies on the differences with respect to energy levels [20] and irradiation techniques [21–26] have been reported; however, the difference with respect to patient body shape has not been reported. In this study, therefore, we compared the dose–volume parameters of the two IMRT modalities for the planning target volume (PTV) and organs at risk (OAR), with special reference to the influence of body size.

MATERIALS AND METHODS

Patient selection

Among over 300 patients treated with linac-based IMRT since 2004, 59 patients with T1–3 N0M0 prostate cancer (who had already completed the treatment between 2005 and 2012) were selected. The patient selection criterion was that IMRT planning data could be properly transferred to the tomotherapy planning workstation. Of the 59 patients, 44 had been treated with 74.8 Gy in 34 fractions at 2.2 Gy daily. The other fractionation schedules used were 77.7 Gy in 37 fractions (2.1 Gy daily) in 4 patients, 78 Gy in 39 fractions (2.0 Gy daily) in 7, and 74 Gy in 37 fractions (2.0 Gy daily) in 4. The 2.0- and 2.1-Gy daily fractionation data were converted to 2.2-Gy daily fractionation data using the linear–quadratic formalism assuming an α/β ratio of 3 Gy (for all organs) [27]. Their median age was 69 years (range, 59–80). In addition, data on 18 patients actually treated between July 2012 and May 2014 using tomotherapy with 74.8 Gy in 34 fractions (2.2 Gy daily) were analyzed. Their median age was 72 years (range, 64–82). IMRT for prostate cancer and publication of the data was approved by the Nagoya City University Institutional Review Board, and all patients gave written informed consent for both their treatment and possible use of their data for research purposes.

Treatment planning

All the patients were immobilized in a supine position with a vacuum bag system (BodyFIX; Medical Intelligence, Schwabmeunchen, Germany) for their whole body. CT

scans were performed at a slice thickness of 3.2 mm using a 4-row multi-detector CT (Mx8000; Philips Medical systems, Best, the Netherlands) for patients treated with linac-based IMRT and a 16-row multi-detector CT (Optima CT 580W; GE Healthcare, Milwaukee, WI, USA) for patients treated with tomotherapy under normal breathing, as described in detail previously [28, 29]. CT images were reconstructed at 2.5-mm thickness.

For 59 patients treated with linac-based IMRT, existing contouring data for each patient was utilized. Our contouring procedures were also described in detail previously [1, 2]. The outlines of the target were delineated on a 3D radiation treatment planning system (Eclipse Version 7.5.14.3; Varian Medical Systems, Palo Alto, CA) by reference to MR images. CT and MRI for treatment planning were taken at 60–90 min after urination, depending on the urinary frequency of patients. The clinical target volume was the whole prostate plus one-third of the seminal vesicle for the T1 stage, plus one-half of the seminal vesicle for the T2, or plus the whole seminal vesicle for the T3. PTV margins were 8 mm in the cranio–caudal and anterior directions, 7 mm in the lateral direction and 6 mm in the posterior direction. The rectum was contoured from 10 mm below to 10 mm above the PTV in the cranio–caudal direction. The whole bladder, including urine, was contoured. Dose constraints in all groups are listed in Table 1. For the 18 patients treated with tomotherapy, contouring was similarly performed.

Their CT and contouring data were exported to the tomotherapy planning station as DICOM data, and tomotherapy

Table 1. Dose constraints for targets and organs at risk

Total dose (Gy)	74.8
PTV	
D95	≥90% of total dose
V90%	≥96% of total dose
Mean	≥99% and ≤103% of total dose
Maximum	≤110% of total dose
Rectum V _x	
≤35%	38.5
≤18%	57.7
= 0%	75.1
Bladder V _x	
≤50%	38.5
≤25%	62.5
= 0%	75.1

PTV = planning target volume, D95 = minimum dose delivered to 95% of the PTV, V90% = percentage of the PTV receiving at least 90% of the prescribed dose, V_x = percentage of the organ receiving at least *x* Gy.

planning was done. Our tomotherapy planning procedures have been described in detail previously [13, 25]. The evaluated parameters were two homogeneity indices (HI95, HIICRU) and a

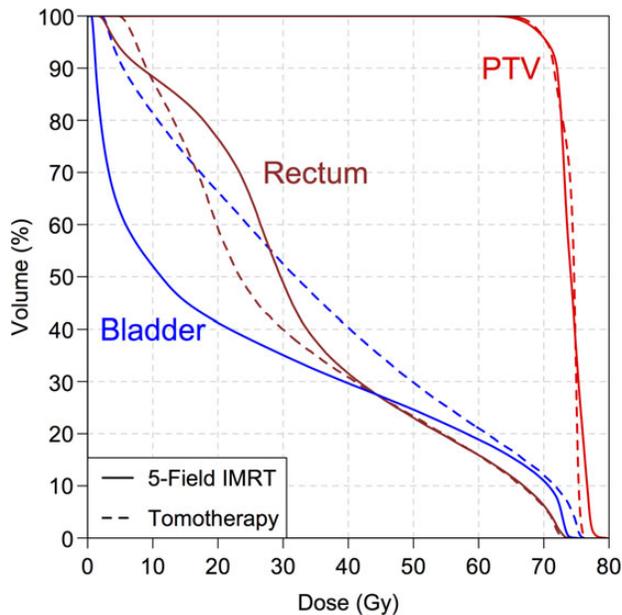


Fig. 1. Representative dose–volume histogram.

conformity index (CI95) for the PTV, D2 (dose received by 2% of the PTV in Gy), D98 (Gy), Dmean (Gy) and $V_{10-70 \text{ Gy}}$ (%) for OARs. HI95 was defined as $D5/D95$, and HIICRU was $(D2-D98)/D50$. CI95 was V_{95}/V_{PTV} : V_{95} = lesion volume (cm^3) covered by 95% of prescribed dose; V_{PTV} = PTV volume (cm^3). Among the 59 patients treated with linac-based IMRT, the body mass index (BMI) {body weight (kg)/[height (m)]²} could be calculated in 37, and the patients were divided into three groups according to BMI (<21; 21–25; and >25 kg/m^2 ; $n = 12, 13$ and 12 , respectively). A BMI >25 kg/m^2 is regarded as indicating overweight. Although the BMI for normal weights ranges from 18.5 to 25 kg/m^2 , the non-overweight patients were divided into two groups by their median BMI, because the patient number with a BMI <18.5 kg/m^2 was small. For the 18 patients treated with tomotherapy, the BMI was <21 kg/m^2 in 1, 21–25 kg/m^2 in 5, >25 kg/m^2 in 5, and unknown in 7.

Statistical analysis

Comparisons of dose–volume parameters between plans were carried out using a *t*-test. All statistical analyses were performed using R statistical software (R Foundation for Statistical Computing, Vienna, Austria.)

Table 2. Dose–volume parameters for all patients

		5-field IMRT (actually treated) $n = 59$	Tomotherapy (planning only) $n = 59$	<i>P</i> -value	Tomotherapy (actually treated) $n = 18$	<i>P</i> -value ^a
PTV	CI95	1.04 ± 0.06	1.22 ± 0.08	<0.001	1.25 ± 0.08	<0.001
	HI95	1.10 ± 0.03	1.07 ± 0.01	<0.001	1.08 ± 0.03	0.01
	HIICRU	0.13 ± 0.04	0.089 ± 0.015	<0.001	0.34 ± 0.017	<0.001
	D95% (Gy)	70.4 ± 1.2	70.9 ± 0.5	<0.001	71.3 ± 1.8	0.06
Rectum	$V_{10 \text{ Gy}}$ (%)	88 ± 6.0	92 ± 5.4	<0.001	89 ± 6.4	0.9
	$V_{20 \text{ Gy}}$ (%)	76 ± 6.7	67 ± 9.7	<0.001	64 ± 12	0.001
	$V_{30 \text{ Gy}}$ (%)	51 ± 6.2	44 ± 8.3	<0.001	41 ± 6.5	<0.001
	$V_{40 \text{ Gy}}$ (%)	33 ± 4.8	32 ± 7.2	0.36	29 ± 3.0	<0.001
	$V_{50 \text{ Gy}}$ (%)	24 ± 4.4	24 ± 6.5	0.08	21 ± 2.1	0.002
	$V_{60 \text{ Gy}}$ (%)	16 ± 4.0	17 ± 5.5	0.006	14 ± 1.5	0.003
	$V_{70 \text{ Gy}}$ (%)	6.8 ± 3.8	7.4 ± 3.6	0.08	6.1 ± 1.3	0.3
Bladder	$V_{10 \text{ Gy}}$ (%)	69 ± 19	89 ± 12	<0.001	80 ± 22	0.04
	$V_{20 \text{ Gy}}$ (%)	55 ± 18	77 ± 15	<0.001	70 ± 22	0.01
	$V_{30 \text{ Gy}}$ (%)	46 ± 17	60 ± 14	<0.001	54 ± 16	0.08
	$V_{40 \text{ Gy}}$ (%)	35 ± 15	44 ± 12	<0.001	39 ± 11	0.3
	$V_{50 \text{ Gy}}$ (%)	28 ± 12	32 ± 10	<0.001	28 ± 8.2	0.8
	$V_{60 \text{ Gy}}$ (%)	21 ± 9.5	23 ± 8.5	0.001	20 ± 6.1	0.8
	$V_{70 \text{ Gy}}$ (%)	12 ± 7.2	13 ± 5.9	0.04	12 ± 3.8	0.6

^aThese *P*-values are for comparison of 5-field IMRT and tomotherapy (actually treated).

Table 3. Dose–volume parameters according to BMI

		5-field IMRT (actually treated)	Tomotherapy (planning only)	P-value	Tomotherapy (actually treated)	P-value ^a	
PTV	CI95	1.04 ± 0.07	1.19 ± 0.08	< 0.001	1.18	–	
		1.04 ± 0.06	1.23 ± 0.07	< 0.001	1.20 ± 0.08	0.01	
		1.02 ± 0.05	1.22 ± 0.08	< 0.001	1.32 ± 0.07	< 0.001	
	HI95	1.12 ± 0.03	1.08 ± 0.01	0.001	1.19	–	
		1.10 ± 0.03	1.07 ± 0.01	< 0.001	1.08 ± 0.01	0.01	
		1.10 ± 0.02	1.07 ± 0.01	< 0.001	1.06 ± 0.01	0.001	
	HIICRU	0.16 ± 0.05	0.10 ± 0.01	0.001	0.31	–	
		0.14 ± 0.04	0.082 ± 0.010	< 0.001	0.35 ± 0.016	< 0.001	
		0.12 ± 0.03	0.086 ± 0.013	< 0.001	0.35 ± 0.014	< 0.001	
	D95% (Gy)	69.0 ± 1.7	70.4 ± 0.4	0.02	65.1	–	
		70.7 ± 0.83	71.2 ± 0.3	0.06	71.8 ± 0.75	0.03	
		70.7 ± 1.0	71.0 ± 0.6	0.3	72.0 ± 1.1	0.04	
Rectum	V _{10 Gy} (%)	90 ± 2.8	96 ± 3.5	< 0.001	87	–	
		86 ± 9.0	91 ± 6.8	0.04	87 ± 4.0	0.8	
		91 ± 2.6	93 ± 5.0	0.3	86 ± 9.5	0.27	
	V _{20 Gy} (%)	77 ± 6.6	77 ± 8.7	0.94	61	–	
		75 ± 8.6	64 ± 10	< 0.001	59 ± 11	0.03	
		79 ± 4.2	66 ± 9.0	< 0.001	66 ± 14	0.10	
	V _{30 Gy} (%)	53 ± 8.2	54 ± 12	0.77	44	–	
		50 ± 8.3	41 ± 5.1	< 0.001	38 ± 3.2	< 0.001	
		53 ± 5.3	42 ± 5.4	< 0.001	43 ± 11	0.11	
	V _{40 Gy} (%)	36 ± 8.3	40 ± 11	0.02	33	–	
		32 ± 3.8	31 ± 4.0	0.18	28 ± 1.9	0.01	
		32 ± 2.4	30 ± 3.0	0.07	29 ± 4.5	0.16	
	V _{50 Gy} (%)	27 ± 8.0	31 ± 10	0.01	23	–	
		24 ± 2.8	23 ± 3.4	0.4	20 ± 2.0	0.07	
		22 ± 2.0	22 ± 0.8	0.4	21 ± 2.7	0.17	
	V _{60 Gy} (%)	20 ± 7.2	22 ± 9.3	0.05	14	–	
		15 ± 2.3	16 ± 3.0	0.04	14 ± 1.8	0.2	
		15 ± 1.6	15 ± 2.5	0.9	14 ± 1.6	0.18	
	V _{70 Gy} (%)	11 ± 6.0	9.8 ± 6.6	0.33	3.2	–	
		6.4 ± 1.7	7.6 ± 2.5	0.02	6.2 ± 1.2	0.8	
		5.8 ± 2.7	6.2 ± 1.8	0.08	6.0 ± 1.4	0.8	
	Bladder	V _{10 Gy} (%)	72 ± 21	91 ± 10	< 0.001	93	–
			68 ± 19	90 ± 12	< 0.001	89 ± 8.0	0.01
			73 ± 15	93 ± 7.0	< 0.001	76 ± 25	0.86
V _{20 Gy} (%)		61 ± 21	81 ± 14	< 0.001	61	–	
		55 ± 19	77 ± 14	< 0.001	79 ± 11	0.01	
		59 ± 15	81 ± 11	< 0.001	67 ± 27	0.56	

Continued

Table 3. *Continued*

	5-field IMRT (actually treated)	Tomotherapy (planning only)	<i>P</i> -value	Tomotherapy (actually treated)	<i>P</i> -value ^a
V _{30 Gy} (%)	53 ± 20	68 ± 17	< 0.001	65	–
	46 ± 18	61 ± 14	< 0.001	59 ± 6.1	0.03
	49 ± 13	63 ± 6.6	< 0.001	52 ± 20	0.80
V _{40 Gy} (%)	43 ± 20	52 ± 17	< 0.001	42	–
	36 ± 15	46 ± 12	< 0.001	42 ± 5.2	0.2
	36 ± 8.9	45 ± 2.8	0.002	36 ± 13	0.96
V _{50 Gy} (%)	33 ± 15	37 ± 16	0.16	28	–
	28 ± 13	34 ± 10	< 0.001	31 ± 4.8	0.46
	28 ± 5.9	32 ± 2.3	0.002	27 ± 9.5	0.91
V _{60 Gy} (%)	25 ± 12	26 ± 13	0.78	18	–
	22 ± 12	25 ± 10	0.02	23 ± 3.9	0.78
	20 ± 4.5	23 ± 1.6	0.02	20 ± 7.1	0.92
V _{70 Gy} (%)	16 ± 8.7	15 ± 7.9	0.43	10	–
	14 ± 9.1	15 ± 8.1	0.03	13 ± 2.7	0.89
	11 ± 4.7	13 ± 2.4	0.11	12 ± 4.4	0.69

For all parameters, data on the first, second and third lines are for patients with BMI < 21, 21–25 and > 25 kg/m², respectively [*n* = 12, 13 and 12, respectively, for 5-field IMRT and tomotherapy (planning only), and *n* = 1, 5 and 5, respectively, for tomotherapy (actually treated)]. ^aThese *P*-values are for comparison of 5-field IMRT and tomotherapy (actually treated).

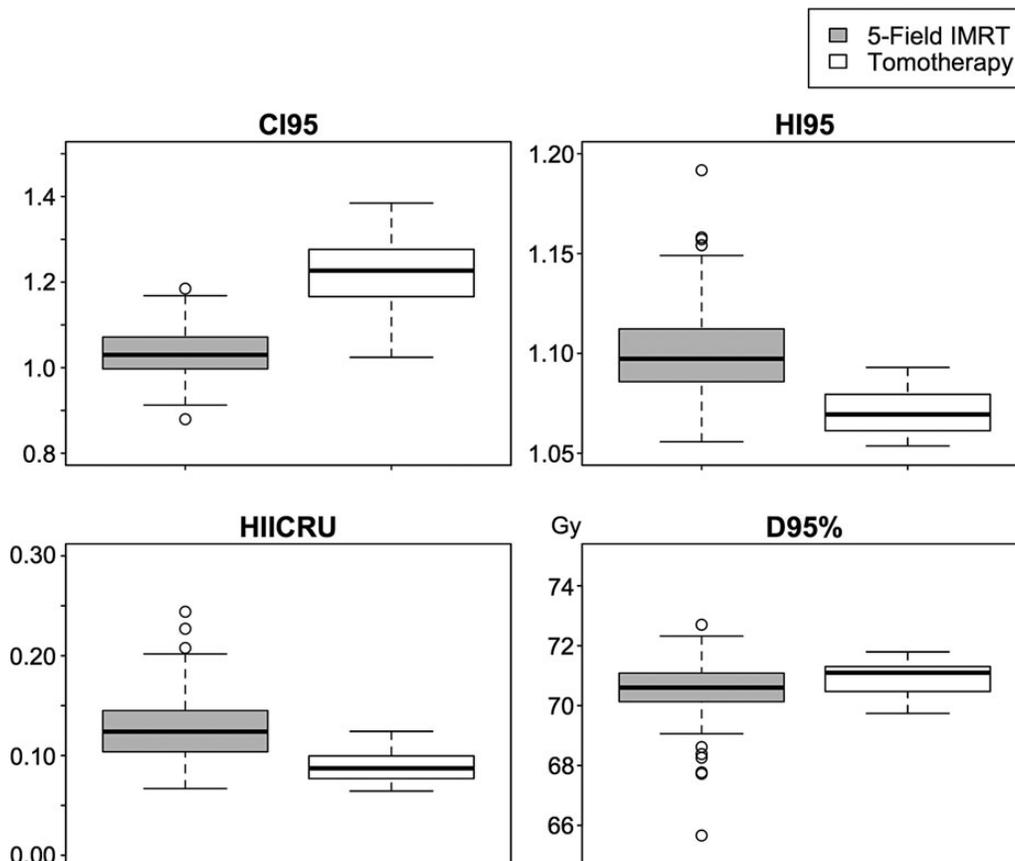


Fig. 2. Comparison of PTV parameters.

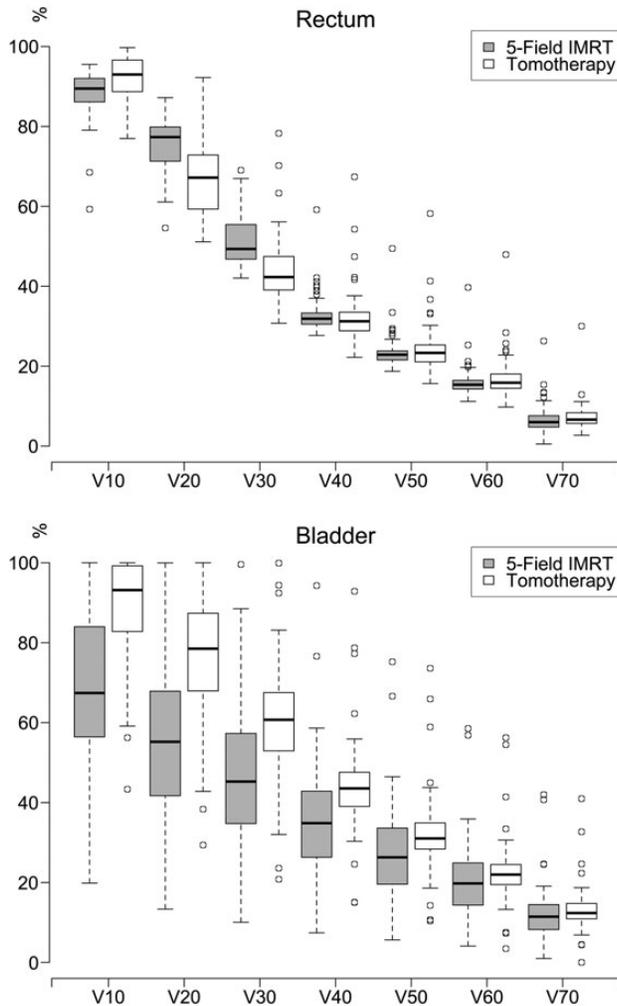


Fig. 3. Comparison of OAR parameters.

RESULTS

A representative dose–volume histogram is illustrated in Fig. 1. On tomotherapy plans, the irradiated volume of the rectum is decreased in middle dose ranges, and the irradiated volume of the bladder is increased in all dose ranges, whereas the PTV coverage is not much different. The dosimetric parameters of all patients ($n = 59$) for PTV and OARs are summarized in Table 2. Both 5-field IMRT and tomotherapy plans satisfied the dose constraints. For the PTV, HI95, HIICRU and V95% were superior and CI95 were inferior in the tomotherapy plans compared with the 5-field linac-based IMRT plans (Fig. 2). For the rectum, $V_{10 \text{ Gy}}$ and $V_{60 \text{ Gy}}$ were significantly higher, whereas $V_{20 \text{ Gy}}$ and $V_{30 \text{ Gy}}$ were lower in the tomotherapy plans. For the bladder, all parameters were significantly higher in the tomotherapy plans (Fig. 3). The dosimetric parameters in the three BMI groups are summarized in Table 3. Although small differences were seen, obvious trends were not observed

with change in body shape. When the 59 patients treated by linac-based IMRT were compared with the 18 patients treated by tomotherapy, small discrepancies were found, but general trends appeared to be similar (Tables 2 and 3).

DISCUSSION

The effects of beam energy and the number of ports on dose distribution in photon-based IMRT for deep-seated targets (such as the prostate) have been reported [30]. The use of 6-MV photons with at least 9 fields would appear to create dose distributions that are equivalent to those generated with higher energy beams. In this study, it was shown that tomotherapy plans generally have superior dose homogeneity and inferior dose conformity for the PTV compared with plans with 18-MV 5-field IMRT. These tendencies were observed in all the body size groups, but both plans appeared to be clinically acceptable. We used BMI as a simple index of body shape; distances from the skin to the PTV may be more relevant for investigating the influence of photon energies, but we found a close correlation between BMI and the distance from the skin to PTV (data not shown). Contrary to our expectation and hypothesis, dose distribution was not much affected by energy level and body shape. This may indicate that the beam delivery system in tomotherapy is so sophisticated that the disadvantage due to the lower photon energy does not become evident.

Late rectal toxicity has been reported as correlated with the rectal volume exposed to high doses of tomotherapy for localized prostate cancer [31], so lowering parameters such as the rectum V60 and V70 is considered to be important. In our previous study, the rectal volume exposed to middle doses like V40 also affected late toxicity [13]. In the 18 patients actually treated with tomotherapy, $V_{20-60 \text{ Gy}}$ of the rectum were lower than those of the 59 patients treated with linac-based IMRT. Based on the results of this study, the outcomes of localized prostate cancer treatment with tomotherapy would be expected to be as good as those of 5-field IMRT. Although high-energy photons have the advantage of creating steeper dose gradients along the PTV, one report implies that they could also lead to an increased risk of secondary malignancy owing to the presence of neutrons generated in the accelerator head at treatment energies $> 8 \text{ MV}$ [32]. On the other hand, the Monte Carlo calculations demonstrated no increased risk of developing a secondary cancer when using high-energy photons [33]. Thus, this issue is controversial, and the advantages and disadvantages of treatment with high-energy photons are not clear at present. From the above considerations, treatment with 6-MV tomotherapy is thought to be comparable with 5-field linac-based IMRT, regardless of patient body shape. Furthermore, the dynamic jaws system is now available for clinical use in order to decrease the irradiated volume at the cranio–caudal ends [34, 35]. Although dose constraints for target volumes

and OARs should be re-evaluated in order to use the dynamic jaw mode, better dose distribution would be expected in plans with tomotherapy. However, the static tomotherapy delivery mode (TomoDirect[®]) has not been demonstrated to be superior to the helical delivery mode (TomoHelical[®]), which was used in the present study [21]. Comparison with volumetric-modulated arc therapy is another topic yet to be investigated. At present, if one modality must be chosen, tomotherapy may be more appropriate than 18-MV 5-field IMRT when considering prostate cancer treatment. Small discrepancies were found between the tomotherapy plans for the 59 patients actually treated with 18-MV 5-field IMRT and those for the 18 patients actually treated with tomotherapy, probably due to the relatively small patient number in the latter group. The clinical data now accumulating (in our institution and also in other institutions) should be evaluated in future decision-making.

In conclusion, the result of our study shows that 6-MV tomotherapy plans have equivalent dose distributions for the PTV and OARs to 18-MV 5-field IMRT, even in large patients. Tomotherapy can be used for prostate cancer treatment in place of IMRT with high-energy photons, regardless of body shape.

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