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FULL PAPER

Comparison of dosimetric parameters and acute toxicity after whole-pelvic vs prostate-only volumetric-modulated arc therapy with daily image guidance for prostate cancer

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Objective: To compare dosimetric parameters and acute toxicity rates between whole-pelvic (WP) and prostate-only (PO) volumetric-modulated arc therapy (VMAT) in patients with localized prostate cancer.

Methods: A total of 224 consecutive patients treated with definitive VMAT to 78 Gy in 39 fractions were enrolled. Of these, 119 patients received initial WP VMAT at 46.8 Gy in 26 fractions using a simultaneous integrated boost technique, and 105 patients received PO VMAT. Image-guided radiotherapy was practised with daily cone beam CT.

Results: The mean rectal dose, the rectal volume receiving ≥ 30 Gy ($V_{30\text{Gy}}$), rectal $V_{50\text{Gy}}$, the mean bladder dose, bladder $V_{30\text{Gy}}$ and bladder $V_{50\text{Gy}}$ were significantly increased in the WP group ($p < 0.05$ each); however, the rectal $V_{70\text{Gy}}$ did not differ between groups ($p = 0.101$),

and the bladder $V_{70\text{Gy}}$ was significantly lower in the WP group ($p = 0.029$). The WP group experienced a significantly increased frequency of acute grade 2 diarrhoea relative to the PO group (5.9% vs 0%; $p = 0.015$). No differences were seen between the WP and PO groups in terms of acute grade 2 proctitis (10.1% vs 6.7%; $p = 0.360$) and genitourinary (GU) toxicity (12.6% vs 10.5%; $p = 0.620$).

Conclusion: Despite larger rectum and bladder volumes at low- and medium-dose levels, WP VMAT resulted in no significant increase in acute proctitis or GU toxicity when compared with PO VMAT.

Advances in knowledge: This study demonstrates that whole-pelvic radiotherapy has comparable acute toxicity to those observed with prostate-only radiotherapy when VMAT with daily image guidance is used.

INTRODUCTION

The benefit of whole-pelvic radiotherapy (WPRT) in patients at high risk for involvement of the pelvic lymph nodes is the subject of ongoing debate, since its effect on survival rates has not yet been clarified. In addition, there is a concern that WPRT could lead to additional toxicity compared with prostate-only radiotherapy (PORT). Two randomized Phase III trials have evaluated WPRT in comparison with PORT for patients with localized prostate cancer using conventional techniques.^{1,2} A subset analysis of the Radiation Therapy Oncology Group (RTOG) 9413 trial demonstrated that a larger field size resulted in a significant increase in acute grade 2 gastrointestinal (GI) and genitourinary (GU) toxicity and late grade 3 or higher GI toxicity among patients treated to the whole-pelvic (WP), mini-pelvis and prostate-only (PO) fields.¹ The GETUG-01 trial from the Groupe

D'Etude des Tumeurs Uro-génitales showed that WPRT resulted in a significant increase in acute grade 3 or higher GU toxicity and no difference in late GI and GU toxicity in comparison with PORT.² Thus, these studies have yielded mixed results. Furthermore, in these studies, the prostate dose was restricted to approximately 70 Gy with conventional fractionation, which has been shown to be suboptimal by current standards in the treatment of localized prostate cancer.³⁻⁵

Previous studies have demonstrated that intensity-modulated radiotherapy (IMRT) provides superior target coverage and organ at risk (OAR) sparing over three-dimensional conformal radiotherapy when performing WPRT.⁶⁻⁸ However, in the context of dose escalation to the prostate, dosimetric and clinical results from the literature comparing WP IMRT with PO IMRT are still limited. In

a planning study, Guckenberger *et al*⁹ predicted similar risks of rectal, bladder and small bowel toxicity in both WP IMRT and PO IMRT. A retrospective study by Deville *et al*¹⁰ comparing the toxicity of WP IMRT and PO IMRT (30 patients in each group) showed a clinically significant increase in acute GI toxicity with WP IMRT, whereas no difference was seen in GU or late GI toxicity.

Volumetric-modulated arc therapy (VMAT) is now widely used clinically,¹¹ since it is capable of delivering IMRT-quality plans with superior treatment delivery efficiency. Although several recent studies have reported early clinical results of VMAT for prostate cancer,^{12–14} to the best of our knowledge, there are no published clinical studies comparing WP VMAT with PO VMAT. Therefore, there is a need to demonstrate whether the use of WPRT could result in increased toxicity when VMAT is performed. Previously, we reported that VMAT for WPRT in prostate cancer is dosimetrically feasible and results in an acceptable rate of acute toxicity.¹⁴ In this study, we further investigated the differences in dosimetric parameters and acute toxicity rates between WP VMAT and PO VMAT with daily cone

beam CT (CBCT)-based image-guided radiotherapy (IGRT) for localized prostate cancer.

METHODS AND MATERIALS

Patient characteristics

This study was based on 224 consecutive patients with clinically localized prostate cancer undergoing definitive VMAT to a total dose of 78 Gy, using daily image guidance, between July 2011 and June 2014. Of these patients, 105 patients received PORT and 119 patients received WPRT. Written informed consent was obtained from all patients, and the Tane General Hospital ethics committee approved the study.

All patients had a biopsy-proven adenocarcinoma that was classified according to the Gleason grading system and were clinically staged according to the 2009 American Joint Committee on Cancer staging classification.¹⁵ The staging evaluation revealed no patients with metastatic disease. The patients were also stratified according to the 2009 National Comprehensive Cancer Network (NCCN) prognostic risk grouping (www.nccn.org). As per our institutional protocol, patients classified as low

Table 1. Patient characteristics and treatment modalities

Characteristic	PO VMAT	WP VMAT	<i>p</i> -value
Number of patients	105	119	
Age (years)			0.086
Median	73	72	
Range	56–87	50–79	
Gleason score			<0.001
4–6	33	6	
7	59	33	
8–10	13	80	
PSA (ng ml ⁻¹)			<0.001
Median	9.5	28.2	
Range	3.9–129.2	4.0–445.0	
Clinical stage			<0.001
T1	42	14	
T2	55	34	
T3	8	63	
T4	0	8	
NCCN risk group			<0.001
Low risk	21	0	
Intermediate risk	63	0	
High risk	21	119	
Diabetes	9	20	0.070
Anticoagulants	18	20	0.947
Androgen deprivation	69	113	<0.001

NCCN, National Comprehensive Cancer Network; PO, prostate-only; PSA, prostate-specific antigen; VMAT, volumetric-modulated arc therapy; WP, whole-pelvic.

Figure 1. Representative dose distributions for (a) prostate-only volumetric-modulated arc therapy (VMAT) and (b) whole-pelvic VMAT. Prostate planning target volumes (PTVs) are shown in red and nodal PTVs are shown in pink. The dose colour wash is from 39 Gy (dark blue) to approximately 81 Gy (red).

or intermediate risk as defined by NCCN criteria were treated to the PO fields. Patients at high risk were mainly treated to the WP fields; however, patients more than 80 years of age or those who did not wish to receive WPRT were treated to the PO fields. Androgen deprivation therapy (ADT) was recommended for 2 years or longer for patients at high risk and for 6 months for patients at intermediate risk. ADT was not recommended for patients at low risk. However, the actual duration of ADT was dependent on the clinical judgment, based on the aggressiveness of the disease. The duration of neoadjuvant ADT was at least 3 months.

Simulation, organ contouring and planning

All patients underwent CT scanning with 1.25-mm-thick slices in the supine position after immobilization with a vacuum-based device (VacLock™; CIVCO Medical Solutions, Kalona,

IA). The patients were instructed to have a comfortably full bladder and an empty rectum for the CT scan and for each treatment. In patients at low risk, the prostate clinical target volume (CTV) was defined as the entire prostate, while for those at intermediate and high risk, the prostate CTV was defined as the entire prostate with a 15-mm area proximal to the seminal vesicles and any visible tumour extension. The prostate planning target volume (PTV) was the prostate CTV with a margin of 8 mm in all directions except posteriorly, where the margin was reduced to 5 mm. Pelvic lymph node volumes were standardized according to RTOG recommendation.¹⁶ The nodal CTV included a 7-mm expansion volume on the obturator vessels in addition to the common, external and internal iliac vessels, while excluding the adjacent bone, muscle, bowel and bladder. Differing from the RTOG recommendation where the pre-sacral nodes were included in the

Figure 2. Average dose-volume histograms for prostate-only (PO) volumetric-modulated arc therapy (VMAT) and whole-pelvic (WP) VMAT for the prostate planning target volume (PTV), rectum and bladder.

Table 2. Dosimetric parameter comparisons of prostate-only volumetric-modulated arc therapy (PO VMAT) and whole-pelvic volumetric-modulated arc therapy (WP VMAT)

Parameter	PO VMAT (mean $\pm$ SD)	WP VMAT (mean $\pm$ SD)	<i>p</i> -value
Prostate PTV			
Volume (ml)	113 $\pm$ 40	93 $\pm$ 23	<0.001
$D_{95\%}$ (Gy)	76.0 $\pm$ 0.5	76.4 $\pm$ 0.3	<0.001
D_{mean} (Gy)	78	78	–
$D_{2\%}$ (Gy)	79.7 $\pm$ 0.3	79.3 $\pm$ 0.2	<0.001
Nodal PTV			
Volume (ml)	–	791 $\pm$ 132	–
$D_{95\%}$ (Gy)	–	44.8 $\pm$ 0.4	–
D_{mean} (Gy)	–	46.8 $\pm$ 0.4	–
Rectum			
Volume (ml)	61 $\pm$ 19	60 $\pm$ 15	0.62
D_{mean} (Gy)	27.7 $\pm$ 4.9	40.0 $\pm$ 2.7	<0.001
$D_{2\%}$ (Gy)	77.6 $\pm$ 0.9	77.1 $\pm$ 1.1	<0.001
$V_{70\%}$ (Gy)	10.7 $\pm$ 3.4	11.5 $\pm$ 3.9	0.101
$V_{50\%}$ (Gy)	22.3 $\pm$ 5.4	26.5 $\pm$ 5.5	<0.001
$V_{30\%}$ (Gy)	37.3 $\pm$ 8.6	64.8 $\pm$ 10.9	<0.001
Bladder			
Volume (ml)	169 $\pm$ 90	198 $\pm$ 87	0.023
D_{mean} (Gy)	28.2 $\pm$ 9.6	43.7 $\pm$ 4.0	<0.001
$D_{2\%}$ (Gy)	78.5 $\pm$ 0.7	78.0 $\pm$ 0.7	<0.001
$V_{70\text{Gy}}$ (%)	12.9 $\pm$ 6.2	11.1 $\pm$ 5.5	0.029
$V_{50\text{Gy}}$ (%)	22.9 $\pm$ 10.2	27.4 $\pm$ 10.8	0.003
$V_{30\text{Gy}}$ (%)	38.2 $\pm$ 15.9	80.3 $\pm$ 11.5	<0.001
Bowel bag			
$D_{2\%}$ (Gy)	14.5 $\pm$ 15.4	47.1 $\pm$ 0.7	<0.001
$V_{45\text{Gy}}$ (ml)	0.2 $\pm$ 0.8	76.0 $\pm$ 30.0	<0.001

D_{mean} , mean dose; $D_{n\%}$, dose to $n\%$ of the volume; PTV, planning target volume; $D_{n\%}$, minimal dose to $n\%$ of the structure; SD, standard deviation; $V_{n\text{Gy}}$, percentage or absolute structure volume receiving $\geq n$ Gy.

Two-sided *p*-values calculated using unpaired Student's *t* test.

nodal CTV, the pre-sacral nodes were excluded in nodal CTV in the current study. The nodal PTV consisted of a 5-mm geometric expansion on the nodal CTV. Contouring of the OARs, including the rectum, bladder, femoral heads and bowel bag, was performed in accordance with RTOG contouring guidelines for the normal pelvic tissue.¹⁷ All OARs were contoured as solid organs. For the rectum, segmentation was performed from the level of the ischial tuberosities to the rectosigmoid flexure. The entire bladder was contoured from the apex to the dome. In terms of the femoral heads, these were delineated to the level of the ischial tuberosities. The bowel bag was defined as the total volume of the peritoneal space to 10 mm above the nodal PTV.

All patients received 78 Gy in 39 fractions of 2 Gy to the prostate PTV. A simultaneously integrated boost technique was

used for the patients undergoing WPRT, who received 46.8 Gy in 1.8-Gy fractions to the nodal PTV for the first 26 fractions. The dose was normalized to the mean dose delivered to the prostate PTV in all patients undergoing WPRT, and the mean dose to the nodal PTV was maintained as close to 46.8 Gy as possible. All VMAT plans were developed in the EclipseTM Treatment Planning System v. 10.0 (Varian Medical Systems, Palo Alto, CA) using 10-MV photons, and the final dose calculation was performed using the Anisotropic Analytical Algorithm v. 10.0.28 (Varian Medical Systems, Palo Alto, CA). The VMAT plans were generated with a single arc for the PO fields and double arcs for the WP fields. Plans were considered acceptable when at least 95% of the PTV received 95% or more of the prescribed dose. Our institutional OAR dose volume constraints were as follows: $V_{70\text{Gy}}$ (the volume receiving ≥ 70 Gy) <20% and $V_{50\text{Gy}}$ <45% for the rectum; $V_{70\text{Gy}}$ <25%

Table 3. Comparisons of acute grade 2 toxicity between prostate-only volumetric-modulated arc therapy (PO VMAT) and whole-pelvic volumetric-modulated arc therapy (WP VMAT)

Toxicity	PO VMAT	WP VMAT	<i>p</i> -value
GI	7 (6.7%)	17 (14.3%)	0.066
Proctitis	7 (6.7%)	12 (10.1%)	0.360
Diarrhoea	0	7 (5.9%)	0.015
GU	11 (10.5%)	15 (12.6%)	0.620
Frequency	9 (8.6%)	14 (11.8%)	0.432
Retention	3 (2.9%)	1 (0.8%)	0.343
Haematuria	2 (1.9%)	1 (0.8%)	0.601
Urinary tract pain	2 (1.9%)	0	0.219
Urgency	1 (1.0%)	0	0.469

GI, gastrointestinal; GU, genitourinary.

and $V_{50\text{Gy}} < 50\%$ for the bladder; $D_{2\%}$ (dose to 2% of the volume) < 50 Gy for the femoral heads; $D_{2\%} < 50$ Gy and $V_{45\text{Gy}} < 195$ ml for the bowel bag.

Online image-guided radiotherapy

The patients were treated with Novalis Tx[™] (Varian Medical Systems in collaboration with Brainlab AG, Feldkirchen, Germany). Radiation was delivered with image guidance using ExacTrac[®] (Brainlab) and CBCT for all patients. After the initial setup according to the marks on the skin of each patient, orthogonal kilovoltage radiographs were obtained using ExacTrac and then matched with the corresponding digitally reconstructed radiographs that were generated from the planning CT. When bone registration was satisfactory, CBCT images were acquired for use in the soft-tissue registration of the target.

Dosimetric analysis

The dose–volume histograms (DVHs) were calculated for the prostate PTV, nodal PTV, rectum, bladder and bowel bag and were averaged over all patients. The parameters chosen for comparison between the PO and WP groups were $D_{2\%}$ and $D_{95\%}$ (dose to 95% of the volume) for the prostate PTV. For the rectum and bladder, the analysis included the mean dose, $D_{2\%}$, $V_{70\text{Gy}}$, $V_{50\text{Gy}}$ and $V_{30\text{Gy}}$. The $D_{2\%}$ and $V_{45\text{Gy}}$ of the bowel bag were also compared.

Acute toxicity

For all patients, the Common Terminology Criteria for Adverse Events v. 4.0 (CTCAE v4.0) was used to retrospectively score the prospectively recorded GI and GU toxicity. The patients were monitored weekly during radiotherapy (RT) and at 2 weeks and 3 months after RT. Acute toxicity was defined as the reported toxicity originating within 90 days after the end of RT. The maximum toxicity grade rates were compared for each group.

Statistical analysis

The characteristics of the patients were compared using unpaired Student's *t*-tests for continuous variables and χ^2 test for

categorical variables. When a categorical variable contained < 5 patients, Fischer's exact test was used in place of the χ^2 test. The dose–volume parameters were compared using the unpaired Student's *t*-test. Either χ^2 test or Fischer's exact test was used to analyze the differences in the frequency of maximum GI and GU toxicities. All reported *p*-values were two tailed, and significance was defined at $p < 0.05$.

RESULTS

The baseline patient characteristics are summarized by treatment modality in Table 1. No significant differences were evident between the groups in terms of age or comorbidities. As a consequence of the patient selection for WPRT, those in the WP group had higher clinical stages, Gleason scores and pre-treatment prostate-specific antigen (PSA) levels and received ADT more frequently.

The representative dose distributions for the PO VMAT and WP VMAT groups are illustrated in Figure 1. The average DVHs for the prostate PTV, rectum and bladder are shown in Figure 2. The DVHs for the prostate PTV were similar in both groups. Although WP VMAT resulted in an increased dose to the rectum and bladder at the low- and medium-dose levels, the high-dose part of the DVH curves (60–80 Gy) for the rectum and bladder overlapped between the WP and PO VMAT groups, as seen in Figure 2. All dose–volume constraints were met for all treatment plans. The mean values of the dosimetric parameters of the PTV and OARs are shown in Table 2. Although there were statistically significant differences in target coverage between the WP and PO groups, the absolute differences in dose were very small. The rectal mean dose, $V_{30\text{Gy}}$ and $V_{50\text{Gy}}$, and bladder mean dose, $V_{30\text{Gy}}$ and $V_{50\text{Gy}}$, were significantly higher in the WP group; however, the rectal $V_{70\text{Gy}}$ did not differ between the groups, and the bladder $V_{70\text{Gy}}$ was significantly lower in the WP group. In addition, rectal $V_{70\text{Gy}}$ in terms of absolute rectal volume did not differ between the WP and PO groups (6.7 ± 2.2 vs 6.4 ± 2.4 ml; $p = 0.284$). Similarly, bladder $V_{70\text{Gy}}$ in terms of absolute bladder volume for the WP and PO groups was 18.6 ± 6.3 ml and 18.3 ± 8.0 ml, respectively, indicating no statistically significant difference

Table 4. Summary of reports on acute toxicities in whole-pelvic radiotherapy (WPRT) vs prostate-only radiotherapy (PORT) with dose escalation to the prostate

Study	Technique	Treatment site	Patients (n)	Total dose (Gy)/number of fractions		Acute GI toxicity (%)			Acute GU toxicity (%)		
				Prostate	Whole pelvis	Grade 3	Grade 2	p-value	Grade 3	Grade 2	p-value
Aizer et al ³¹	3D-CRT, IMRT	WPRT	68	75.6/42	45/25	10	34	0.048	2	18	0.090
		PORT	209		–	6	25		3	7	
Guckenberger et al ²⁸	IMRT	WPRT	25	73.91–76.23/32–33	46/25	0	12	1.00	0	44	0.81
		PORT	75		–	0	12		5	36	
Deville et al ¹⁰	IMRT	WPRT	30	79.2/44	45/25	0	50	0.006	3	50	0.587
		PORT	30		–	0	13		0	50	
Current study	VMAT	WPRT	119	78/39	46.8/26	0	14	0.066	0	13	0.620
		PORT	105		–	0	7		0	11	

3D-CRT, three-dimensional conformal radiotherapy; GI, gastrointestinal; GU, genitourinary; IMRT, intensity-modulated radiotherapy; VMAT, volumetric-modulated arc therapy.

between the groups ($p = 0.830$). The bowel bag $D_{2\%}$ and $V_{45\text{Gy}}$ were markedly increased in the WP group.

All patients completed RT and 3 months of follow-up. There was no acute GI or GU toxicity $\geq$ grade 3. The maximal acute toxicity is detailed in Table 3. Despite a statistically significant increase in the incidence of acute grade 2 diarrhoea in the WP group, only 7 (5.9%) patients experienced this side effect. No significant differences were noted between both groups with regard to acute grade 2 proctitis or GU toxicity.

DISCUSSION

In this study, we have examined the differences in both the dosimetric parameters and the acute toxicities between WP and PO VMAT with daily CBCT-based IGRT in patients with localized prostate cancer. While the volumes of the irradiated rectum and bladder differed at the low- and medium-dose levels, the volumes exposed to high-dose levels were equivalent in both groups. The maximum acute toxicity was limited to grade 2. In addition, there was no difference in the rates of acute grade 2 proctitis and GU toxicity. However, WP VMAT resulted in a statistically significant increase in acute diarrhoea. Although this study was limited by its retrospective nature, it was novel in that all patients were treated in a consistent manner with image-guided VMAT, with dose escalation to the prostate.

There are limited data in the literature with regard to dosimetric comparisons between WP and PO IMRT. In a planning study by Guckenberger et al⁹ with a series of 10 patients, WP IMRT resulted in increased doses to the rectum at the low-dose level (≤ 30 Gy) and to the bladder at the low- and medium-dose levels (≤ 50 Gy) when compared with PO IMRT, whereas no difference was observed at the high-dose levels for the rectum and bladder. In a report by Deville et al,¹⁰ 60 patients received either WP IMRT or PO IMRT, and there was no dosimetric difference at the high-dose levels ($V_{65\text{Gy}}$ and $V_{70\text{Gy}}$) for the rectum and bladder. Similar results were obtained in our study when we compared WP VMAT with PO VMAT. This result can be explained by the fact that the in-field rectum and bladder volumes were greater in WP VMAT owing to the increased overlap with the nodal PTV, which caused an increase at the low- and medium-dose levels assessed for the rectum and bladder.

The dosimetric differences in the volume of the rectum and bladder irradiated at the low- and medium-dose levels did not transfer to statistically significant differences in the rates of acute proctitis and GU toxicity between WP and PO VMAT. In previous reports discussing the relationship between acute proctitis and rectal dose–volume parameters, no clear dose–volume effect for acute proctitis could be found.^{18–20} In contrast, the Quantitative Analyses of Normal Tissue Effects in the Clinic (QUANTEC) review demonstrated that most rectal dose–volume parameters for doses ≥ 60 Gy were significantly associated with late rectal toxicity, with the exception of faecal incontinence.²¹ Because late faecal incontinence has been associated with medium doses to larger volumes of the rectum,²² it is likely that these larger volumes irradiated at medium-dose levels in the WP group of this study may have influenced the late toxicity profile. For the bladder, there is no clear correlation

between the DVH parameters and the incidence of acute and late toxicity,²³ since the DVH obtained from a single planning CT image is unlikely to represent the true dose distribution delivered to the bladder during the treatment course. Furthermore, GU toxicity may be partly caused by the effects of radiotherapy on the prostatic urethra and part of the bladder neck, which are unavoidable parts of the target volume and are likely to receive similar doses, independent of the radiation field size.^{24,25} In contrast, WP VMAT resulted in a significant increase in acute grade 2 diarrhoea because most bowel bag volumes were outside the PTV with PO VMAT, while the bowel bag and PTV partially overlapped in cases that underwent WP VMAT. In this study, the bowel bag V_{45Gy} was 0.2 ± 0.8 and 76.0 ± 30.0 ml for PO and WP VMAT, respectively. However, the incidence of grade 2 diarrhoea was only 5.9%.

IMRT has become the standard of treatment for dose-escalated external beam RT in patients with localized prostate cancer. In terms of acute GI and GU toxicities $\geq$ grade 2, the rates reported from PO IMRT series are from 1.9% to 32.4% and 9–64%, respectively.^{10,24–28} For WP IMRT, acute GI and GU toxicities $\geq$ grade 2 have been reported from 12% to 50% and 44–51.7%, respectively.^{10,28–30} Although the use of different toxicity scales makes comparison difficult, in our study, both PO and WP VMAT with daily CBCT-based IGRT provided acceptably low rates of acute GI and GU toxicity when compared with the results presented in other studies.^{10,24–30}

Data comparing acute toxicities between WPRT and PORT in the setting of dose escalation to the prostate are limited. Table 4 summarizes the available reports in comparison with our findings. All of the reports showed that there was no difference in acute GU toxicity, as in the present study. However, there was a statistically significant or tendency towards higher rates of acute GI toxicity in the WPRT groups, except for the report by Guckenberger et al.⁹ Unlike the other reports, the one by Aizer et al.³¹ reported acute grade 3 GI toxicity in the WPRT group. This high-grade toxicity is potentially explained by the fact that the patients in the WPRT group were treated with three-dimensional conformal radiotherapy, whereas IMRT in combination with IGRT, such as CBCT or the ultrasound-guided system for anatomic positioning verification, was used for WPRT in the other studies.^{10,28} Given these findings, although

there is a trend towards increased acute grade 2 GI toxicity in WPRT, it is conceivable that the incidence of severe acute GI and GU toxicities is infrequent and is similar when comparing WPRT with PORT in the setting of IMRT/VMAT using IGRT.

The pelvic lymph node volumes were similar to those recommended by the RTOG consensus,¹⁶ except for the exclusion of the pre-sacral nodes. The pre-sacral lymph nodes were not irradiated in many WP IMRT series in the context of conventionally fractionated^{8,10,30,32} and hypofractionated^{33,34} RT. Similar to other institutions,^{10,34} the reason for the nodal CTV definition used at our institution is that inclusion of the pre-sacral nodes could potentially increase the volume of the rectum, bladder and bowel bag irradiated at the low- to medium-dose levels, which could further impact GI and GU toxicities.

There are several limitations in the present study. First, although the pre-treatment patient characteristics, such as age and comorbidities, were similar in both groups, patients in the WP group received ADT more frequently because this cohort consisted only of patients with high-risk prostate cancer. Whether androgen suppression is correlated with increased toxicity is a controversial issue in the literature.^{35,36} However, we cannot exclude the possibility that prostate volume reduction after ADT likely yielded the low incidence of acute bladder and rectal toxicity in the WP group. Second, there was a short follow-up period. While a lower incidence of acute toxicity might reduce the development of subsequent late toxicity,^{25,37,38} WPRT could result in worse late toxicity because the field is larger than that irradiated during PORT. Therefore, late toxicity should be assessed during longer follow-up.

CONCLUSION

WP VMAT resulted in larger rectum and bladder volumes at low- and medium-dose levels, but similar or smaller volumes at high-dose levels than PO VMAT. Both WP and PO VMAT with daily image guidance provided acceptably low rates of acute GI and GU toxicity. Although WP VMAT resulted in a significant increase in acute diarrhoea, the larger volumes of irradiated rectum and bladder in the WP group did not lead to a significant increase in acute proctitis and GU toxicity when compared with the PO group. Further follow-up is needed to assess late toxicity.

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