



Risk factors for rectal bleeding after volumetric-modulated arc radiotherapy of prostate cancer

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ABSTRACT

Background: It is crucially important to understand the risk factors for rectal bleeding after volumetric-modulated arc radiotherapy (VMAT) for prostate cancer to prevent subsequent rectal bleeding. We assayed clinical and dosimetric data to investigate the risk factors for rectal bleeding after VMAT of prostate cancer.

Materials and methods: This study included 149 patients with prostate cancer who received VMAT from February, 2012 to June, 2020. Irradiated total doses were 78 Gy/39 fractions in 33 patients (22.1%), 76 Gy/38 fractions in 89 (59.7%), 74 Gy/37 fractions in 4 (2.7%), and 72 Gy/36 fractions in 23 (15.4%). We investigated multiple clinical and dosimetric factors with reference to rectal bleeding.

Results: The median observation period was 38 months. Fourteen patients (9.4%) experienced rectal bleeding: five (3.4%) were classified as Grade 2, and nine (6.0%) as Grade 1. There were significant differences between Grade ≥ 1 and Grade 0 patients in the overlap region of the planning target volume (PTV) and the rectum, the rectal V30–75, and the mean rectal dose ($p < 0.05$). There were significant differences between Grade 2 and Grade 0–1 patients in rectal V30–65 and mean rectal dose ($p < 0.05$).

Conclusions: Rectal bleeding occurred, but its grades and rate of occurrence were permissible. Higher rectal doses were shown to be related to rectal bleeding, and reduction of low/intermediate and mean rectal doses will be important for preventing rectal bleeding.

Key words: prostate cancer; radiotherapy; volumetric-modulated arc radiotherapy; rectal bleeding

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Introduction

Prostate cancer is one of the most common malignant tumors in men [1], and the number of patients who need the treatment is increasing. In radiation therapy for prostate cancer, both tumor control

and reduction of adverse events are very important. According to several studies, dose escalation for the treatment of prostate cancer has the benefit of tumor control [2–4]. However, the prostate is surrounded by critical organs, such as the rectum and urinary bladder, and dose escalation has

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the risk of adverse events to these organs, especially the rectum. Prevention of rectal bleeding can be as important as tumor control for long-term prostate cancer patients because rectal bleeding has a direct impact on quality of life.

Intensity modulated radiation therapy (IMRT) has enabled both dose escalation and sparing of the rectum. Dose escalation using three-dimensional conformal radiotherapy (3D-CRT) has the risk of rectal toxicity. IMRT improved the conformality of dose distributions around the planning target volume (PTV) compared with 3D-CRT [5–7]. Zelefsky et al. reported that the 2-year actuarial risk of Grade 2 rectal bleeding was 2% for IMRT and 10% for conventional 3D-CRT, and that IMRT significantly reduced the risk of rectal bleeding compared with 3D-CRT [8]. However, there are still a small number of patients who suffer from rectal bleeding after IMRT treatment.

Volumetric-modulated arc therapy (VMAT) is a complex treatment strategy for IMRT and may be the most efficient treatment option [9]. VMAT is a rotational treatment, and the field shapes change dynamically during irradiation. Compared with step-and-shoot IMRT, the treatment time when using VMAT is short. We have used VMAT for prostate treatment since 2012 because of its high throughput.

It is crucially important to understand the risk factors for rectal bleeding after VMAT for prostate cancer to prevent subsequent rectal bleeding. In this study, we assayed clinical and dosimetric data to investigate the factors of rectal bleeding after VMAT for prostate cancer.

Materials and methods

All patients gave their informed consent for treatment, and for the use of their records for this retrospective study. Our institutional ethics committee approved this study. The requirement for informed consent was waived.

Patients

The patient population for this retrospective study consisted of a single-institution registry of 156 consecutive patients with clinically localized prostate cancer who underwent VMAT at our hospital from February 2012 to June 2020 and were observed for at least 12 months. Seven patients

were excluded because their radiation treatment plans were not able to be summed up and it was difficult to evaluate their rectal dose in detail. One hundred one patients (67.8%) received hormone therapy. Rectal bleeding complications were recorded at 1- to 6-month intervals during regular follow-up visits. Rectal bleeding was quantified using the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0. Grade 1 is defined as mild symptoms, intervention not indicated; Grade 2 is defined as moderate symptoms, intervention indicated; and Grade 3 is defined as transfusion indicated, invasive intervention indicated, and/or hospitalization. We regarded a case in which rectal bleeding occurred and endoscopic clipping or argon plasma coagulation (APC) was performed as Grade 2. We measured PSA every 3 months for 3 years after radiation treatment, then every 6 months thereafter. PSA failure was determined according to the Phoenix criteria [10]. Patient clinical characteristics are summarized in Table 1.

Planning optimization and treatment delivery

We prescribed patients magnesium oxide and dimethicone about one week before the planning CT to empty their rectum. We asked them to take medicines orally during the treatment. Planning CT was performed using Optima CT580 (GE Healthcare Japan, Tokyo, Japan) with a slice thickness of 2.5 mm. Pelvic MRI was carried out at the same time, and axial T2-weighted images were fused with CT images using ECLIPSE Ver. 15.1 (VARIAN Medical Systems, Palo Alto, CA, USA). The contouring volume of the target and organ at risk were completed in ECLIPSE.

The prostate was considered the clinical target volume (CTV) in the low-risk group. The prostate and proximal (1 cm) seminal vesicle were considered the CTV in the intermediate-risk group, and the prostate and proximal (2 cm) seminal vesicle were considered the CTV in the high-risk group. The planning target volume (PTV) was generated based on the CTV and a margin of 0.6 cm in all directions except posteriorly, which had a margin of 0.4 cm.

The contouring volume of the rectum was defined as a solid organ in transverse planes where the PTV existed.

Table 1. Baseline and treatment characteristics of patients (n = 149)

Characteristics	Patients, n	%
Median age	71 (50-85) years	
Age [years]		
< 70	58	38.9
≥ 70	91	61.1
T stage		
≤ T1c	50	33.6
≥ T2a	99	66.4
Gleason score		
≤ 6	43	28.9
7	51	34.2
≥ 8	55	36.9
PSA [ng/mL]		
< 10	91	61.1
10–20	35	23.5
> 20	23	15.4
D'Amico classification		
Low	27	18.1
Intermediate	42	28.2
High	80	53.7
Total dose [Gy]		
72	23	15.4
74	4	2.7
76	89	59.7
78	33	22.1
Hormonal therapy		
Yes	101	67.8
No	48	32.2
Anticoagulants or anti-aggregants*		
Yes	24	16.1
No	122	81.9
Hypertension**		
Yes	80	53.7
No	67	45.0
Diabetes mellitus***		
Yes	28	18.8
No	118	79.2
Smoking****		
Yes	24	16.1
No	110	73.8

PSA — prostate specific antigen; *Data were available in 146 patients;

Data were available in 147 patients; *Data were available in 146 patients;

****Data were available in 134 patients

Planning optimization and treatment delivery was conducted using CLINAC ix (VARIAN

Medical Systems, Palo Alto, CA, United States) and ECLIPSE Ver. 15.1. All radiotherapy involved the delivery of 10-MV X-rays. The arc creation was 1 full rotation in all cases, and the angle of the collimator was 30 degrees in most cases. Basically, the prescribed dose followed the PTV: 74 Gy/37 fractions in the low-risk group, 76 Gy/38 fractions in the intermediate-risk group, and 78 Gy/39 fractions in the high-risk group. Initially, the prescribed dose followed the PTV as follows: 72 Gy/36 fractions in the low-risk group, 76 Gy/38 fractions in the intermediate-risk and high-risk group. Beginning around September 2017, the prescribed dose in the high-risk group was raised to 78 Gy/39 fractions; starting April 2019, the prescribed dose in the low-risk group was raised to 74 Gy/37 fractions.

All prescribed doses were adopted to the mean of the PTV. We identified the overlap region of the PTV and the rectum as “PTV & Rectum”. We identified the region of the PTV without the rectum as “PTV sub Rectum”. We expanded the rectum with a margin of about 1 cm in consideration of peristaltic motion and identified the region of the expanded rectum without the PTV as “Rectum sub PTV”. In order to reduce the rectal dose, we used PTV & Rectum, PTV sub Rectum, and Rectum sub PTV at the inverse planning and complied with the rectum dose constraints as strictly as possible.

Cone beam CT (CBCT) was performed on a daily basis. If there was an unacceptable rectum distension, we requested that the patient empty his rectum. If CBCT revealed severe inconsistencies, re-planning using an update CT was performed. Six patients (4.0%) underwent re-planning. The dose distributions for each plan were summed up on the first planning CT, and the total dose-volume histogram was evaluated using ECLIPSE Ver. 15.1.

Statistical analysis

The following clinical and dosimetric data were considered for each patient: age, T stage, Gleason score, PSA, total dose, hormonal therapy, use of anticoagulants or anti-aggregants, coexistence of hypertension and diabetes mellitus, smoking, PSA failure, volume of prostate, CTV, PTV, PTV & Rectum, rectal volume, rectal V30, V50, V60, V65, V70 and V75, and rectal mean dose. The relationship of each factor with Grade ≥1 rectal bleeding was determined by means of Kaplan-Meier curves. Comparisons were made using the log-rank test

and the Cox proportional hazards model. Potential prognostic factors (which showed $p < 0.05$) were additionally evaluated in multivariate analysis using the Cox proportional hazards model. The cut-off value for each variable correlating with the risk for Grade ≥ 1 rectal bleeding was determined using an ROC curve and the Youden index (sensitivity + specificity - 1).

The correlations of each factor with the risk of Grade 2 rectal bleeding were assessed using univariate analysis by means of the Wilcoxon rank sum test for continuous variables and Fisher's exact test for categorical variables, because of the small number of patients with Grade 2 rectal bleeding. In all analyses, differences with $p < 0.05$ were considered statistically significant. Data analysis was performed using R version 4.1.2.

Results

Median observation periods were 38 (range, 12–103) months. Fourteen patients (9.4%) had rectal bleeding with a median timing for occurrence of 14.5 (range, 4–29) months. Five patients (3.4%) were classified with Grade 2 bleeding and nine (6.0%) with Grade 1 bleeding; no patient showed Grade 3 bleeding. PSA failure was observed in five patients (3.4%). No patient died of prostate cancer. Six patients (4.0%) died of other diseases.

Patient dosimetric data

Patient dosimetric data are summarized in Table 2.

Patients with Grade ≥ 1 rectal bleeding

Grade ≥ 1 rectal bleeding was observed in 14 (9.4%) patients. Event-free survival (EFS) for Grade ≥ 1 rectal bleeding was calculated from the last day of radiotherapy. Patients who were free from events were censored at the date of last observation. As shown in Figure 1, Kaplan-Meier curves for EFS regarding Grade ≥ 1 rectal bleeding were generated. In univariate analysis, the following factors significantly worsened EFS for Grade ≥ 1 rectal bleeding: a PTV & Rectum volume $\geq 1.9 \text{ cm}^3$, a rectal V30 $\geq 43.9\%$, V50 $\geq 21.3\%$, V60 $\geq 12.7\%$, V65 $\geq 11.9\%$, V70 $\geq 7.2\%$, and V75 $\geq 0.4\%$, and a mean rectal dose $\geq 32.7 \text{ Gy}$ (Tab. 3). Multivariate analysis was performed for the following factors, which had a significant association when evaluated

Table 2. Patients' dosimetric data (n = 149)

Characteristics	Mean \pm SD
Prostate volume [cm ³]	31.20 \pm 15.32
CTV [cm ³]	35.82 \pm 15.51
PTV [cm ³]	92.01 \pm 28.48
PTV & Rectum volume [cm ³]	1.92 \pm 1.20
Rectal volume [cm ³]	32.78 \pm 12.77
Rectal V30 (%)	41.59 \pm 13.63
Rectal V50 (%)	19.72 \pm 6.88
Rectal V60 (%)	12.35 \pm 5.28
Rectal V65 (%)	8.67 \pm 4.46
Rectal V70 (%)	4.55 \pm 3.56
Rectal V75 (%)	0.68 \pm 1.37
Rectal mean dose [Gy]	30.79 \pm 5.94

CTV — clinical target volume; PTV — planning target volume; V30–V75 — volume receiving ≥ 30 –75 Gy; SD — standard deviation

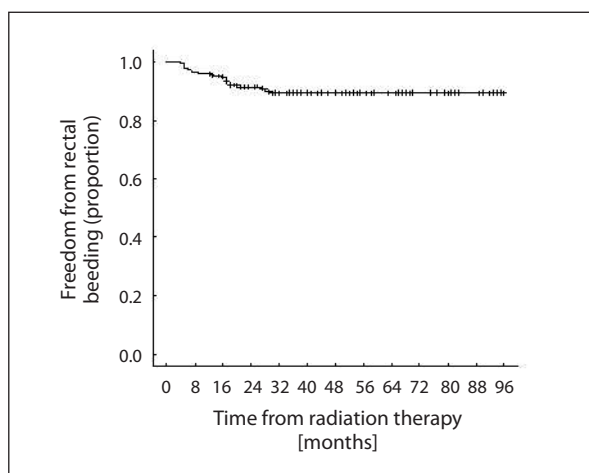


Figure 1. Kaplan-Meier plot for \geq Grade 1 rectal bleeding

using univariate analysis: a PTV & Rectum volume $\geq 1.9 \text{ cm}^3$, a rectal V30 $\geq 43.9\%$, V50 $\geq 21.3\%$ and V70 $\geq 7.2\%$, and a mean rectal dose $\geq 32.7 \text{ Gy}$. We identified V30 as a low dose, V50 as an intermediate dose, and V70 as a high dose. We did not use V60, V65 and V75 for multivariate analysis. There was strong collinearity among values for rectal V30, V50 and V70, and the mean rectal dose. Therefore, we did not test these factors concurrently, but rather, tested them independently with PTV & Rectum volume. In multivariate analysis, a rectal V30 $\geq 43.9\%$, V50 $\geq 21.3\%$ and V70 $\geq 7.2\%$, and mean rectal dose $\geq 32.7 \text{ Gy}$ remained significant whereas PTV & Rectum volume $\geq 1.9 \text{ cm}^3$ was significant only in analysis 1 (Tab. 4).

Table 3. Univariate analysis for \geq Grade 1 rectal bleeding

Variables	Category	Cox's proportional hazards model		1-year EFS (%)	p (log rank test)
		Hazard ratio (95% CI)	p		
Age [years]	< 70	1.00	0.161	96.6	0.1
	\geq 70	2.50 (0.70–8.95)		95.6	
T stage	\leq T1c	1.00	0.262	100	0.3
	\geq T2a	2.08 (0.58–7.46)		93.9	
Gleason score	< 8	1.00	0.111	97.9	0.1
	\geq 8	2.36 (0.82–6.81)		92.7	
PSA [ng/mL]	< 4.6	1.00	0.786	100	0.8
	\geq 4.6	1.33 (0.17–10.14)		95.6	
Total dose [Gy]	< 76	1.00	0.282	100	0.3
	\geq 76	3.05 (0.40–23.35)		95.1	
Hormonal therapy	Yes	1.82 (0.51–6.52)	0.359	94.1	0.3
	No	1.00		100	
Anticoagulants or anti-aggregants	Yes	0.40 (0.05–3.04)	0.374	95.8	0.4
	No	1.00		95.9	
Hypertension	Yes	0.86 (0.30–2.46)	0.782	93.8	0.8
	No	1.00		98.5	
Diabetes mellitus	Yes	0.69 (0.15–3.09)	0.628	96.4	0.6
	No	1.00		95.8	
Smoking	Yes	1.16 (0.32–4.18)	0.816	95.8	0.8
	No	1.00		95.4	
PSA failure	Yes	2.52 (0.33–19.28)	0.374	80.0	0.4
	No	1.00		96.5	
Prostate [cm ³]	< 23.1	1.00	0.183	96.4	0.2
	\geq 23.1	2.38 (0.66–8.56)		95.7	
CTV [cm ³]	< 30.2	1.00	0.136	97.1	0.1
	\geq 30.2	2.42 (0.76–7.73)		95.0	
PTV [cm ³]	< 87.1	1.00	0.063	97.4	0.05
	\geq 87.1	3.01 (0.94–9.60)		94.4	
PTV & Rectum volume [cm ³]	< 1.9	1.00	0.013*	98.8	0.006*
	\geq 1.9	5.08 (1.42–18.22)		92.5	
Rectal volume [cm ³]	< 33.1	1.00	0.303	95.7	0.3
	\geq 33.1	1.73 (0.61–4.95)		96.4	
Rectal V30 (%)	< 43.9	1.00	0.002*	100	< 0.001*
	\geq 43.9	24.54 (3.21–187.70)		89.3	
Rectal V50 (%)	< 21.3	1.00	0.002*	100	< 0.001*
	\geq 21.3	24.89 (3.25–190.50)		89.3	
Rectal V60 (%)	< 12.7	1.00	0.004*	100	< 0.001*
	\geq 12.7	19.53 (2.55–149.40)		90.8	



Table 3. Univariate analysis for \geq Grade 1 rectal bleeding

Variables	Category	Cox's proportional hazards model		1-year EFS (%)	p (log rank test)
		Hazard ratio (95% CI)	p		
Rectal V65 (%)	< 11.9	1.00	< 0.001*	98.3	< 0.001*
	\geq 11.9	9.13 (3.05–27.32)		86.2	
Rectal V70 (%)	< 7.2	1.00	< 0.001*	98.3	< 0.001*
	\geq 7.2	8.61 (2.88–25.75)		86.7	
Rectal V75 (%)	< 0.4	1.00	0.017*	98.1	0.01*
	\geq 0.4	3.66 (1.26–10.59)		91.3	
Rectal mean dose [Gy]	< 32.7	1.00	0.002*	100	< 0.001*
	\geq 32.7	23.57 (3.08–180.30)		89.7	

Asterisks show the significant values; PSA — prostate specific antigen; CTV — clinical target volume; PTV — planning target volume; V30–V75 — volume receiving \geq 30–75 Gy; CI — confidence interval; EFS — event-free survival

Table 4. Multivariate analysis for \geq Grade 1 rectal bleeding

Characteristics	Hazard ratio (95% CI)	p
Analysis 1		
PTV & Rectum volume [cm ³]	4.11 (1.14–14.76)	0.030*
Rectal V30 (%)	21.75 (2.84–166.63)	0.003*
Analysis 2		
PTV & Rectum volume [cm ³]	2.58 (0.71–9.42)	0.152
Rectal V50 (%)	18.98 (2.41–149.25)	0.005*
Analysis 3		
PTV & Rectum volume [cm ³]	2.33 (0.56–9.80)	0.248
Rectal V70 (%)	5.86 (1.71–20.03)	0.005*
Analysis 4		
PTV & Rectum volume [cm ³]	3.47 (0.96–12.52)	0.057
Rectal mean dose [Gy]	19.31 (2.50–148.87)	0.005*

Bold numbers show the significant values; PTV — planning target volume; V30–V70 — volume receiving \geq 30–70 Gy; CI — confidence interval

Patients with Grade 2 rectal bleeding

Grade 2 rectal bleeding was observed in five (3.4%) patients. Univariate analysis indicated that rectal bleeding was significantly associated with rectal V30, V50, V60, V65, and rectal mean dose (Tab. 5).

Discussion

The grade and rate of rectal bleeding were thought to be permissible in this study. Only 5 (3.4%) out of 149 patients were classified with Grade \geq 2 rectal bleeding, and an acceptable level of moderate/severe late rectal bleeding was reported to be < 5–10% [11]. Our grade and rate of rectal bleeding might be better than those in other

reports, although our study has limitations and we need a longer observation period.

The PTV & Rectum volume and rectal dose were significant factors for rectal bleeding, and the low/intermediate rectal dose and the rectal mean dose were thought to be especially important factors. Our results suggested that the PTV & Rectum volume, rectal V30, V50, V60, V65, V70 and V75, and rectal mean dose were significant predictors for Grade \geq 1 rectal bleeding, and hazard ratios of the rectal V30, V50, and V60, and rectal mean dose were higher than those of the other factors. The rectal V30, V50, V60, and V65, and rectal mean dose were significant predictors for Grade 2 rectal bleeding.

A high rectal dose was significant for Grade \geq 1 rectal bleeding. Several investigators have demonstrated that keeping the rectal V70 and V75 below 25% and 5%, respectively, is predictive of a very low incidence of late bleeding [11–15]. However, a high rectal dose was not a significant risk for Grade 2 rectal bleeding in this study. We suggest that this is because our dose planning protocol worked effectively to restrict the high-dose area. The rectal V70 values of all patients were below 25%, and the V75 values of almost all patients were below 5%, so severe bleeding did not occur frequently. With more patients enrolled in the study, the rectal V70 and V75 might have become significant factors for Grade 2 rectal bleeding.

The low/intermediate rectal dose and the rectal mean dose were significant for both Grade \geq 1 and Grade 2 rectal bleeding. In line with our study, some investigators have reported the importance

Table 5. Factors associated with Grade 2 rectal bleeding

Variables	Median (range)		P
	Grade 0-1 (n = 144)	Grade 2 (n = 5)	
Clinical factors			
Age (years)	71 (50–85)	70 (65–76)	0.833
T stage (\leq T1c/ \geq T2a)	49/95	1/4	0.664
Gleason score	7 (4–10)	8 (7–10)	0.132
PSA [ng/mL]	8.46 (2.11–127.70)	5.53 (4.60–9.08)	0.110
Total dose [Gy]	76 (72–78)	76 (76–78)	0.585
Hormonal therapy (Yes/No)	96/48	5/0	0.176
Anticoagulants or anti-aggregants (Yes/No)	23/118	1/4	1.000
Hypertension (Yes/No)	77/65	3/2	1.000
Diabetes mellitus (Yes/No)	27/114	1/4	1.000
Smoking (Yes/No)	106/23	4/1	1.000
PSA failure (Yes/No)	4/140	1/4	0.159
Dosimetric factors			
Prostate [cm ³]	26.1 (6.1–98.3)	33.7 (18.4–43.4)	0.639
CTV [cm ³]	31.3 (9.0–98.3)	41.0 (20.2–56.0)	0.490
PTV [cm ³]	84.4 (42.0–188.9)	103.9 (71.8–139.0)	0.223
PTV & Rectum volume [cm ³]	1.7 (0–7.0)	3.4 (1.4–4.3)	0.057
Rectal volume [cm ³]	30.2 (13.3–96.2)	31.2 (18.0–37.0)	0.587
Rectal V30 (%)	38.3 (18.1–83.2)	58.7 (50.7–79.7)	0.003*
Rectal V50 (%)	18.9 (4.8–35.4)	35.6 (21.6–43.1)	0.003*
Rectal V60 (%)	12.0 (1.5–27.0)	25.9 (12.7–31.5)	0.009*
Rectal V65 (%)	8.1 (0.3–22.3)	20.2 (7.6–24.9)	0.028*
Rectal V70 (%)	3.7 (0–15.9)	13.1 (0.5–16.7)	0.085
Rectal V75 (%)	0.1 (0–6.3)	0.5 (0–6.4)	0.291
Rectal mean dose [Gy]	30.1 (17.8–43.6)	40.2 (34.0–44.3)	0.001*

Bold numbers show the significant values; PSA — prostate specific antigen; CTV — clinical target volume; PTV — planning target volume; V30–V75 — volume receiving \geq 30–75 Gy

of the rectal volume irradiated with an intermediate dose [16, 17]. We think it quite possible that the restriction of the high rectal dose by IMRT resulted in an increase of the low/intermediate rectal dose and the rectal mean dose. When treating with IMRT, maintaining strict attention to low/intermediate and mean rectal doses, as well as the high rectal dose, seems important for preventing any grade of rectal bleeding.

The PTV & Rectum volume was significant for Grade \geq 1 rectal bleeding. This factor would be related to rectal dose. Katahira-Suzuki et al. reported that the rectal volume was one of the significant predictors for Grade \geq 1 late rectal bleeding [16], but the rectal volume was not a significant factor in our study. No patient received pelvic lymph node irradiation in our study, while more than half of

their patients received it. Their study showed that pelvic lymph node irradiation increased the rectal dose according to the rectal volume. In our study the radiation therapy was concentrated on the PTV related to the prostate and proximal seminal vesicle; therefore, the rectal volume close to the PTV would be related to the rectal dose.

Our data suggest that a smaller PTV margin might be useful for preventing rectal bleeding when using VMAT. The PTV & Rectum volume, which was a significant factor for Grade \geq 1 rectal bleeding, depends on the PTV margin. In this study, the PTV margin was set at 0.6 cm in all directions, except for posteriorly, where the margin was 0.4 cm. According to the Japanese Society for Radiation Oncology (JASTRO) guideline, the PTV margin should be about 0.8–1.0 cm in all directions,

except for the rectal-side margin, where the margin should be about 0.4–0.5 cm [18]. Since our margin is smaller than that of the JASTRO guideline, precise daily registration becomes more essential. When using one-rotation VMAT, the treatment ends in only 2 minutes from the daily position adjustment with CBCT [9], so misregistration is kept to the minimum. In spite of the smaller margin in this study, PSA failure occurred in five (3.4%) out of the 149 patients; this PSA failure rate was nevertheless thought to be permissible [18, 19].

No clinical factors were significant for rectal bleeding. Other studies have identified factors other than those strictly correlated with dose/volume parameters of the rectum to be associated with rectal bleeding in patients treated with radiotherapy for prostate cancer [11]. Herold and Skwarchuk reported diabetes as a risk factor [20, 21]. Feinberg and Sanguineti found androgen deprivation as a risk factor [22, 23]. The use of anticoagulants or anti-aggregants was also associated with rectal bleeding, according to Choe [24]. Those clinical factors might not have proven significant in our study because the number of patients and the observation period were limited.

Conclusions

Our study showed that rectal bleeding after VMAT of prostate cancer occurred, but the grade and rate of rectal bleeding were permissible. A higher rectal dose was shown to be related to rectal bleeding, and the reduction of rectal dose, especially low/intermediate and mean doses, will be important for reducing the incidence of rectal bleeding.

Conflict of interest

The authors declare that they have no conflict of interest

Financial disclosure

Authors have not any financial disclosure.

Ethical statement

Informed consent was obtained from all individual participants included in the study. The institutional ethics committee of Oita Koseiren Tsurumi Hospital approved this retrospective study. All applicable institutional and/or national guidelines for care were followed.

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