**Research Article**

# Dose–Volume Constraints in Rectum in Patients with Prostate Cancer after 74-Gy 3-Dimensional Conformal Radiotherapy

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## Abstract

**Purpose:** To clarify the dose–volume relationship with late rectal toxicity (LRT) in prostate cancer patients after 74-Gy 3-dimensional conformal radiotherapy (3DCRT) using the 7-fields technique.

**Materials and Methods:** Between June 2004 and December 2011, 221 patients with localized prostate cancer [median age, 71 (48–89) years] were treated by 74-Gy 3DCRT using the coplanar 7-fields technique. Patients were classified according to the National Comprehensive Cancer Network risk group classification as low-risk, 20 patients (9%); intermediate-risk, 106 patients (48%); and high-risk, 95 patients (41.6%). Furthermore, 126 (57%) and 46 (20.9%) patients received androgen deprivation and anticoagulant therapy, respectively. For 3DCRT, the Clinical Target Volumes (CTV) included the prostate and at least half of the seminal vesicles in the intermediate and high-risk groups and the prostate alone in the low-risk group. We analyzed the relationship between the incidence rate of rectal bleeding and rectal wall Dose–Volume Histograms (DVHs). Late rectal bleeding (>90 days after radiotherapy) was evaluated according to the Common Terminology Criteria for Adverse Events v 4.0.

**Results:** The median follow-up period was 48 (range, 6–103) months, with a 4-year cumulative incidence rate for grade ≥2 LRT of 11.0%. Univariate analysis (UA) determined the cutoff values of rectal wall DVHs for grade of ≥2 LRT: V60 <38.9%, V65 <22.5%, V70 <17.8% and V72 <12.6%. UA also determined the cutoff values of rectal wall DVHs for grade of ≥1 LRT: V10 <92.2%, V20 <76.7%, V30 <64.8%, V40 <66.5%, V50 <38.9%, V60 <22.5%, V70 <17.8, V72 <12.6%, $D_{max}$ <74.1Gy, $D_{mean}$ <50.9Gy, $D_{median}$ <47.6 Gy, and rectal wall volume of >23.6 cm$^3$.

**Conclusion:** This study is the first to show a clear correlation between LRT and rectal DVHs after 74-Gy 3DCRT using the 7-fields technique and that it is acceptable.

## ABBREVIATIONS

LRT: Late Rectal Toxicity, LPC: Localized Prostate Cancer, 3DCRT:3-Dimensional Conformal Radiotherapy, NCCN: The National Comprehensive Cancer Network Risk Group Classification, CTV: Clinical Target Volumes, PTV: Planning Target Volume, DVHs: Dose–Volume Histograms, EBRT: External Beam Radiotherapy, IMRT: Intensive Modulated Radiotherapy, PSA: Prostate Specific Antigen, GS: Gleason Score, DRR: Digitally Reconstructed Radiographs, CT: Computed Tomography, ROC: Receiver-Operating Characteristic, AUC: Area Under The Curve, UA: Univariate Analysis, APC: Argon Plasma Coagulation, HBO: Hyperbaric Oxygen Therapy

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## INTRODUCTION

Prostate cancer is among the most common malignancies in men. Currently, the majority of prostate cancers are detected at an early stage and designated as localized prostate cancer (LPC). External beam radiotherapy (EBRT) is among the principal treatment options for such cancers. Three-dimensional conformal radiotherapy (3DCRT) allows a high-dose volume to be fitted to the target, resulting in the irradiation of smaller volumes of normal tissue and reduced late rectal toxicity (LRT) [1-5].

In the early 1990s, the local target volume doses used to treat prostate cancer patients were <70 Gy. High-dose 3DCRT radiotherapy treatment, defined as a local dose of >70 Gy, has been associated with better clinical outcomes in prostate cancer patients [6-8]. However, dose escalation introduces an increased risk of developing LRT, particularly late rectal bleeding for Japanese LPC patients with thin fatty layer between rectum and prostate; therefore, the identification of predictive parameters of LRT is of importance.

New techniques such as intensive modulated radiotherapy (IMRT), stereotactic radiotherapy, image-guided radiotherapy, and particle radiotherapy with proton and carbon ion beams have offered new possibilities for dose escalation while sparing the surrounding normal tissues. However, some concerns remain regarding the costs and benefits of these new techniques. Furthermore, it would be difficult to implement these new techniques for each LPC patient in every institution. In many Japanese institutions, 3DCRT is generally the common therapeutic technique for LPC patients. Therefore, in 2004, we performed dose-escalataion without IMRT to 74 Gy from 70 Gy for LPC patients, particularly those in the intermediate or high-risk groups. In the present study, we evaluated the rectal dose constraints for 3DCRT with 74 Gy to reduce late rectal bleeding.

The definition of rectal dose constraints after EBRT is complex. Some reports have identified numerous clinical factors related to LRT, and several authors have identified the presence of acute rectal toxicity as a significant factor. Skwarchuk et al. and Herold et al. reported that the incidence of diabetes correlated with LRT [9,10]. Other authors have reported correlations between grade 2 and 3 late rectal bleeding and the use of anticoagulation therapy [11]. On the other hand, several publications have described a relationship between LRT and the rectal dose–volume histogram (DVH) [12]. Previous studies reported that rectal injuries occurred at the maximum dose sites on the anterior rectal wall and that the incidence of serious late rectal toxicity was unusual with doses <60 Gy [13]. According to Boersma et al., the rectal wall dose-constraints associated with the incidence of severe rectal bleeding were the high-dose regions of V65 >40–50%, V70 >30%, and V75 >5% [14]. Jackson et al. reported that a dose of 40–50 Gy, which is considered moderate, correlated with late rectal bleeding [15].

In recent years, the number of patients using anticoagulation therapies consequent to circulatory and cerebrovascular diseases has increased. Choe et al. also demonstrated that the use of anticoagulation therapy was associated with improved Prostate Specific Antigen (PSA) control in patients with LPC. Therefore, many prostate cancer patients may receive anticoagulation therapy [16].

In this study, we evaluated the incidence of LRT and the rectal wall dose–volume relationship in the absence of anticoagulation therapy in prostate cancer patients after 74-Gy 3DCRT with the 7-fields technique.

## MATERIALS AND METHODS

Between June 2004 and Dec 2011, 221 patients with LPC were treated with external photon beam 3DCRT at our institution. When conducting dose-escalation, the authors conformed to the ethical guidelines of the 1975 Declaration of Helsinki (revised in 2000) and obtained written informed consent from all of patients. Eligible patients had been diagnosed with biopsy-confirmed Union for International Cancer Control prostate cancer TNM stage T1-3N0M0 adenocarcinoma of the prostate and have been classified as low, intermediate, or high-risk according to the National Comprehensive Cancer Network (NCCN) guidelines (available at http://www.nccn.com). Patients with T1–T2a clinical stage tumors, a Gleason score (GS) of 2–6, or a pretreatment PSA level of <10 ng/mL were classified as low risk. Patients with T2b or T2c clinical stage tumors (GS = 7) or a pretreatment PSA level of 10–20 ng/mL were classified as intermediate risk. Patients with ≥T3a clinical stage tumors (GS = 8–10) or a pretreatment PSA level of >20 ng/mL were classified as high-risk.

The patient characteristics are shown in Table 1.The median age at treatment was 71 years (range, 48–89 years). Regarding the NCCN risk classification, 20 patients (9%) were classified as low risk, 106 patients (48%) as intermediate risk, and 95 patients (41.6%) as high risk. Regarding T-staging, 96 patients (43.5%) were staged as T1, 55 patients (24.9%) as T2, and 35 patients (15.8%) as T3; an additional 35 patients (15.8%) were not otherwise specified. Regarding GS, 33 patients (15%) had scores of 2–6, 115 (52%) had scores of 7, and 68 (30.7%) had scores of 8–10. Furthermore, 126 patients (57%) received androgen deprivation therapy, and 46 patients (20.9%) were treated with anticoagulants Table 1.

**Table 1:** Patient and tumor characteristics.

|  | **N or range** |  |
|---|---|---|
| No. of patients | 221 |  |
| Age (years) | 48–89 | 71 (median) |
| Gleason score |  |  |
| 2-6/7/8-10/unknown | 33/115/68/5 | 15.0%/52.0%/30.7%/2.1% |
| Tstage |  |  |
| T1/ T2/T3/unknown | 96/55/35/35 | 43.5%/24.9%/15.8%/15.8% |
| NCCN risk group |  |  |
| Low risk/ Intermediate risk / High risk | 20/106/95 | 9.0%/48.0%/43.0% |
| Use of ADT (Yes/No) | 126/95 | 57.0%/43.0% |
| Medication with anticoagrants (Yes/ No) | 46/175 | 20.9/79.1 |

NCCN,National Comprehensive Cancer Network; ADT,androgen deprivation therapy.

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## Radiotherapy

All 3DCRT-treated patients were immobilized in the supine position with their feet placed in a vacuum bag system. Computed Tomography (CT) scans were performed at a slice thickness of 0.25-mm with a multi-detector CT scanner (GE Light Speed Qxi; GE Healthcare, Waukesha, WI, USA). The patients were instructed to urinate immediately before CT scanning and before each treatment. Eclipse (release 6.5; Varian Medical Systems, Palo Alto, CA, USA) was used for dose calculations during 3DCRT planning. The daily dose was 2.0 Gy per fraction and was administered on 5 days per week.

The Clinical Target Volume (CTV) included the prostate and half to two-thirds of the seminal vesicles for the intermediate and high-risk groups, whereas the low-risk group CTV contained only the prostate. CTV was expanded in 3 dimensions with 0.7–1.0-cm margins to yield the planning target volume (PTV) except at the prostate–rectal interface, where a 0.5-cm margin was adopted to decrease rectal involvement. The rectum was defined as the rectal wall (excluding air and feces) with a 0.2-cm inner margin from the rectal contour. The anal verge was considered the inferior limit, and beyond 0.5 mm from the PTV upper edge was considered the superior limit (Figure 1).

Patients were initially treated with 46-Gy dose to the isocenter, given in 2-Gy fractions, using 10–15 MV photons with a conventional 4-field box technique. After 46-Gy, a 7-fields technique was used to boost irradiation to the prostate at a dose of 28 Gy, given in 2-Gy fractions. The 7-fields coplanar arrangement comprised 1 anterior field, 2 lateral fields at 90° or 270°, and 4 oblique fields at 45° above or below the lateral field (Figure 2).

After treatment planning, 1 pair of orthogonal (anteroposterior and right-lateral) Digitally Reconstructed Radiographs (DRR) was constructed, in which the bony anatomical positions could be located. This image set comprised the reference image pair. To verify the treatment fields on each RT day, the therapist acquired 1 pair of orthogonal Electronic Portal Images (EPI) with the AP and left-right set-up fields; these comprised the comparison image set. The portal images were obtained with (Varian Oncology Systems, Palo Alto, CA) that was mounted on a dual-energy Clinac 2100EX accelerator (Varian). Daily repositioning of
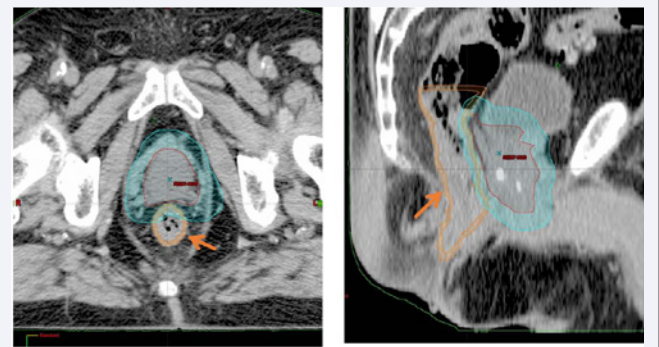


**Figure 1** Image of the 74-Gy 3-dimensional conformal radiotherapy with the coplanar 7-field technique for prostate cancer.



**Figure 2** Image of the axial and sagittal rectal wall contours, which were defined as the rectal wall with a 0.2-cm inner margin from the rectal contour. The anal verge was considered the inferior limit, and >0.5-mm from the PTV upper edge was considered the superior limit.

the patients before the administration of each treatment fraction was accomplished through matching the EPI to the reference DRR based on the bony anatomy.

## Follow-up

Follow-up evaluations after treatment completion were performed at 3–6-month intervals for 5 years and every 6 months thereafter.

## Toxicity scoring

LRT appeared no earlier than 90 days after the initiation of EBRT and was scored according to the Common Terminology Criteria for Adverse Events, version 4.0. In brief, intermittent bleeding was considered grade 2 morbidity, and any laser cauterization or blood transfusion consequent to rectal bleeding was considered grade 3 toxicity (Table 2). Patients who had been followed for <2 years after treatment were excluded from this analysis.

## Statistical analysis

The complication rates were determined from Kaplan–Meier estimates. The clinical parameters were investigated in univariate analyses (log-rank test). The Receiver-Operating Characteristic (ROC) curves were used to derive the dose–volume constraints from the retrospective clinical data. In this study, ROC curves were used to determine the optimal DVH cutoff values to predict late rectal bleeding. Patients were categorized into groups above and below the optimal cutoff values. Those who had been treated with anticoagulation therapy were excluded from the DVH analysis. The statistical analyses were performed with the JMP software package, version 10 (SAS Institute Inc., Cary, NC, USA). In all analyses, a p value of <0.05 was considered statistically significant.

## RESULTS

### Incidence of late rectal bleeding

Data were collected from 221 patients who had been treated with 74-Gy 3DCRT with the 7-fields technique, with follow-up periods ranging from 6–103 months (median, 48 months). Thirty-eight patients who had been followed for <2 years after treatment were excluded. Data with which to analyze the incidence of LRT
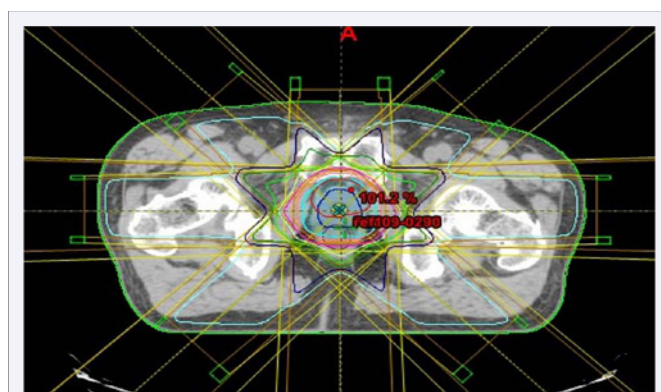
were available from 183 patients, with follow-up periods of 24–103 months (median, 51 months). Of these, 47 patients (25.6 %) experienced grade 1 LRT, 19 (10.3%) experienced grade 2 LRT, and 3 (1.6%) experienced grade 3 LRT. No patient developed grade 4 LRT. The median time to development of grade ≥2 LRT was 14 months (range, 8–65 months). No grade ≥2 LRT appeared earlier than 6 months after radiation therapy. All grade ≥2 LRT patients were treated with steroid suppositories; in addition, 3 patients were treated with argon plasma coagulation (APC) and 5 with Hyperbaric Oxygen therapy (HBO).

The 4-year cumulative incidence rate for grade ≥2 LRT in all of patients was 11.0% (95% CI: 7.0–16.7%; Figure 3). The 4-year cumulative incidence rate for grade ≥2 LRT without anticoagulant therapy was 9.1% (95% CI: 5.0–16.1%). The 4-year cumulative incidence rate for grade ≥2 LRT with anticoagulant therapy was 24.8% (95% CI: 12.9–42.4%). The Kaplan–Meier curves differed significantly between the patients with grade ≥2 LRT who received and did not receive anticoagulant therapy (p < 0.05; Figure 3,4).

### Rectal wall DVH analysis

Data from 110 patients were available for the DVH analysis. Patients who had received anticoagulant therapy or had been followed for <2 years after treatment were excluded. Figure 5 shows the comparison of the median rectal wall DVHs for patients treated with and without anticoagulants Figure 5.

### Grade <2 vs. grade ≥2 rectal wall DVHs

Table 3 shows the results of a rectal wall DVH analysis (grade <2 vs. grade ≥2). This table lists the dose–volume parameters and each optimal cutoff point obtained from the ROC curve analysis.

**Table 2:** Common Terminology Criteria for Adverse Events (CTCAE) version 4.0.

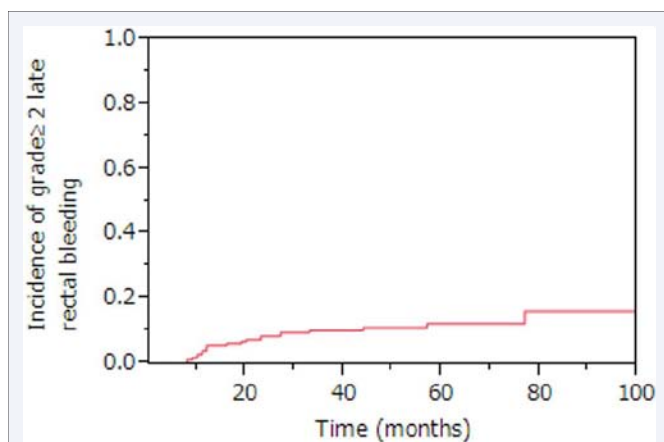| Grade 1 | Grade 2 | Grade 3 | Grade 4 |
|---|---|---|---|
| Slight bleeding | Intermittent bleeding | Bleeding requiring surgery, any laser cauterization or blood, transfusion resulting | Necrosis, perforation, fistula |



**Figure 3** The 4-year cumulative incidence of late rectal toxicity after 74-Gy 3-dimensional conformal radiotherapy with the coplanar 7-field technique for prostate cancer (Kaplan–Meier method).
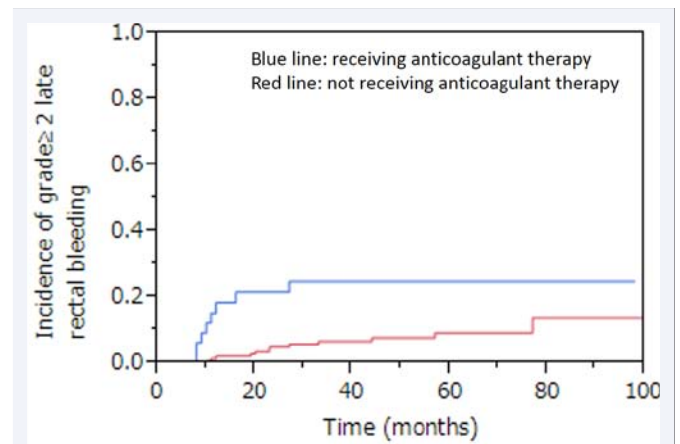


**Figure 4** Kaplan–Meier curves for patients receiving anticoagulant therapy versus those not receiving anticoagulant therapy.
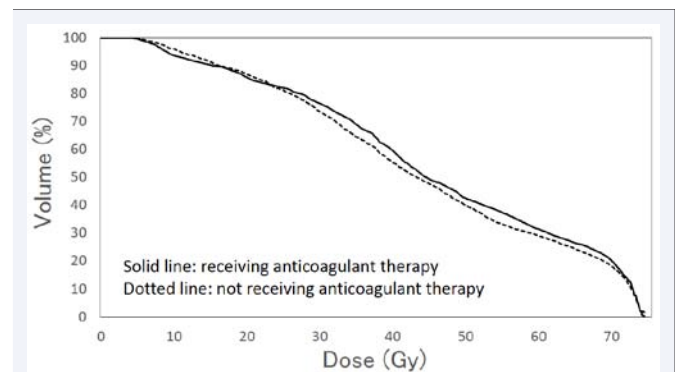


**Figure 5** Cumulative dose–volume histogram (DVH) of the rectal wall. The median DVH for patients receiving anticoagulant therapy patients is shown as a solid line, whereas the median DVH for those not receiving anticoagulant therapy is shown as a dotted line.

The area under the curve (AUC) values from the ROC plots for V10, V20, V30, V40, V50, V60, V65, V70, V72, $D_{max}$, $D_{mean}$, $D_{median}$ and the rectal wall volume were 0.56, 0.53, 0.52, 0.57, 0.62, 0.65, 0.62, 0.69, 0.70, 0.55, 0.60, 0.61, and 0.51, respectively; the p values of V60–72 were <0.05. The optimal cutoff point values were defined as the highest peaks on each ROC plot. The cutoff values were as follows: V60, <38.9%; V65, <22.5%; V70, <17.8%; and V72, <12.6% Table 3.

### Grade <1 vs. grade ≥1 rectal wall DVHs

Table 4 shows the results of another rectal wall DVH analysis (grade <1 vs. grade ≥1). This table lists the dose–volume parameters and each optimal cutoff point obtained from the ROC curve analysis. The area under the curve (AUC) values from the ROC plots for V10, V20, V30, V40, V50, V60, V65, V70, V72, $D_{max}$, $D_{mean}$, $D_{median}$, and the rectal wall volume were 0.60, 0.63, 0.63, 0.67, 0.68, 0.66, 0.68, 0.71, 0.75, 0.64, 0.68, 0.67, and 0.53, respectively; all p values were <0.05. The optimal cutoff point values were the highest peaks on each ROC plot. The cutoff values were as follows: V10, <92.2%; V20, <76.7%; V30, <64.8%; V40, <66.5%; V50, <38.9%; V60, <22.5%; V70, <17.8%; V72, <12.6%; $D_{max}$, <74.1 Gy; $D_{mean}$, <50.9 Gy; $D_{median}$, <47.6 Gy; and rectal wall volume, >23.6 cm$^3$ Table 4.

## DISCUSSION

This study adopted the 7-fields technique to reduce the incidence of high-dose-related posterior rectal wall lesions and prescribed more uniform doses to the prostate, compared to those obtained with the 4 or 6-fields techniques. To date, there have been few investigations into the use of 3DCRT with the 7-fields technique to treat LPC patients. In addition, this was the first investigation to report a highly significant correlation between the rectal wall DVH and the incidence of late rectal bleeding in LPC patients consequent to the use of the 7-fields technique without anticoagulant therapy.

3DCRT and IMRT were used to treat LPC, and late radiotoxicity-related complications including rectal bleeding. In our study, grade ≥2 LRT after 3DCRT occurred in 22 patients with a 4-year cumulative incidence rate of 11.0%. Furthermore, 3DCRT, >15% of LPC patients who underwent high-dose 3DCRT with the 4 or 6-fields techniques developed LRT. Incidences of late rectal

**Table 3:** Rectal wall DVHs analysis of the grade<2 vs. grade≧2.

|  | AUC | Cut-off | P value (log-rank) |
|---|---|---|---|
| V10 | 0.56 | < 92.2% | 0.08 |
| V20 | 0.53 | < 76.7% | 0.2 |
| V30 | 0.52 | < 64.8% | 0.09 |
| V40 | 0.57 | < 66.5% | 0.07 |
| V50 | 0.62 | < 38.9% | 0.1 |
| V60 | 0.65 | < 38.9% | 0.01* |
| V65 | 0.62 | < 22.5% | 0.02* |
| V70 | 0.69 | < 17.8% | 0.01* |
| V72 | 0.70 | < 12.6% | 0.005* |
| $D_{max}$ | 0.55 | < 74.1Gy | 0.3 |
| $D_{mean}$ | 0.60 | < 50.9 Gy | 0.05 |
| $D_{median}$ | 0.61 | < 47.6 Gy | 0.08 |
| Rectal wall volume | 0.51 | > 23.6 cm$^3$ | 0.27 |

*p<0.05

**Table 4:** Rectal wall DVHs analysis of the grade<1 vs. grade≧1.

|  | AUC | Cut-off | P value (log-rank) |
|---|---|---|---|
| V10 | 0.60 | < 92.2% | 0.01* |
| V20 | 0.63 | < 76.7% | 0.001* |
| V30 | 0.63 | < 64.8% | 0.009* |
| V40 | 0.67 | < 66.5% | 0.0003* |
| V50 | 0.68 | < 38.9% | 0.0009* |
| V60 | 0.66 | < 38.9% | 0.0005* |
| V65 | 0.68 | < 22.5% | 0.0006* |
| V70 | 0.71 | < 17.8% | 0.002* |
| V72 | 0.75 | < 12.6% | 0.00001* |
| $D_{max}$ | 0.64 | < 74.1Gy | 0.001* |
| $D_{mean}$ | 0.68 | < 50.9 Gy | 0.0003* |
| $D_{median}$ | 0.67 | < 47.6 Gy | 0.0003* |
| Rectal wall volume | 0.53 | > 23.6 cm$^3$ | 0.02 |

*p<0.05

bleeding have been reported to range from 10.7–25% [17-22] after 3DCRT for LPC, which are higher than our results with the 7-field technique (11.0%). This difference in the frequency of late rectal bleeding between the 7-fields and other 3DCRT techniques may be because the 7-fields technique administers lower doses than that administered by other techniques as a result of the absent posterior field. Regarding IMRT, the frequency of LRT in LPC patients after IMRT has been reported to be 2–11% [22-25]. Although IMRT reportedly offers advantages over 3DCRT, the incidence of late rectal bleeding was not drastically improved with this technique. In addition, it would be difficult to administer IMRT to all LPC patients in every Japanese institution. Therefore, it is necessary to improve the incidence rate of late rectal bleeding after 3DCRT.

Our results showed a relationship between V10–V72 and grade ≥1 LRT and a significant correlation between the high-dose V60–V72 region and grade ≥2 LRT. Several authors have reported correlations between the moderate-dose region and LRT. Jackson et al. suggested only a correlation between late bleeding and the volume irradiated at a moderate dose (approximately 40–50 Gy) [15]. Fiorino et al. also reported a correlation between the intermediate-dose region (V50–V60) and LRT [26]. However, there were no reports regarding the low-dose region (V10–V30). On the other hand, grade ≥2 LRT did not correlate with the low-dose region in our study. The reason for this difference may have been that the low-dose region was predictive of the incidence rather than the severity of LRT.

In our results, the following rectal wall dose-volume constraints were obtained: V60, <38.9%; V65, <22.5%; V70, <17.8%; and V72, <12.6%. Several publications have described the correlation between rectal wall DVHs and grade ≥2 LRT. According to Huang et al., a V60 >40% and V70 >25% increased the risk of grade ≥2 LRT. Greco et al. also reported rectal dose constraints of V40 <60%, V50 <50%, V60 <60%, V72 <25%, and V76 <5% [18]. Many studies have reported that patients in whom >25% of the rectum was irradiated with >70 Gy developed Grade ≥2 complications [27]. However, in our study, the rectal wall DVH cutoff values were less than those in other reports. This might have been because patients character of except for anticoagulant therapy patients.

There have been some reports regarding the correlation between anticoagulant therapy and LRT in patients with LPC. Choe et al. reported that patients treated with anticoagulants were at a substantial risk of developing acute or late bleeding after EXRT for prostate cancer [16]. Takeda et al. reported a correlation between anticoagulant/anti-aggregant treatment and with LRT [11]. In our study, the Kaplan–Meier curves for patients who received and did not receive anticoagulant therapy differed significantly with regard to the incidence of grade ≥2 LRT (p < 0.05). On the other hand, there have been few reports regarding the correlation between anticoagulation therapy and LRT in patients with LPC. Therefore, it is important to exclude the impact of anticoagulants on patients with LPC when analyzing rectal DVHs.

Our study has some limitations. The median 48-month follow-up period may be too short to make definitive statements regarding late toxicities because late radiation-induced reactions

often occur after 5 years. Furthermore, the definition of the rectal DVH was an important factor that affected the DVH analysis. DVH analyses encounter problems when switching between hollow organs (e.g., the rectum) and solid organs (e.g., the lung and liver). In general, DVH data should be used to evaluate solid organs (e.g., the lung and liver). However, Michalski et al., in a preliminary toxicity report from an intergroup trial, observed that the relative risk of LRT development was 2-fold greater if the total rectal volume receiving the radiation dose exceeded 100 $cm^3$; therefore, the rectum was contoured as a solid organ [28]. On the other hand, 2 types of data, the rectal DVH and rectal wall DVH, exist to analyze the dose constraints. The rectal wall DVH, dose-wall histograms, and dose-surface histograms are commonly used to evaluate treatments and provide estimates of the risk of toxicity.

An additional limitation is that it is difficult to determine the total rectal organ volume and thus the impact of the rectal contouring method is very important. Contouring becomes a significant factor that determines the risk of rectal toxicity when dose restrictions are applied to the rectum [29]. If the superior and inferior rectal limits are extensive, the DVH evaluation will yield a lower value. However, several reports have not clearly defined the range of rectal contouring. According to Fiorino et al., the rectum was drawn on CT slices from just above the anal verge to the point at which it transitioned into the sigmoid colon [26]. Vargas et al. reported rectal contouring from the anal verge or ischial tuberosities to the sacroiliac joints or rectosigmoid junction [20]. Marzi et al. defined the inferior limit as the anal verge and the superior limit as the sigmoid flexure [30]. In this study, the inferior limit was defined as the anal verge and the superior limit as >0.5 mm from the PTV upper edge.

Finally, the impact of organ motion is another important uncertainty factor between simulation and treatment rectal wall DVHs. Studies that have investigated organ motion reported movement of ≥1 cm in the anteroposterior directions, most likely due to rectal filling with gas and stool [31]. The rectal wall volume may be altered by the presence of gas and stool and this may affect the DVH analysis. In our study, a log-rank test of rectal wall volumes of >23 $cm^3$ and <23 $cm^3$ revealed a significant difference with respect to the incidence of grade of ≥1 LRT (p < 0.05).

## CONCLUSION

This study is the first to report a clear correlation between LRT and the rectal DVHs in prostate cancer patients treated with the 7-fields technique. The DVH parameters between grade ≥1 and grade <1 were related to LRT onset, whereas the DVH parameters between grade ≥2 and grade <2 were related to LRT severity. The use of these parameters may facilitate reductions in the incidence and severity of late rectal bleeding.

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