

## Error Detectability of Isodose Volumes as ROIs in Prostate Intensity-modulated RT QA

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**Abstract.** *Background/Aim:* To evaluate the quality of error detectability with a three-dimensional verification system using isodose volumes as regions of interest (ROIs) in quality assurance (QA) of intensity-modulated radiation therapy. *Patients and Methods:* Treatment plans with four types of intentional errors were created from the data of 20 patients with localized prostate cancer. These plans underwent QA using the three-dimensional verification system. The datasets of another 30 cases without inserted errors were assessed as controls. The ROIs used in the evaluations were those used in our conventional method (planning target volume, rectum, and bladder). The isodose volume method (5%, 50% and 95% isodose volume) and the error detection rates (measurement above the tolerance values, as set from the other 30 cases) were assessed and compared. *Results:* There was significantly higher multileaf collimator systematic closed error detectability with the isodose volume method compared to the conventional method (A-side 0.2 mm:  $p=0.005$ , A-side 0.35 mm:  $p=0.002$ , B-side 0.2 mm:  $p=0.001$  and B-side 0.35 mm:  $p=0.010$ ). There were no error types for which the error detection rate of the isodose volume method was lower than that of the conventional method. *Conclusion:* The isodose volume method was able to evaluate the irradiated ROIs that could be delineated, and improved error detectability. This method has the potential to provide a wider margin of safety in intensity-modulated radiation therapy.

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**Key Words:** IMRT verification, error detection, isodose volume.

Intensity modulated radiation therapy (IMRT) is an irradiation technique that can create a steep dose gradient to deliver a high dose to the target while avoiding normal tissue (1, 2). Volumetric-modulated arc therapy (VMAT) is an IMRT technique that uses a dynamic multileaf collimator (MLC) and varies the dose rate while rotating the gantry to rapidly deliver IMRT (3, 4). In order to ensure safe delivery of VMAT, it is recommended that each treatment plan created by a treatment planning system (TPS) be verified to detect inherent errors and to verify dose accuracy (5). The IMRT verification methods include absolute dose verification using a dosimeter (6) and dose distribution verification using a two-dimensional detector or radiochromic film (7-11). In absolute dose verification, a phantom is used in a three-dimensional treatment plan. The absolute dose is verified by comparing the results calculated with the phantom's CT scan data with those doses measured using the phantom and a dosimeter. The verification of dose distribution is evaluated comparing distribution recalculated by the TPS with those obtained using radiochromic film or two-dimensional detectors. A gamma analysis is often used as the evaluation method (12-14).

A recently developed three-dimensional dose verification system can predict the dose distribution in the patient body from the phantom measurement results obtained using a two-dimensional detector (15, 16). It can be evaluated using a dose volume histogram (DVH), which can predict the dose delivered to organs at risk (OARs) and targets, allowing the treatment plan to be evaluated from a clinical perspective. In the three-dimensional dose verification system, each organ is set as a region of interest (ROI), and each evaluation is performed only for that ROI. Areas outside of ROIs (*e.g.*, rectus abdominis muscle, subcutaneous fat) are not evaluated and errors may be overlooked. In recent years, TPSs have been equipped to create isodose volumes as ROIs based on the dose distribution. By using this function, low-dose areas that have not been evaluated in the conventional QA procedure can be evaluated, and we expect that the use of ROIs that follow the dose distribution will improve dose error detectability. Therefore, the purpose of this study was to evaluate the improvement of error detectability by



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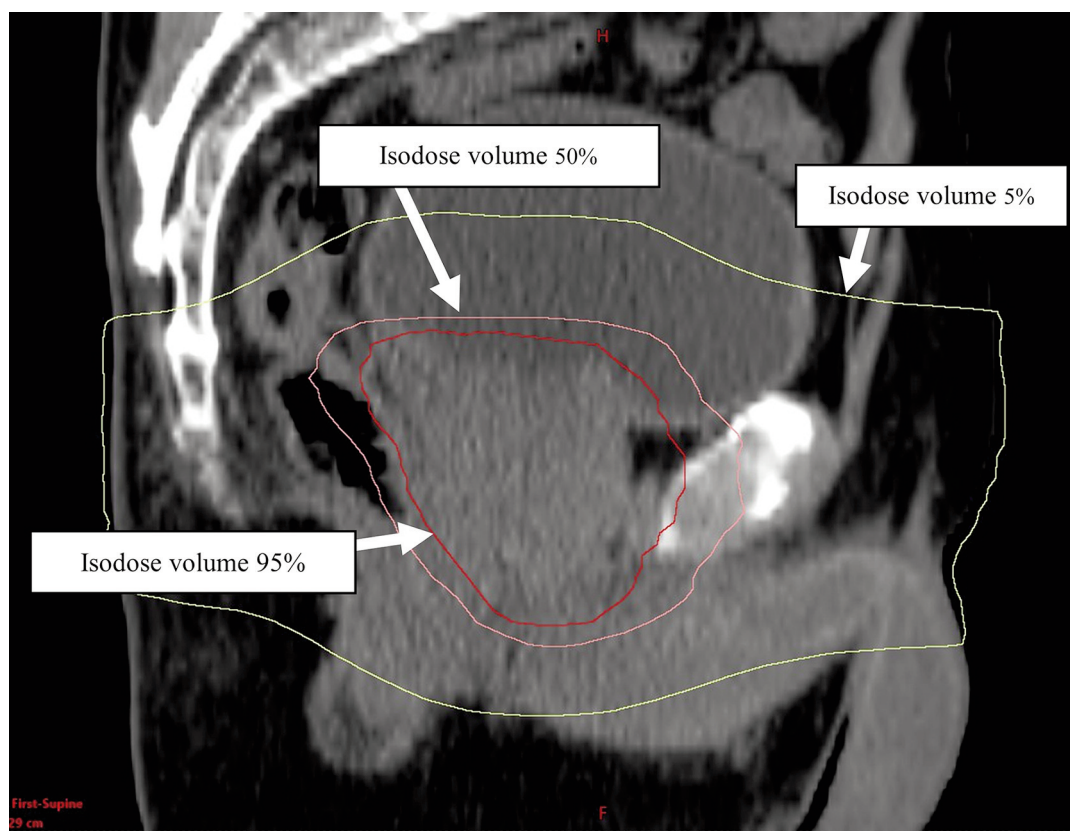


Figure 1. Overview of the isodose volume method. Isodose volume 5%, Isodose volume 50%, and Isodose volume 95% refer to the volumes included by isodose lines at 5%, 50%, and 95% of the prescribed dose.

using isodose volumes as ROIs for the evaluation of IMRT verification using a three-dimensional dose verification system.

## Patients and Methods

**Linear accelerator and three-dimensional dose verification system.** A linear accelerator [Novalis Tx (17), Brainlab, Feldkirchen, Germany and Varian Medical Systems, Palo Alto CA, USA] was used. This system is equipped with multiple image-guidance methodologies [on-board imaging (OBI), cone-beam CT, an electronic portal imaging device (EPID)] and a high-definition MLC. There are 60 pairs of MLC leaves; the central 32 pairs are 2.5 mm thick and the outer 28 pairs are 5 mm thick. They are installed under upper and lower jaws. The upper jaw is formed in the direction perpendicular to the MLC, while the lower jaw is formed in the direction parallel to the MLC. We used a three-dimensional system that can evaluate the dose distribution in a patient's body based on the measurements of a two-dimensional array of detectors (COMPASS system with MatriXX, IBA Dosimetry, GmbH, Schwarzenbruck, Germany) (16). The MatriXX is a two-dimensional ionization chamber with 1020 ion chambers in parallel in a 32×32 array. It was mounted on the gantry head of the linear accelerator together with a 5 cm water phantom as a build-up. The COMPASS system is an instrument that can calculate the dose distribution in the patient's body in three dimensions from the fluence acquired from the two-dimensional ionization chamber array using collapsed cone convolution/superposition

(CCC) as the dose calculation algorithm. Recalculation using Digital Imaging and Communications in Medicine Structured Reporting (DICOM)-RT data exported from the TPS (Eclipse® version 10.0, Varian Medical Systems) was also performed, allowing comparison under calculation by CCC of the dose distributions generated by the TPS with those generated by measurement data. The patients were imaged using a 16-row multislice CT (Optima CT580W; GE Healthcare, Waukesha, WI, USA) with an FOV of 50 cm, tube voltage of 120 kVp, tube current under automatic exposure control, slice thickness of 2.5 mm, and matrix of 512×512.

**Patient population and region of interest.** Among patients with localized prostate cancer treated at Tane General Hospital, the TPS data of 20 patients determined to be at intermediate risk according to the National Comprehensive Cancer Network classification were used for error detectability. Radiation therapy was delivered with the VMAT technique to all patients. The prescribed dose to the PTV was 78 Gy in 39 fractions, which was the mean dose to the PTV. The minimum CTV dose was >95% of the prescribed dose. The calculation grid size was 2.5 mm. The Analytical Anisotropic Algorithm was used for the dose calculation algorithm. Written informed consent was obtained from all patients, and the study was approved by the Ethics Committee of Tane General Hospital (approval no. 2021-07) and Hyogo Medical University (approval no. 3868). The clinical target volume (CTV) was defined as the entire prostate plus the proximal 1.5 cm of the seminal vesicles by radiation oncologists. The planning target volume (PTV)

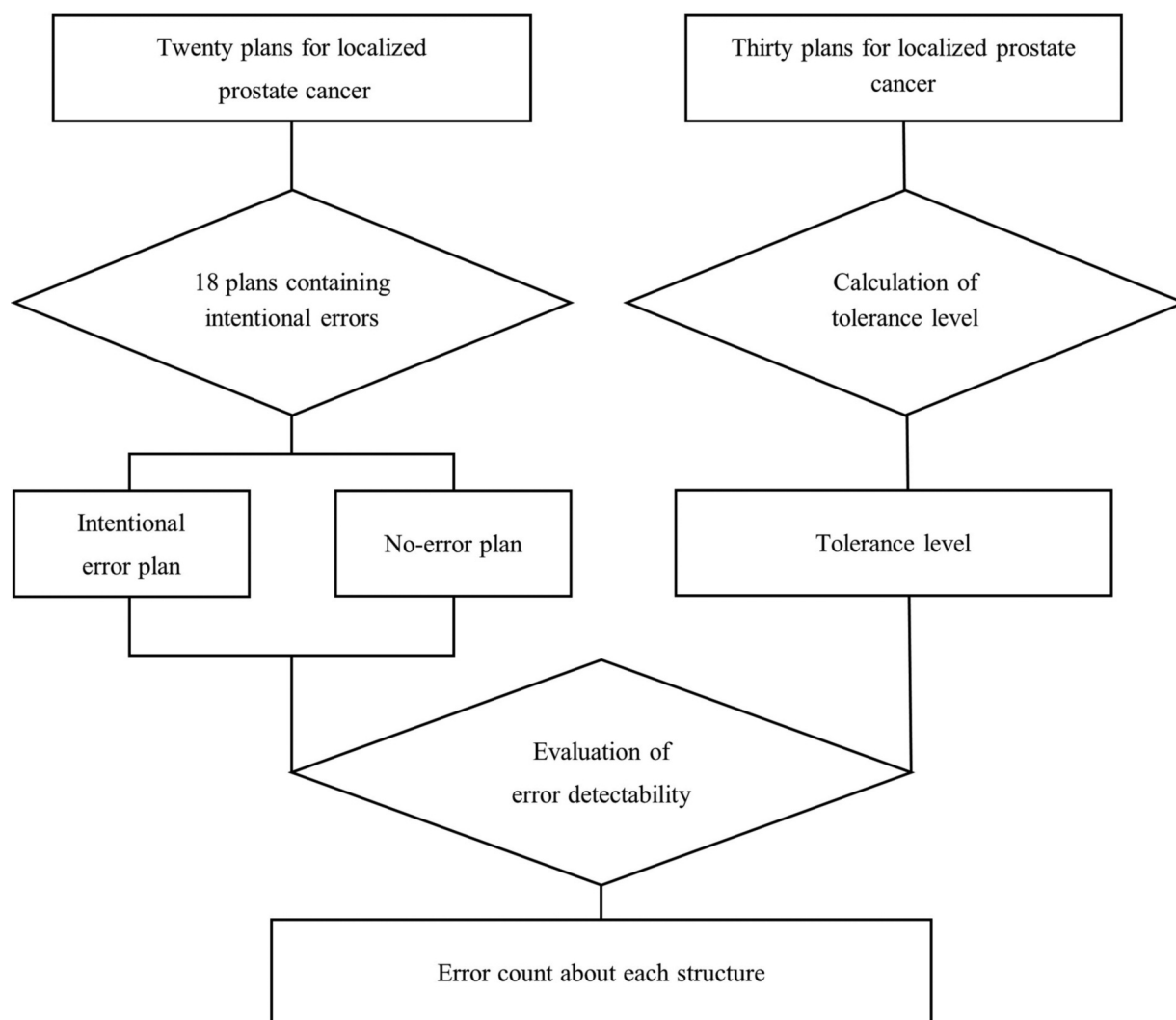


Figure 2. Flow that the study of error detection. Treatment plans with 18 patterns of intentional errors, which were created for each of the 20 cases and were validated using the three-dimensional verification system for the treatment plans with errors and without errors. The tolerance value, which is an index of error detection, was calculated from the measurement results of the other 30 cases.

was generated by adding an 8 mm margin to the CTV in all directions except posteriorly, where a 5 mm margin was used. The rectum and bladder were contoured as solid organs. The rectum was segmented from the level of the ischial tuberosities to the rectosigmoid flexure, and the bladder was contoured from its apex to the dome. The volume surrounded by equal doses was defined as the isodose volume, and contouring was performed for 5%, 50%, and 95% isodose volumes of the prescribed dose using the functions attached to the TPS (Figure 1).

*Adding errors to the treatment plan data.* The flow of this study is shown in Figure 2. For each patient, the following four types of error were added to the treatment plan:

a) The monitor unit (MU) output values were increased by 1% and 3% from the original treatment plan. This assumed that an error would affect the overall dose distribution. In this study, we define this error as “output error.”

b) Jaw retraction error was created by widening the lower jaw by 5 mm and 3 cm over the width in the treatment plan, widening only one jaw and also widening both jaws. Because the lower jaw shields the leaked dose from the MLC outside the PTV, it was assumed to influence the medium- and low-dose areas outside the PTV.

c) MLC systematic open errors were created for the A-side and B-side of the MLC by systematically opening the MLC 0.2 mm, 0.35 mm, and 0.5 mm on one side at a time.

MLC systematic closed errors of 0.2 mm, 0.35 mm, and 0.5 mm of narrowing were created for the A side and B side of the MLC, in a similar fashion.

The treatment plans without added errors were evaluated to determine false positives.

*Assessment of error detectability and statistical analysis.* The DVHs from TPS data calculated by the CCC (computed) and the

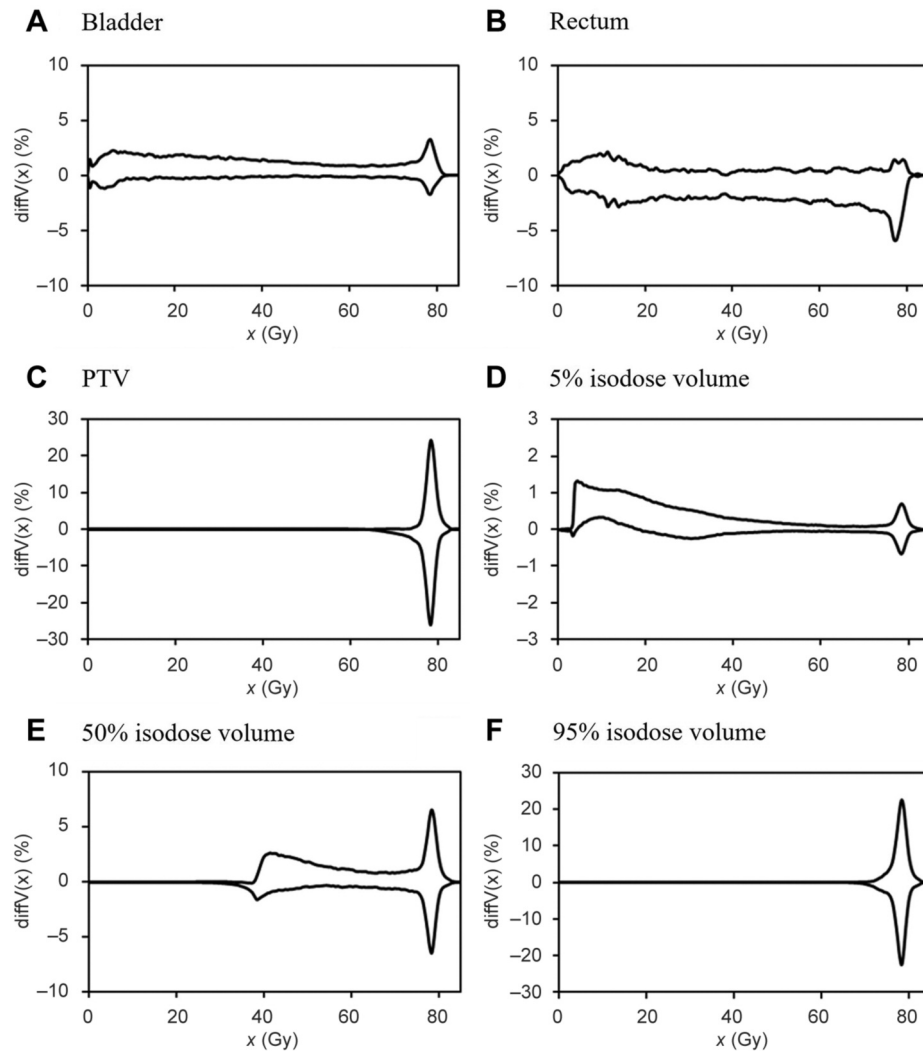


Figure 3. The tolerance values of each region of interest. The curves are the upper and lower limit values of the tolerance. PTV: Planning target volume.

results of dose distributions calculated by result of measurement using the two-dimensional ionization chamber array (measured) DVHs were evaluated.

To confirm the influence of the intentional errors, the DVH was recalculated with the COMPASS system. In this study,  $V_m(x)$ , the “measured” volume of the ROI receiving  $x$  Gy and  $V_c(x)$ , and the volume of the ROI “computed” by the TPS receiving  $x$  Gy, were evaluated. The ROIs were as follows: the PTV, rectum, bladder, 5% isodose volume, 50% isodose volume, and 95% isodose volume. The difference between  $V_m(x)$  and  $V_c(x)$  was calculated every 0.5 Gy from 0 Gy to 85 Gy. The differences at each dose [ $\text{Diff } V(x)$ ] were evaluated using the Equation (1) below:

$$\text{Diff } V(x) = V_m(x) - V_c(x) \quad (1)$$

Errors were considered detected when one or more of the  $\text{Diff } V(x)$  in each ROI exceeded the tolerance value. The tolerance values were defined as the mean value  $\pm 3$  standard deviations for each  $\text{Diff } V(x)$ ,

which were calculated from the data of the 30 other prostate cancer patients (Figure 2).

As a method to evaluate error detectability, the method by using PTV, bladder and rectum was defined as the conventional method, and the method by using 5%, 50%, and 95% isodose volume was defined as the isodose volume method. The number of intentionally added errors detected in each ROIs were evaluated for each plan, and the error detection rates with the two different types of validation method were evaluated using Fisher’s direct method, with  $p < 0.05$  considered significant. We used SPSS statistics version 22 for statistical analysis (SPSS, Chicago, IL, USA).

## Results

The upper and lower limits of tolerance values for each ROI (PTV, rectum, bladder, 5% isodose volume, 50% isodose volume and 95% isodose volume) are shown in Figure 3. The



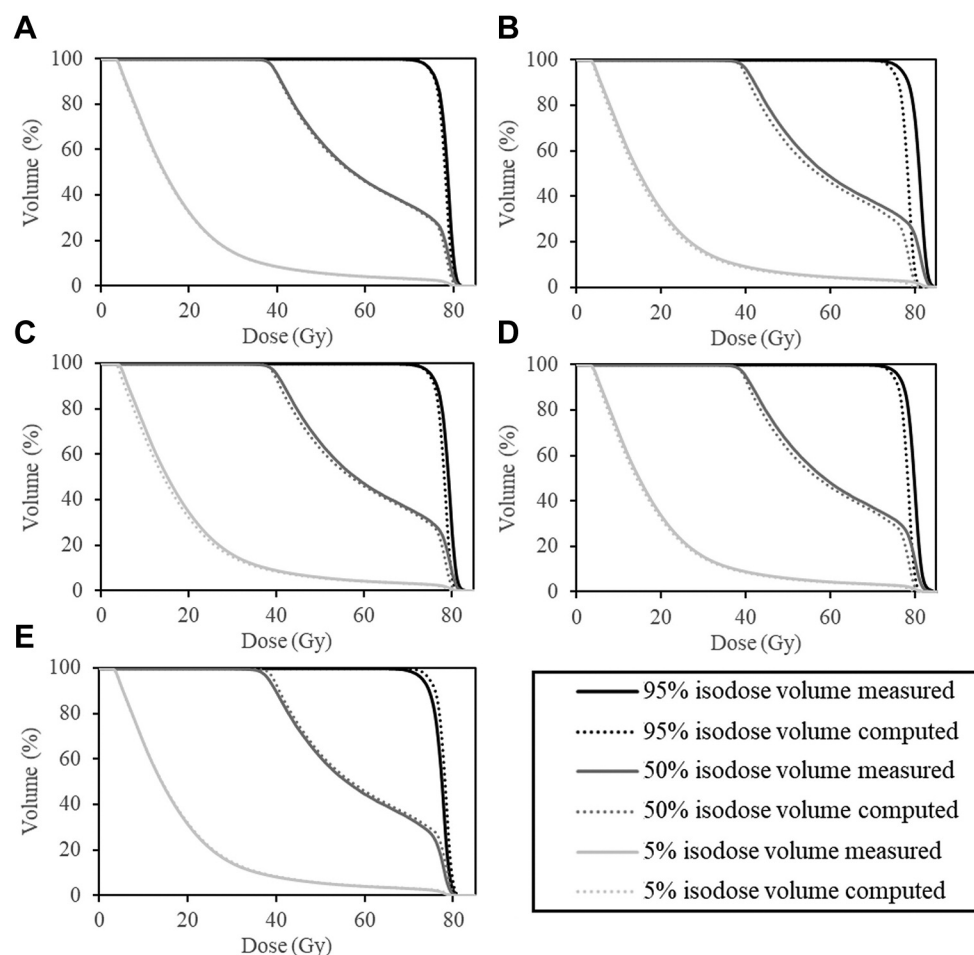


Figure 4. A case of dose volume histogram that resulted of “measured” and “computed” using three-dimension verification system. The solid line in each graph represents “measured” and the dotted line represents “computed”. The errors are as follows: (A) no error, (B) output error 3%, (C) jaw retraction error both sides 30 mm, (D) MLC systematic open error A-side 0.5 mm, (E) MLC systematic closed error A-side 0.5 mm.

range of the tolerance values for the conventional ROIs, which spread into low-dose regions such as bladder and rectum, tended to be wide (Figure 3A and B), and the tolerance values for the ROIs, which spread over a limited range in the high-dose regions, such as PTV, ranged approximately  $\pm 20\%$  (Figure 3C). The 5% isodose volume, which spreads into low-dose regions, tended to have a wide range similar to that of the bladder and rectum (Figure 3D). The 50% isodose volume had a narrower range than the 5% isodose volume, but the tolerance value was  $\pm 5\%$  (Figure 3E). The curves for the 95% isodose volume were similar in shape to those of the PTV (Figure 3F).

Figure 4 shows the DVHs of “measured” (two-dimensional ionization chamber array) and “computed” (CCC) values in one of 20 cases. Despite the absence of added errors, there were differences between “measured” and “computed” in the high-dose range (Figure 4A). With the 3% output error, the “measured” dose was generally higher than the “computed” dose of all isodose volumes from middle- to high-dose ranges,

especially in the range of 80 Gy (Figure 4B). With jaw retraction of 30 mm, the “measured” dose tended to be higher in all ROIs, especially in the low-dose range of <20 Gy of the 5% isodose volume (Figure 4C). With MLC systematic errors, the 95% isodose volume displayed major differences in the high-dose range (approximately 80 Gy) with both open and closed errors (Figure 4D and E).

The detection rate of an output error = 1% was higher in the 5% isodose volume (95%, 19/20), 50% isodose volume (100%, 20/20), and 95% isodose volume (80%, 16/20) than that of the PTV (65%, 13/20), rectum (45%, 9/20) and bladder (70%, 14/20) (Table I). In terms of jaw retraction error = 5 mm, the error detection rate was higher in the 5% isodose volume (one side: 70%, 14/20; both sides: 95%, 19/20) and rectum (one side: 60%, 12/20; both sides: 90%, 18/20), which contains many low-dose areas, than other ROIs (Table II). The error detection rate of the MLC systematic error in the 5% isodose volume and PTV, which was predicted to affect the periphery

Table I. Detection rate of output error.

		PTV	Rectum	Bladder	5% Isodose volume	50% Isodose volume	95% Isodose volume
Output error	Error	65%	45%	70%	95%	100%	80%
	1%	(13/20)	(9/20)	(14/20)	(19/20)	(20/20)	(16/20)
	Error	100%	100%	95%	100%	100%	100%
	3%	(20/20)	(20/20)	(19/20)	(20/20)	(20/20)	(20/20)

PTV: Planning target volume; x% isodose volume: isodose volume x% of the prescribed dose.

Table II. Detection rate of jaw retraction error.

		PTV	Rectum	Bladder	5% Isodose volume	50% Isodose volume	95% Isodose volume
Jaw retraction error	One side	5 mm	20% (4/20)	60% (12/20)	35% (7/20)	70% (14/20)	25% (5/20)
		30 mm	35% (7/20)	100% (20/20)	55% (11/20)	100% (20/20)	70% (14/20)
	Both sides	5 mm	20% (4/20)	90% (18/20)	40% (8/20)	95% (19/20)	40% (8/20)
		30 mm	60% (12/20)	100% (20/20)	65% (13/20)	100% (20/20)	95% (19/20)

PTV: Planning target volume; isodose volume x%: isodose volume x% of the prescribed dose.

of the target, was higher than that of other ROIs (Table III). Among all ROIs, the 5% isodose volume had the highest number of errors detected.

Table IV shows the results of comparing the error detection rates by the conventional method and the isodose volume method. For all errors, the isodose volume method showed higher rates than the conventional method; however, the only significant differences in error detection were of those involving the MLC systematic closed errors.

## Discussion

Compared with conventional radiotherapy, the use of IMRT has been reported to reduce OAR dose and adverse effects (18, 19), and the benefits of IMRT to patients are noteworthy. In areas where the target and OAR are close to each other, dose distributions with steep dose gradients are often necessary, and the motion of the treatment device tends to be more complicated (20). In recent years, planning devices that can perform treatment planning for VMAT using machine learning have become commercially available, but treatment plans created by machine learning are reported to be more complex in terms of MLC movements than those created manually (21, 22). As treatment plans become more complex, MLC positioning accuracy increases in importance (23), and

patient-specific verification is more important for the safe delivery of radiation therapy. Several studies have considered the evaluation of ROI settings to improve error detectability in verification using a three-dimensional verification system (24, 25). To our knowledge, however, the present study is the first to directly evaluate isodose volume and error detectability in detail. Among all ROIs in the conventional method and the isodose volume method, the 5% isodose volume, the ROI that covers a large volume including both low- and high-dose regions and evaluates the widest area in this method, had the highest error detection capacity. For relatively small errors such as the MLC systematic 0.2 mm error, for which the error detectability of the conventional method was limited, the error detectability of the 5% isodose volume was significantly better. In addition, slight improvements in error detectability were also observed by adding other isodose volumes to the evaluation; however, it should be noted that the addition of evaluation items led to increased complexity of the verification process.

In jaw retraction error, the jaw is intentionally opened to increase the medium-to-low-dose areas. Therefore, the error detectability in the rectum that was located dorsal to the PTV and the 5% isodose volume containing the low-dose region were high. On the other hand, the error detectability of the bladder located cephalad to the target was low. In all

Table III. Detection rate of MLC systematic open and closed error.

		PTV	Rectum	Bladder	5%	50%	95%	
					Isodose volume	Isodose volume	Isodose volume	
MLC systematic open error	A-side	0.2 mm	65% (13/20)	45% (9/20)	45% (9/20)	90% (18/20)	80% (16/20)	75% (15/20)
		0.35 mm	95% (19/20)	95% (19/20)	100% (20/20)	100% (20/20)	100% (20/20)	95% (19/20)
		0.5 mm	100% (20/20)	95% (19/20)	100% (20/20)	100% (20/20)	100% (20/20)	100% (20/20)
	B-side	0.2 mm	55% (11/20)	50% (10/20)	40% (8/20)	90% (18/20)	65% (13/20)	65% (13/20)
		0.35 mm	65% (13/20)	95% (19/20)	65% (13/20)	100% (20/20)	100% (20/20)	90% (18/20)
		0.5 mm	80% (16/20)	95% (19/20)	90% (18/20)	100% (20/20)	100% (20/20)	100% (20/20)
MLC systematic closed error	A-side	0.2 mm	30% (6/20)	25% (5/20)	0% (0/20)	70% (14/20)	60% (12/20)	40% (8/20)
		0.35 mm	50% (10/20)	40% (8/20)	15% (3/20)	100% (20/20)	90% (18/20)	85% (17/20)
		0.5 mm	80% (16/20)	55% (11/20)	35% (7/20)	100% (20/20)	100% (20/20)	95% (19/20)
	B-side	0.2 mm	30% (6/20)	25% (5/20)	10% (2/20)	80% (16/20)	65% (13/20)	55% (11/20)
		0.35 mm	70% (14/20)	30% (6/20)	10% (2/20)	100% (20/20)	90% (18/20)	100% (20/20)
		0.5 mm	95% (19/20)	65% (13/20)	10% (2/20)	100% (20/20)	100% (20/20)	100% (20/20)

MLC: Multileaf collimator; PTV: planning target volume; x% isodose volume: x% isodose volume of the prescribed dose.

treatment plans in this study the collimator was rotated 30 degrees, and the influence of jaw retraction error on the cephalad direction was small in this situation. Coleman *et al.* (18) reported on the analysis of gamma and DVH with intentional errors added to MLC in prostate cases. They added open and close errors from 0.25 mm to 1 mm to the MLC and performed a gamma analysis. They reported that errors were not detected when the MLC was closed by 0.25 mm. In this study, the isodose volume method was able to detect errors as small as 0.2 mm, which is superior to the error detection in their report. Tamborra *et al.* (25) stated that gamma analysis is insufficient for verification, and instead proposed the isodose structure method using isodose volume and clinical structures. They reported that the accuracy of validation was improved by adding spatial indices to DVH

evaluation using the overlapping ratio (OR) and volume ratio (VR) factors of the isodose volumes. However, in the present study, the error detectability with isodose volume was improved by using the tolerance value that was calculated from the plans without introduced errors.

The use of only 95% isodose volume was inadequate for IMRT verification, because the shape of the 95% isodose volume was similar to the shape of the PTV and the region out of the delineated structures was not evaluated. On the other hand, the 5% isodose volume included most of the irradiated volume, and the error detectability using 5% isodose volume was higher than that using the target and OARs. The error detectability using the isodose volume method was higher than the conventional method and errors in the low-dose regions were detectable in this study. The isodose volume

Table IV. Comparison of error detection rates between conventional method and isodose volume method.

			Conventional method	Isodose volume method	p-Value
Output error	Error 1%		85% (17/20)	100% (20/20)	0.115
	Error 3%		100% (20/20)	100% (20/20)	–
Jaw retraction error	One side	5 mm	80% (16/20)	80% (16/20)	0.653
		30 mm	100% (20/20)	100% (20/20)	–
	Both side	5 mm	95% (19/20)	95% (19/20)	0.756
		30 mm	100% (20/20)	100% (20/20)	–
MLC systematic error	Open error	A-side	0.2 mm	80% (16/20)	0.171
			0.35 mm	100% (20/20)	–
			0.5 mm	100% (20/20)	–
		B-side	0.2 mm	90% (18/20)	0.500
			0.35 mm	100% (20/20)	–
			0.5 mm	100% (20/20)	–
	Closed error	A-side	0.2 mm	35% (7/20)	0.005
			0.35 mm	60% (12/20)	0.002
			0.5 mm	90% (18/20)	0.244
		B-side	0.2 mm	40% (8/20)	0.001
			0.35 mm	70% (14/20)	0.010
			0.5 mm	95% (19/20)	0.500

The denominator of the numbers in parentheses indicates the total number of errors, and the numerator indicates the number of error counts. IV: Isodose volume.

method is useful in the safe execution of radiotherapy. The errors that can be detected from IMRT verification are those that affect the dose distribution, and the evaluation method using isodose volume with the above characteristics has the potential to be used to adjust ROIs for cases.

This study has several limitations. Only prostate cancer patients were evaluated, and the number of cases was small. Further, the datasets of these prostate cancer patients were similar in terms of target shape, size, and location of OAR. Therefore, additional studies using case- and site-independent tolerances are necessary. In addition, this evaluation method has not been automated and requires complex procedures using an in-house program. It is necessary to prepare a program for evaluation to use this method in clinical practice.

## Conclusion

In conventional IMRT QA using a three-dimensional verification system, there were regions that were not evaluated spatially. The isodose volume method was able to evaluate most of the irradiated volume and improved the error detectability, to make IMRT verification more effective. The

isodose volume method has the potential to be used for diseases other than prostate cancer, and its use could accordingly be substantially expanded with additional research.

## Conflicts of Interest

The Authors declare that they have no conflicts of interest in relation to this study.

## Authors' Contributions

Ryuta Nakahara contributed to the design of the study, data collection, analysis, and writing of the manuscript. Masayuki Fujiwara and Haruyuki Takaki contributed to the analysis and interpretation of data and drafting of the article. Masao Tanooka, Kentaro Ishii, Ryu Kawamorita, and Koichiro Yamakado provided critical analysis and revision of the paper. All Authors discussed the results and contributed to the final manuscript.

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