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ノート

Consideration of the optimum dose rate in intensity-modulated radiation therapy for patients with prostate cancer

前立腺癌患者の強度放射線治療における最適な線量率の検討

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Key words: MLC,　Gamma pass rate,　IMRT, Dose rate,　Radiochromic film

【Abstract】

This study aimed to determine the optimum dose rate (DR) of intensity-modulated radiation therapy (IMRT) for patients with prostate cancer in relation to the multileaf collimator (MLC) position errors based on the DR and gamma pass rate (GPR). A gamma evaluation was performed using a 3% dose difference and 2 mm distance-to-agreement criteria with a dose threshold of 10%. The MLC position error was measured using DynaLog files. The GPR was measured using MapCHECK2 and EBT3. The delivery time decreased from 97 sec to 83 sec when the DR increased from 500 to 600 monitor units per minute (MU/min). However, the difference between DR 500 and 600 MU/min was not significant ($p > 0.05$). The MLC position errors increased with increasing DR but no significant difference was observed in the maximum root mean square errors between the DRs of 300 and 400 MU/min, 400 and 500 MU/min, and 500 and 600 MU/min ($p > 0.05$). The mean percentage GPRs of 97.6%, 96.2%, 97.0%, and 95.7% were observed for the DRs of 300, 400, 500, and 600 MU/min, respectively, in EBT3. However, no significant difference was observed in the GPRs of DRs 300, 400, 500, and 600 MU/min ($p > 0.05$). The GPR of a DR 600 MU/min using EBT3 were at the very limit of 95% criteria. Therefore, we suggested that a DR of 500 MU/min was the most acceptable rate considering clinical safety.

【要 旨】

線量率（DR）に基づいたマルチリーフコリメーター（MLC）の位置誤差とガンマパス率（GPR）の関係から，前立腺癌患者の強度変調放射線治療における最適なDRを検討した．MLCの最大RMS誤差は，300と400 MU/min，400と500 MU/min，500と600 MU/minで有意差はなかった．ガンマ解析は，MapCHECK2とEBT3で，DR300, 400, 500および600 MU/minで有意差はなかった．EBT3解析の600 MU/minのGPRは，95%基準の限界寸前であり臨床的安全を考慮すると，500 MU/minが最も許容可能なDRであることを示唆した．

Introduction

The intensity-modulated radiation therapy (IMRT) technique uses a multileaf collimator (MLC) to modify the beam fluence in the same treatment field in order to improve the conformity of the prescribed dose distribution around the tumor region[1-5]. This modulation using MLC can be achieved using the sliding window (dynamic MLC [DMLC]) technique. DMLC is a treatment technique in which both the dose rate (DR) and leaf velocity (LV) are continually adjusted by MLC shapes when the beam is on. An increase in the DR greatly reduced the delivery time[6, 7], thus decreasing the burden on the patient; in particular, a longer delivery time causes result in patient repositioning or movement during a therapeutic session. However, increasing DR cause the faster LV, and a DR of 300 monitor units per minute (MU/min) or 400 MU/min is routinely applied in DMLC-IMRT because higher LV affects the MLC position accuracy[8-10]. Vorwerk et al.[9] recommended that the DR for sliding window IMRT should be 300 MU/min or 400 MU/min for patients with prostate cancer according to the dose volume histograms of the organs at risk. Kaviarasu et al.[10] examined the effect of DR on treatment accuracy using portal dosimetry gamma evaluation (GE) and created a workflow for pretreatment IMRT quality assurance (QA) using portal dosimetry with a default DR of 400 MU/min for the approved treatment plan. Thus, a higher DR of 500 or 600 MU/min was not applicable.

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On the contrary, Ghasroddashti et al.[6] conducted a survey of the relationship between DR and the number of MUs; however, they did not explicitly indicate which DR was acceptable, and a higher DR will possibly allow sufficient time to increase the number of patients treated in a day. Furthermore, Slosarek et al.[7] suggested that the difference between DRs of 100 MU/min and 600 MU/min, measured using the radiation planning index, was minor, and a low DR of 100 MU/min did not have a significant impact on the differences in treatment accuracy even if larger MLC position errors occurred in DR 600 MU/min than that in DR 100 MU/min. These studies can potentially apply a higher DR of 500 or 600 MU/min.

Although these studies evaluated dose distribution using GE, few studies have evaluated proportion of MLC position errors in detail based on DR changes in the clinical radiation plan. Furthermore, the optimal DR has not been determined such as previous studies[6-10]. This study aimed to determine the optimal DR in DMLC-IMRT for patients with prostate cancer in terms of relationship with the MLC position errors according to the DR and the influence of DR on dose distribution.

Materials and Methods

Patient data

Data of 15 patients with prostate cancer treated using DMLC-IMRT in our institution between June 2019 and January 2020 were retrospectively obtained. Their median age was 71 years (range, 56–81 years). According to the Comprehensive Cancer Network Risk classification for Prostate cancer (ver. 4, 2018), four patients had low-grade prostate cancer and 11 had intermediate-grade prostate cancer[11]. All patients were treated for prostate cancer with a dose of 76 Gy (2 Gy per fraction) using a 7 field IMRT with 10 MV photon beams energy.

Computed tomography simulation and delineation

Computed tomography (CT) axial scans with a slice thickness of 2.5 mm were performed for all patients using a 16 slice CT scanner (Bright Speed Elite Pro Vision; GE Healthcare, USA). The CT images were then transferred to a treatment planning system (TPS; Varian Medical Systems, Palo Alto, CA, USA) for treatment planning. The target volumes were contoured by a physician. The clinical target volumes (CTVs) were the prostate, the proximal 1 cm of the seminal vesicle for intermediate-risk patients, and the prostate for low-risk patients. The planning target volumes (PTVs) consisted of the CTV with a posterior 5 mm margin and a 7 mm margin for other directions (superior, inferior, anterior, right lateral, and left lateral). The prescribed dose was planned to be 95% of the PTV.

Linear accelerator and treatment planning system

The treatment plans were calculated using a Clinac iX (Varian Medical Systems, Palo Alto, CA, USA) linear accelerator equipped with a Millennium 120-leaf MLC (central: 20 cm of field, 5 mm leaf width; outer: 20 cm field, 10 mm leaf width) capable of IMRT delivery for different DRs (300, 400, 500, and 600 MU/

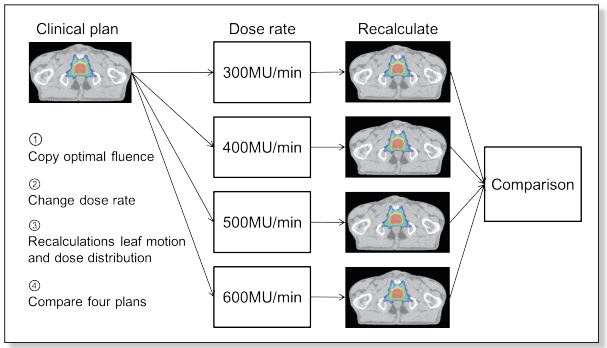

Fig.1 Flow of copied clinical plans for four DRs: 300, 400, 500, and 600 MU/min.

First, the clinical plan was copied, and optimization process was not modified; second, the clinical plan was changed based on the four DRs: 300, 400, 500, and 600 MU/min; and third, the leaf motion calculator was rerun for each field, and the dose distribution was recalculated in four copied plans.

Table1 Dosevolumehistgramparametersofthecopiedfourplans.

Structure	Constrainttype	Doserate (MU/min) 300	400	500	600
PTV	Max (Gy)	80.33	80.34	80.34	80.35
	Mean (Gy)	77.84	77.84	77.83	77.81
	D99% (%)	97.46	97.49	97.52	97.53
Rectum	V76Gy (%)	2.39	2.43	2.47	2.49
	V70Gy (%)	8.43	8.45	8.47	8.49
	V65Gy (%)	11.06	11.08	11.10	11.12
	V60Gy (%)	13.36	13.39	13.40	13.42
	V50Gy (%)	17.99	18.03	18.05	18.08
	V40Gy (%)	24.05	24.10	24.14	24.19
Bladder	V75Gy (%)	8.80	8.80	8.76	8.76
	V65Gy (%)	16.41	16.42	16.41	16.41
	V40Gy (%)	34.89	34.91	34.92	34.96

Dataarepresentedasmeanvalues.
PTV,planningtargetvolume

min). All plans were created using Varian's Eclipse TPS incorporating the Anisotropic Analytical Algorithm version 13.6, and the associated leaf motion calculator version 13.6 (Varian Medical Systems, Palo Alto, CA, USA). The linear accelerator was equipped with a maximum LV of 2.5 cm/sec. In addition, the number of segment settings for DMLC-IMRT was automatically calculated in the TPS. Clinical plans (DR 600 MU/min) were copied for four DRs: 300, 400, 500, and 600 MU/min. Figure 1 shows the flow of the four copied plans. The optimal fluence patterns determined during the initial optimization process were not modified, and the only DRs were changed for all plans. Table 1 lists the dose volume histogram parameters for four copied plans. These parameters were much the same values in spite of the different DRs.

MLC position error

The positional accuracy of the DMLC was evaluated from a DMLC log (DynaLog) file containing MLC details[12-14]. These log files contained DMLC delivery details recorded every 50 ms to analyze the inaccuracy in MLC motion for banks A and B. We analyzed the log files of all IMRT copied plans while changing only the DRs using the DoseLab v.6.8 FractionLab software (Mobius Medical Systems, TX, USA). We assessed the following factors: delivery time, number of MU, number of segments, and proportion of MLC position errors (0–0.05, 0.05–0.5, 0.5–1.0, and 1.0–1.5 mm). The MLC position errors represent the differences in the MLC positions between the planned and actual delivery positions. The analysis value of DynaLog files was expressed as the root mean square (RMS). The RMS errors are used to condense a set of errors into a single representative value[15]. The RMS errors are always greater than or equal to the mean of the absolute value of the errors. FractionLab software is used to calculate the RMS errors for individual leaves in files, ranges of gantry angles in files, and entire leaf banks in a collection of files. For a set of n errors (differences between the set and delivered positions), the RMS errors were calculated using the following formula:

$$\text{RMS error} = \sqrt{\frac{\Sigma(\text{Error})^2}{n}}$$

Gamma evaluation (two-dimensional diode array detector)

To evaluate the influence of DRs on the dose distribution, all IMRT copied plans were measured using MapCHECK2 (Sun Nuclear Corporation, Melbourne, FL, USA) to compare the dose distributions between the calculated and measured doses; a GE was performed using a 3% dose difference and 2 mm distance-to-agreement criteria with a dose threshold (TH) of 10% (3%/2 mm) to remove the noise, as recommended by the American Association of Physicists in Medicine Task Group (AAPM TG) 21[16, 17]. MapCHECK2 has a measuring

area of 26 cm × 32 cm that consists of 1,527 solid-state SunPoint diode detectors with a resolution of 0.8 mm × 0.8 mm, diagonal detector spacing of 7.07 mm, and parallel detector spacing of 10 mm. MapCHECK2 was set up under an 8 cm water-equivalent phantom (Solid Water HE; GAMMEX-RMI, Middleton, WI, USA) and placed in a plane with an isocenter. All treatment parameters in the copied plans were the same as those in the clinical plan, excluding the gantry and collimator angles set to 0° for all fields. Before the GE, MapCHECK2 was calibrated according to the manufacturer's guidelines. A GE was performed at an absolute dose. The calculated and measured dose distributions were compared using the SNC Patients™ v. 6.7.4 (Sun Nuclear Corporation, Melbourne, FL, USA). In addition, Woon et al.[18] reported that the criterion of 3%/1 mm was the most sensitive gamma criterion for MapCHECK2 to detect systematic MLC errors. Therefore, we conducted a GE using the criterion of 3%/1 mm in the additional investigation.

Gamma evaluation (Film)

The radiochromic film used in this study was a Gafchromic EBT3 (International Specialty Products, Wayne, NJ, USA) with sheet dimensions of 20.3 cm × 25.4 cm. The film was used according to the methods described in the AAPM TG-55 report[19]. To obtain the calibration curve, the EBT3 film was cut into smaller pieces measuring 6 cm × 6 cm in size, and 12 of the smaller films were selected. Each piece of film was placed under a 10 cm solid water phantom with a 10 cm space underneath to provide adequate backscatter, a field size of 10 cm × 10 cm, and a 90 cm source-to-surface distance. The films were then irradiated using the Clinac iX linear accelerator with a 10 MV photon beam energy in the range of 0 MU to 500 MU (0, 10, 25, 50, 100, 150, 200, 250, 300, 350, 400, and 500 MU). To evaluate the influence of DR on dose distributions, the EBT3 film was sandwiched between I'mRT phantoms (IBA Dosimetry, GmbH, Schwarzenbrunk, Germany) and placed in the sagittal plane at the center of the phantom (Fig.2). After irradiation, the films were kept in a box in order to protect them from fluorescent light for 24 h after irradiation exposure, and an unexposed film was scanned using a flatbed scanner (Epson Expression DS-G20000; Epson Tokyo, Japan) in 48-bit RGB mode (red, 16-bit color; green, 16-bit color; and blue, 16-bit color) with a resolution of 75 dots/inch. All treatment parameters in the copied plans were the same as those in the clinical plan, including the gantry and collimator angles. The calculated and measured dose distributions were compared using the DoseLab dose comparison software ver.6.8 (Mobius Medical Systems, USA). A GE was performed with an absolute dose using criteria of 3%/2 mm, TH10%.

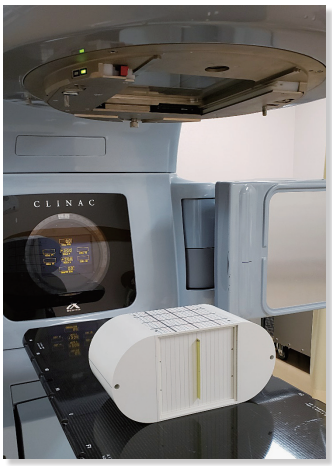

Fig.2 Experimental set-up for film evaluation using I'mRT phantom.

To evaluate the influence of dose rate on the dose distribution, the EBT3 film was sandwiched between I'mRT phantoms and located in the sagittal plane at the center of the phantom. Because sagittal plane could draw the most rectum which was organ at risk, we verified the dose distribution using sagittal plane. We evaluated the dose distribution at the center of the PTV.

Dose rate dependence (preliminary experiment)

Actually delivered DRs of linear accelerator were measured using two-dimensional (2D) diode array detector (Profiler2 model1174; Sun

Nuclear Corporation, Melbourne, FL, USA). The measurement were 20 cm × 20 cm open field size for 300 MU of 10 MV photon beams using DRs of 300, 400, 500, and 600 MU/min. In addition, to verify the variations of radiation output with DR in Clinac iX, a cylindrical ion chamber (Farmer 30013; PTW GmbH, Freiburg, Germany) and an electrometer (RAMTEC Smart; TOYO Medic, Tokyo, Japan) were used. The measurements were made in water with a depth 10 cm and in an open filed size of 10 cm × 10 cm for 100 MU of 10 MV photon beams using the DRs of 300, 400, 500, and 600 MU/min. The measurement values for each DR were obtained from ten measurements. Furthermore, we confirmed the DR dependence of MapCHECK2 by measuring 100 MU in 10 cm × 10 cm open fields with 10 MV photon beams in the same setup (under an 8 cm solid water).

Statistical analysis

A comparison of Dynalog files for MLC position errors between the four copied plans was performed by repeated-measures ANOVA or the Friedman test and post hoc comparisons with Bonferroni/Dunn's test or Steel–Dwass test. Statistical significance was set at $P < 0.05$. All statistical analyses were performed using Excel 2015 software (Microsoft, Redmond, WA, USA) with the add-in software application Statcel4 (OMS Publishing Inc. Tokyo, Japan).

Results

In the preliminary experiment

Table 2 shows the results of actually delivered DRs. The actually delivered DR of 600 MU/min was slightly lower than that of nominal value. Delivery beams for other DRs (400, and 500 MU/min) measured by Profiler2 were the equivalent magnification values as nominal values normalized with a dose rate of 300 MU/min. Figure 3 shows the results of DR dependence for ion chamber and MapCHECK2 in the preliminary experiment. The output of the machine with a 10 MV photon beam energy measured by the ion chamber was quite constant for this range of DRs with a maximum variation of 0.04% for DR of 600 MU/min (normalized with a DR of 300 MU/min). The response of MapCHECK2 increased with increasing DR value, with a maximum variation of 0.4%, which is equivalent and comparable to the value of 0.21%–0.35% from previous studies[20, 21].

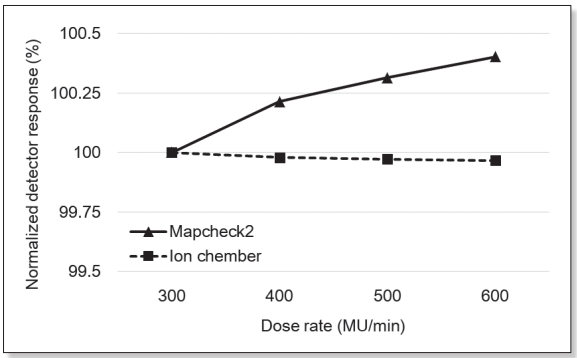

Fig.3 Results of the dose rate (DR) dependence for ion chamber and MapCHECK2.

The output of the Clinac iX with 10 MV photon beams measured by the ion chamber was quite constant for this range of DRs with the maximum variation of 0.04% for the DR of 600 MU/min (normalized with the DR of 300 MU/min). The response of the MapCHECK2 increased with increasing DR value with a maximum variation of 0.4%.

MLC position error

Tables 3 and 4 show the differences in the DRs analyzed based on the MLC position errors in this study. Table 5 shows the results

Table 2 Results of actually delivered dose rates of linear accelerator

Dose rate (MU/min)	300	400 (×1.33)	500 (×1.67)	600 (×2.0)
Profiler2 (pulse/sec)	180	240 (×1.33)	300 (×1.67)	350 (×1.94)

The number in parentheses indicated the magnification values normalized with a dose rate of 300 MU/min.

of the statistical analysis of MLC position errors. The delivery time decreased from 97 sec to 83 sec when the DR increased from 500 to 600 MU/min. However, the difference between DR 500 and 600 MU/min was not significant ($p > 0.05$, Table 4). The MU values normalized with a DR of 300 MU/min were expressed as a percentage increase in increased DRs, and gains of 3.12% were achieved for 400 MU/min, 6.47% for 500 MU/min, and 9.80% for 600 MU/min; however, no significant difference was observed in the respective comparisons ($p > 0.05$, Table 4). No significant differences were also observed between the DRs of 300 and 400 MU/min, 400 and 500 MU/min, and 500 and 600 MU/min for the number of segments ($p > 0.05$, Table 3). Expressed in terms of percentage increased in MUs per 100 MU/min increase DR, we observed gains of approximately 3.3% which was approximately the same and comparable to the value of 4.1% from a previous study[6]. The number of MUs and segments increased with increasing DR but MU per segment was slightly lower with increasing DR (Table 3). Moreover, no significant difference was

Table 3 Results of MLC position errors based on the dose rates.

	300 MU/min	400 MU/min	500 MU/min	600 MU/min
Delivery time (sec)	151.85 ± 21.64	116.82 ± 15.89	97.22 ± 12.75	83.71 ± 10.66
Monitor unit (MU)	757.27 ± 108.49	780.87 ± 107.73	806.27 ± 106.41	831.47 ± 106.43
Segment	668.27 ± 51.10	696.87 ± 63.63	735.33 ± 65.83	770.07 ± 65.70
MU per segment	1.13	1.12	1.09	1.08
Leaf speed Minimum (cm/sec)	0.20 ± 0.06	0.24 ± 0.06	0.28 ± 0.07	0.33 ± 0.09
Leaf speed Maximum (cm/sec)	2.10 ± 0.08	2.20 ± 0.07	2.24 ± 0.08	2.26 ± 0.07
Mean RMS error (mm)	0.18 ± 0.03	0.23 ± 0.03	0.27 ± 0.03	0.30 ± 0.03
Max RMS error (mm)	0.47 ± 0.07	0.54 ± 0.07	0.59 ± 0.07	0.64 ± 0.08
MLC bank A				
0-0.05 mm (%)	41.53 ± 13.58	36.51 ± 13.45	33.16 ± 13.26	30.58 ± 13.01
0.05-0.5 mm (%)	54.74 ± 14.13	57.32 ± 13.14	57.99 ± 15.03	57.47 ± 16.35
0.5-1.0 mm (%)	3.47 ± 2.52	5.49 ± 3.73	7.96 ± 5.03	10.32 ± 5.68
1.0-1.5 mm (%)	0.24 ± 0.37	0.55 ± 0.57	0.89 ± 0.76	1.36 ± 0.94
MLC bank B				
0-0.05 mm (%)	42.39 ± 12.43	36.58 ± 12.97	33.02 ± 12.87	30.49 ± 12.15
0.05-0.5 mm (%)	54.25 ± 12.63	57.53 ± 13.13	58.72 ± 13.56	58.90 ± 13.44
0.5-1.0 mm (%)	3.13 ± 2.27	5.08 ± 3.22	7.23 ± 4.03	9.43 ± 4.89
1.0-1.5 mm (%)	0.22 ± 0.35	0.52 ± 0.56	0.83 ± 0.73	1.28 ± 0.98

Data are presented as mean ± standard deviation.
MLC, multi leaf collimator; RMS, root mean square.

Table 4 Results of DynaLog files based on the dose rates.

Analysis of variance						
Data		Delivery time	Monitor unit	Segment	Leaf speed	
					Minimum	Maximum
p-value		2.84E-33	4.12E-38	1.17E-65	3.22E-07	1.02E-06
Post hoc comparisons						
comparison		Delivery time	Monitor unit	Segment	Leaf speed	
Dose rate 1	Dose rate 2				Minimum	Maximum
300	400	**	n.s.	n.s.	n.s.	*
	500	**	n.s.	*	*	**
	600	**	n.s.	**	**	**
400	500	**	n.s.	n.s.	n.s.	n.s.
	600	**	n.s.	*	*	n.s.
500	600	n.s.	n.s.	n.s.	n.s.	n.s.

Analysis of variance was calculated using repeated measures of analysis of variance or the Friedman test. The Bonferroni/Dunn's test or Steel-Dwass test was used for post hoc comparisons. n.s., not significant; *, $p < 0.05$; **, $p < 0.01$.

Table 5 Results of the statistical analysis of MLC position errors.

Analysis of variance											
Leaf position		Mean RMS error	Max RMS error	0-0.05 mm		0.05-0.5 mm		0.5-1.0 mm		1.0-1.5 mm	
				bank A	bank B	bank A	bank B	bank A	bank B	bank A	bank B
p-value		7.66E-44	2.70E-32	6.91E-66	2.92E-104	2.33E-12	1.10E-17	5.46E-66	1.2E-65	4.4E-60	2.7E-60
Post hoc comparisons											
comparison		Mean RMS error	Max RMS error	0-0.05 mm		0.05-0.5 mm		0.5-1.0 mm		1.0-1.5 mm	
Dose rate 1	Dose rate 2			bank A	bank B	bank A	bank B	bank A	bank B	bank A	bank B
300	400	**	n.s.	**	**	n.s.	n.s.	**	**	**	**
	500	**	**	**	**	n.s.	*	**	**	**	**
	600	**	**	**	**	n.s.	*	**	**	**	**
400	500	**	n.s.	n.s.	n.s.	n.s.	n.s.	**	**	**	**
	600	**	**	**	**	n.s.	n.s.	**	**	**	**
500	600	*	n.s.	n.s.	n.s.	n.s.	n.s.	**	**	**	**

Analysis of variance was calculated using repeated measures of analysis of variance or the Friedman test. The Bonferroni/Dunn's test or Steel-Dwass test was used for post hoc comparisons. n.s., not significant; *, $p < 0.05$; **, $p < 0.01$. MLC, multi leaf collimator; RMS, root mean square.

observed in the maximum RMS between the DRs of 400 and 500 MU/min, and 500 and 600 MU/min ($p > 0.05$, Table 4).

The proportion of MLC position errors in approximately > 90% of the total errors in the DRs 300, 400, 500, and 600 MU/min in banks A and B were within 0–0.05 mm and 0.05–0.5 mm (Table 3). No significant difference was observed in the MLC position errors between the DRs of 300 and 400 MU/min, 400 and 500 MU/min, 400 and 600 MU/min, and 500 and 600 MU/min in banks A and B (range 0.05–0.5 mm) ($p > 0.05$, Table 5). In addition, no significant difference was observed in the MLC position errors between the DRs of 400 and 500 MU/min, 500 and 600 MU/min in banks A and B (range: 0 mm–0.05 mm) ($p > 0.05$, Table 4). Furthermore, no significant difference was observed in the Max RMS errors between 300 and 400 MU/min, 400 and 500 MU/min, and 500 and 600 MU/min ($p > 0.05$, Table 5). On the contrary, MLC position errors of the all comparisons in banks A and B (range: 0.5–1.0 mm and 1.0–1.5 mm) were statistically differences. ($p < 0.05$, Table 5).

Gamma evaluation

Figure 4 shows the mean values of gamma pass rates (GPRs) for MapCHECK2 and EBT3 according to DRs. The mean percentage GPRs of 99.6%, 99.5%, 99.4%, and 99.5% were observed for the DRs of 300, 400, 500, and 600 MU/min, respectively, in MapCHECK2. The mean percentage GPRs of 97.6%, 96.2%, 97.0%, and 95.7% were observed for the DRs of 300, 400, 500, and 600 MU/min, respectively, in EBT3. Based on the GE of EBT3 films, the GPR of a DR of 600 MU/min was lowest than that of other DRs. However, no significant difference was observed in the GPRs of DRs 300, 400, 500, and 600 MU/min ($p > 0.05$).

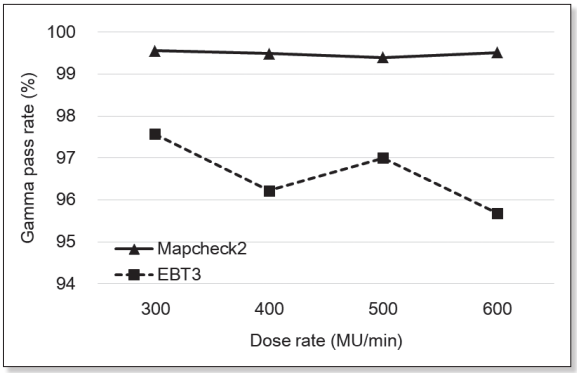

Fig.4 Gamma pass rates (GPRs) for MapCHECK2 and EBT3 according to the varying dose rates (DRs).

The mean percentage GPRs of 99.6%, 99.5%, 99.4%, and 99.5% were observed for the DRs of 300, 400, 500, and 600 MU/min, respectively, with the gamma criteria of 3%/2 mm in MapCheck2. The mean percentage GPRs of 97.6%, 96.2%, 97.0%, and 95.7% were observed for the DRs of 300, 400, 500, and 600 MU/min, respectively, with the gamma criteria of 3%/2 mm in EBT3.

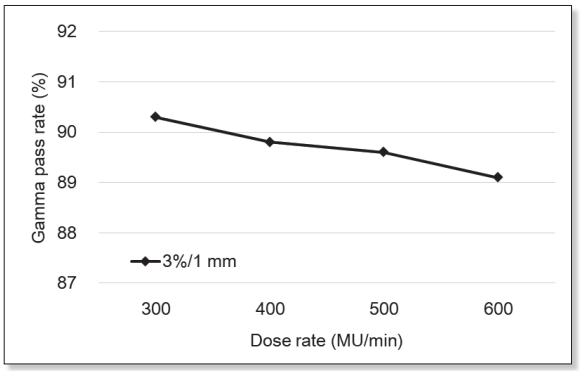

Fig.5 Gamma pass rate (GPR) with the most sensitive criterion 3%/1 mm for MapCHECK2 [18].

The mean percentage GPRs of 90.3%, 89.8%, 89.6%, and 89.1% were observed for the DRs of 300, 400, 500, and 600 MU/min, respectively, with the gamma criteria of 3%/1 mm in MapCHECK2.

Figure 5 shows the mean values of GPRs with the most sensitive criterion 3%/1 mm for MapCHECK2 according to DRs. The mean percentage GPRs of 90.3%, 89.8%, 89.6%, and 89.1% for DRs of 300, 400, 500, and 600 MU/min, respectively, were observed (Fig.5). The GPRs decreased with increasing DR; the GPR of a DR of 600 MU/min was lowest value as well as in EBT3. However, no significant difference was observed in the GPRs of DRs 300, 400, 500, and 600 MU/min ($p > 0.05$).

Discussion

In this study, we evaluated the MLC position errors between the planned and actual delivery positions using DynaLog files. These log files of the delivered IMRT contain significant information used to assess the routine IMRT QA and are commonly used for patient-specific IMRT QA[22, 23]. Furthermore, these log files are a promising tool for IMRT QA automation that reduces the time spent on IMRT QA and can be used to analyze the entire IMRT day-to-day delivery[24]. In this study, DynaLog files were considered to reflect the accuracy of the MLC position, and our results were highly reliable.

The number of MUs increased with increasing DR (Table 3), suggesting a larger number of small MU segments. Previous studies demonstrated that a small MU segment may result in delivery inaccuracy in IMRT[25-27]. Huang et al.[28] reported that the presence of small MU segments has a strong impact on GPRs. However, these studies did not investigate a small MU segment with MUs fewer than 1. Therefore, small MU segments had a little effect on the GPRs in this study because the MU per segment value was much the same based on the DR (Table 3). In a comprehensive multicenter study, Kerns et al.[29] revealed that the parameters, including gantry angle, number of beam holdoffs, and number of segments, commonly thought to affect MLC performance were found to have no such effect. Therefore, we considered that increasing the number of small MU segments had no effect on the GPRs and MLC position errors.

A patient-specific QA for IMRT is extremely important for ensuring the quality of care for patients with cancer during radiotherapy. Various methods, including the use of an ion chamber, 2D array detectors, and an electronic portal imaging device (EPID), have been employed during pretreatment verification to detect possible errors between the calculated dose and the measured dose[30-32]. The MapCHECK2 used in this study has a detection accuracy and a stability of GPR equivalent to those of MatriXX (ion chamber 2D array) and EPID[33]. MapCHECK2 showed that a systematic MLC error of up to 0.5 mm was not detected with a gamma criterion of 3%/1 mm[18]; in this study, almost all MLC position errors in banks A and B were within 0–0.05 mm and 0.05–0.5 mm (Table 3). Therefore, MapCHECK2 with a GE of 3%/2 mm could not detect a slight difference in the dose distribution according to the difference in DRs (Fig.4). However, the GPRs decreased with increasing DR using criteria of 3%/1 mm (Fig.5). Previous studies were demonstrated that 1 mm MLC position error produced about

5% errors in dose delivery and decreased in average GPRs[34, 35]. We considered that decreasing GPRs were influenced by MLC position errors within 0.5–1.0 mm and 1.0–1.5 mm (Table 5) .

By contrast, Gafchromic films were designed for IMRT and QA because they have high resolution and can detect slight differences in the dose distribution[36, 37]. Furthermore, Marroquin et al.[38] evaluated the uncertainty in an EBT3 film dosimetry system, including the dynamic reproducibility, uniformity, and orientation. They noted that higher uncertainties were found because of the relative orientation of the film and the uniformity in the response of the scanner. However, they reported that one must strictly control the position and orientation of the film, so that the total uncertainties are considerably reduced. We considered that the GE using EBT3 had a little uncertainty because we performed the film analysis in the same position on the scanner and in the same orientation. In addition, Borca et al.[39] evaluated DR dependence in IMRT (6 MV and 15 MV) among various DRs (100, 300, and 600 MU/min). In another study by Ataei et al.[40], DR dependence (6 MV and Co-60 gamma rays) was observed between DRs of 200 and 400 cGy/min. These studies found that DR dependence was not significantly different between the EBT3 films. Therefore, results of the GE using the EBT3 films were not affected by the difference in DRs, and the decrease in the GPR with increasing DR in EBT3 was considered to mainly reflect the inaccuracy of MLC position errors according to the DRs.

Vorwerk et al.[9] recommended that mechanical and technical aspects limit for the LV of 2.5–3.0 cm/sec and for the DR of 300–400 MU/min should be respected for prostate patients. In addition, we considered that MLC position errors were less in the same DRs because maximum LV was 2.5 cm/sec in our study. Furthermore, Kaviarasu et al.[10] indicated that some fields of a DR 500 MU/min showed the worse gamma value than DR 400 MU/min. They discussed that increasing the DR increased the number of control points per min and increased the complexity of the MLC delivery, but they did not investigate the MLC. In addition, average gamma values were same values for 400 and 500 MU/min, and the maximum gamma value of a DR 400 MU/min was slightly better (0.08 point) than that of a DR 500 MU/min, and difference of point absolute dose using ion chamber showed that < 1% mean deviation for 400 and 500 MU/min. These results showed that there were few difference between the DR 400 and 500 MU/min same as our study. More importantly, we considered that intrafractional displacement of the prostate during IMRT had a greater effect on dose distribution than slightly difference of MLC position errors between the DR 400 and 500 MU/min. Previous studies demonstrated that the average 3D displacements of intrafraction prostate were approximately 2–3 mm according to the immobilization system and duration of radiotherapy[41, 42]. Furthermore, Kontaxis et al.[43] reported that the average drops in D99% coverage due to displacement of the intrafraction prostate for the PTV and CTV during radiation delivery were 11% and 2.1%, respectively, using combined 1.5T magnetic resonance imaging and a linear accelerator system. Therefore, we considered the influence for dose distribution, the delivery time should be as short as possible.

These results indicated that a DR of 500 or 600 MU/min was the acceptable rate when reducing the delivery time. However, no significant difference was observed between DR 500 and 600 MU/min for the delivery time (Table 4). Those causes were considered that actually delivered DR of 600 MU/min was slightly lower than that of nominal value. In addition, the GPRs of a DR 600 MU/min was larger decreased compared to DR 400 and 500

MU/min using MapCHECK2 with a gamma criterion 3%/1 mm (Fig.5). Furthermore, the GPR of a DR 600 MU/min using EBT3 were at the very limit of 95% criteria deciding by TG 218[17] (Fig.4). Therefore, we suggested that a DR of 500 MU/min was the most acceptable rate considering clinical safety.

With regard to the limitations, according to our analysis, the MU values in DMLC-IMRT increased with increasing DR. The usage of greater MUs results in an increase in scattered radiation and radiation leakage, causing secondary malignancies[44-46]. In addition, the transmitted radiation dose, which depends on the transmission through the leaves, is also higher[47] and consequently increases the integral dose to the organ at risk because of inter- and intraleaf transmission leakage and scatter. Decreasing these radiation doses is important for the protection of organs at risk and in normal tissues. However, we did not consider these influences in terms of radiation exposure in this study.

Conclusion

We considered the influence of DR on the MLC position errors and GPR and found that a DR of 500 MU/min was the most acceptable rate when reducing the delivery time while maintaining the MLC positional accuracy and GPR.

Conflict of interest

The authors declare that they have no conflict of interest.

Statement of human rights

This study was approved by the Ethics Committees of Akita Kousei Medical Center (approval No. 2020-155).

図の説明

Fig.1 4つの線量率への臨床計画のコピーの流れ
第1に臨床計画をコピーし，最適化過程は変更しませんでした．第2に計画は4つの線量率に基づいて変更しました．第3にリーフモーション計算機で，各フィールドに対して再計算を行い，線量分布が4つのコピー計画により再計算を行いました．

Fig.2 I'mRTファントムを使用したフィルム評価のための実験装置
線量分布に対する線量率の影響を評価するために，EBT3フィルムをI'mRTファントムの間に挟み，ファントムの中心の矢状面に配置しました．矢状面は危険臓器である直腸を最も多く描出することができるため，矢状面を用いて線量分布を確認しました．PTV中心の線量分布を評価しました．

Fig.3 イオンチェンバーとMapCHECK2の線量率依存性の結果
電離箱によって測定された10 MV光子ビームを使用したClinaciXの出力は，この範囲の線量率で非常に一定であり，600 MU/minの線量率で最大変動は0.04%でした（300 MU/minのDRで正規化）．MapCHECK2の応答は，線量率の値の増加とともに増加し，最大変動は0.4%でした．

Fig.4 線量率変化によりMapCHECK2とEBT3のガンマパス率
ガンマ基準が3%/2 mmにおけるMapCheck2の平均ガンマパス率は，線量率が300，400，500および600 MU/minで，それぞれ99.6%，99.5%，99.4%，99.5%でした．ガンマ基準が3%/2 mmにおけるEBT3の平均ガンマパス率は，線量率が300，400，500，600 MU/minで，それぞれ97.6%，96.2%，97.0%，95.7%でした．

Fig.5 MapCHECK2の最も感度の高い基準3%/1 mmのガンマ通過率（GPR）[18]
MapCHECK2のガンマ基準が3%/1 mmの時，線量率が300，400，500および600 MU/minで，平均ガンマパス率は，それぞれ90.3%，89.8%，89.6%，89.1%でした．

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