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FULL PAPER

Gating window dependency on scanned carbon-ion beam dose distribution and imaging dose for thoracoabdominal treatment

SHINICHIRO MORI, PhD, MASATAKA KARUBE, MD, SHIGEO YASUDA, MD, NAOYOSHI YAMAMOTO, MD, HIROSHI TSUJI, MD and TADASHI KAMADA, MD

Research Center for Charged Particle Therapy, National Institute of Radiological Sciences, Chiba, Japan

Address correspondence to: Dr Shinichiro Mori
E-mail: mori.shinichiro@qst.go.jp

Objective: To explore the trade-off between dose assessment and imaging dose in respiratory gating with radiographic fluoroscopic imaging, we evaluated the relationship between dose assessment and fluoroscopic imaging dose in various gating windows, retrospectively.

Methods: Four-dimensional (4D) CT images acquired for 10 patients with lung and liver tumours were used for 4D treatment planning for scanned carbon ion beam. Imaging dose from two oblique directions was calculated by the number of images multiplied by the air kerma per image. Necessary beam-on time was calculated from the treatment log file. Accumulated dose distribution was calculated. The gating window was defined as tumour position not respiratory phase and changed from 0-100% duty cycle on 4DCT. These metrics were individually evaluated for every case.

Results: For lung cases, sufficient dose conformation was achieved in respective gating windows [D_{95} -clinical target

volume (CTV) > 99%]. V_{20} -lung values for 50%- and 30%-duty cycles were 2.5% and 6.0% of that for 100%-duty cycle. Maximum doses (cord/oesophagus) for 30%-duty cycle decreased 6.8%/7.4% to those for 100%-duty cycle. For liver cases, V_{10} -liver values for 50%- and 30%-duty cycles were 9.4% and 12.8% of those for 100%-duty cycle, respectively. Maximum doses (cord/oesophagus) for 50%- and 30%-duty cycles also decreased 17.2%/19.3% and 24.6%/29.8% to those for 100%-duty cycle, respectively. Total imaging doses increased 43.5% and 115.8% for 50%- and 30%-duty cycles to that for the 100%-duty cycle.

Conclusion: When normal tissue doses are below the tolerance level, the gating window should be expanded to minimize imaging dose and treatment time.

Advances in knowledge: The skin dose from imaging might not be counterbalanced to the OAR dose; however, imaging dose is a particularly important factor.

INTRODUCTION

Our facility introduced carbon-ion pencil-beam scanning (C-PBS) treatment without respiratory gating in the second quarter of 2011 and as of 2015 has treated over 800 patients. Scanning beam treatment and intensity-modulated radiotherapy could have caused the presence of hot/cold spots within the target, which arise due to inconsistency between beam motion and target motion (interplay effect).¹⁻⁵ Several approaches to minimize the interplay effect have been introduced elsewhere.^{1-3,6-8} Using three techniques (gating,⁹ phase-control² and rescanning³), we began clinical trial of the thoracoabdominal area with carbon-ion pencil-beam scanning and amplitude-based gating using radiographic fluoroscopic imaging system in the first quarter of 2015.¹⁰

One general solution to improving dose conformity to a moving target is to use a small gating window to minimize the magnitude of tumour displacement during

irradiation, especially in scanning irradiation.¹ However, the use of a small gating window will still often result in treatment time being longer than with a larger gating window, because a small gating window could increase the probability that the tumour is positioned out of the gating window region. Also, the tumour out of the gating window due to respiratory pattern variation will increase treatment time even when the tumour is located within the gating window at the start of treatment.

Moreover, when respiratory gating is performed using a radiographic fluoroscopic imaging system, which is now commercially available (CyberKnife® Robotic Radiosurgery System; Accuray, Inc., Sunnyvale, CA; and SyncTraX®; Shimadzu, Kyoto, Japan), the longer treatment time increases imaging dose. Our group previously reported that phase-controlled rescanning (PCR) improved dose conformation to a moving target even when tumour

Table 1. Patient characteristics and centre of mass for clinical target volume (CTV) displacement

No.	Location		Prescribed dose [Gy (RBE)]	No. fraction	Respiratory cycle 4DCT (s)	Centre of mass for CTV displacement in 4DCT (mm)				CTV volume (cm ³)	Actual treatment gating window
						T00–T90	T20–T80	T30–T70	T40–T60		
1	Lung	Right S1	48.0	4	3.8	1.8	1.5	0.3	0.1	15.3	T30–T70
2	Lung	Right S9	57.6	12	4.0	10.7	10.7	9.2	4.1	115.7	T30–T60
3	Lung	Right S1	60.0	4	3.5	1.0	1.0	1.0	0.4	34.9	T30–T70
4	Lung	Left S9	60.0	4	4.1	21.4	10.7	5.3	0.8	5.6	T30–T70
5	Lung	Left S10	60.0	4	3.7	7.1	5.4	3.5	1.3	6.4	T30–T70
6	Liver	S3	48.0	2	4.1	6.9	4.9	2.9	0.7	27.2	T30–T70
7	Liver	S8	48.0	4	2.2	16.5	12.9	9.7	4.3	211.7	T30–T60
8	Liver	S7–S8	64.8	12	3.3	3.1	1.8	0.8	0.1	453.3	T30–T70
9	Liver	S8	48.0	2	4.9	6.3	4.7	2.3	0.5	121.3	T30–T60
10	Liver	S7	60.0	4	3.4	19.6	14.8	10.2	3.4	59.2	T30–T60

4DCT, four-dimensional CT; RBE, relative biological effectiveness.

displacement was large.¹ The actual treatment (clinical trial) selected an approximate 50% gating (from mid-inhalation to mid-exhalation), albeit that the gating window should be considered with regard to both the dose to organs at risk (OARs) and the fluoroscopic imaging dose.

In this study, we aimed to analyze the size of the gating window for individual patients by evaluating dose assessment and fluoroscopic imaging dose with various gating window sizes by reusing the actual treatment data, retrospectively.

METHODS AND MATERIALS

Patient and image acquisition

We enrolled 10 subjects (mean age 67.7 ± 7.9 years) selected from among inpatient participants in the clinical trials of C-PBS treatment at our hospital, 5 each with lung or hepatocellular carcinoma. All patients consented to participate, and the study was approved by the institutional review board of our institution. Patient characteristics are summarized in Table 1.

Treatment planning CT was performed under free-breathing conditions using a 320 multislice CT (Aquilion One™ Vision®; Toshiba Medical Systems, Otawara, Japan). All patients were immobilized on the treatment couch with a shell device (Shellfitter®; Keraray Co., Ltd., Osaka, Japan) and water-hardening urethane resin (Moldcare®; Alcare, Tokyo, Japan).

Respiration was monitored during four-dimensional (4D) CT (AZ-733V®; Anzai Medical Co., Tokyo, Japan). The 4DCT data sets were subdivided into 10 phases (T00 = peak inhalation, T50 = peak exhalation).

The respiratory pattern of patients often varies in clinical situations due to intra-/interfractional changes, and it is questionable whether tumour position remains the same, even in exhalation. We therefore used the amplitude-base gating technique with markerless tumour tracking using radiographic fluoroscopic unit to directly detect tumour position.^{11–13} This method allows targeting of the treatment beam to the absolute tumour position as defined in treatment planning using 4DCT, in contrast to phase-based gating, in which the beam is generally on at exhalation even though the respiratory phase is different.⁹ The gating window was defined as positions not respiratory phase to cover intrafractionally tumour displacement on the 4DCT. The gating window of T00–T90 in the amplitude-based gating, therefore, was not ungated treatment. In this study, we used the expression of Tn, which is defined as absolute tumour position acquired in 4DCT imaging. To achieve this, the tumour position was captured in real time using two radiographic fluoroscopic units.¹⁴ Fluoroscopic imaging was performed during treatment. Dynamic flat-panel detectors (PaxScan® 3030+; Varian Medical Systems, Palo Alto, CA) are installed on both sides of the vertical irradiation port, whereas the corresponding X-ray tubes are installed under the floor. The room isocentre and source–image

Table 2. Dose assessment metrics averaged over all patients for lung and liver treatment

Dose assessment metrics		Gating window				
		T00–T90 (absolute value)	T20–T80 (ratio)	T30–T70 (ratio)	T40–T60 (ratio)	T50 (ratio)
Mean $\pm$ SD (lung)	D_{95} –CTV	99.4 ± 0.1	1.00 ± 2.07	1.00 ± 1.32	1.00 ± 2.07	1.00 ± 1.11
	V_{20} –lung	8.7 ± 5.6	1.00 ± 1.01	0.97 ± 1.00	0.94 ± 0.99	0.94 ± 1.00
	$D_{\max}$ –cord	12.9 ± 6.8	0.95 ± 1.02	0.94 ± 1.06	0.93 ± 1.06	0.91 ± 1.03
	$D_{\max}$ –oesophagus	9.1 ± 7.9	0.96 ± 0.96	0.94 ± 0.95	0.93 ± 0.94	0.90 ± 0.91
Max–min (lung)	D_{95} –CTV	99.5–99.3	1.00–1.00	1.00–1.00	1.00–1.00	1.00–1.00
	V_{20} –lung	17.3–3.6	1.00–1.00	0.98–0.89	0.95–0.78	0.95–0.78
	$D_{\max}$ –cord	17.2–1.6	1.00–1.00	1.00–0.25	1.00–0.25	1.00–0.25
	$D_{\max}$ –oesophagus	13.6–0.0	1.00–1.00	1.00–1.00	1.00–1.00	1.00–1.00
Mean $\pm$ SD (liver)	D_{95} –CTV	98.8 ± 0.6	1.00 ± 0.77	1.00 ± 0.78	1.00 ± 0.78	1.00 ± 0.76
	V_{10} –liver	36.9 ± 17.8	0.96 ± 0.95	0.91 ± 0.92	0.87 ± 0.88	0.86 ± 0.88
	$D_{\max}$ –cord	10.7 ± 14.9	0.92 ± 0.93	0.83 ± 0.84	0.75 ± 0.78	0.72 ± 0.76
	$D_{\max}$ –oesophagus	6.1 ± 8.5	0.89 ± 0.89	0.81 ± 0.81	0.70 ± 0.70	0.61 ± 0.60
Max–min (liver)	D_{95} –CTV	99.4–97.8	1.00–1.00	1.00–1.00	1.00–1.00	1.00–1.00
	V_{10} –liver	56.1–10.0	0.94–0.93	0.89–0.86	0.85–0.83	0.84–0.82
	$D_{\max}$ –cord	30.4–0.0	0.95–1.00	0.88–1.00	0.83–1.00	0.83–1.00
	$D_{\max}$ –oesophagus	17.6–0.0	0.91–1.00	0.82–1.00	0.70–1.00	0.57–1.00

CTV, clinical target volume; GW, gating window; max, maximum; min, minimum; SD, standard deviation.

Results for the GW(T00–T90) are expressed by the absolute values; however, those for other gating windows are expressed by the ratio to the those for the GW(T00–T90).

Figure 1. Accumulated carbon-ion beam dose distributions for a liver case (Patient 8) with the gating windows of (a) T00–T90, (b) T30–T70 and (c) T50, and (d) dose differences (T00–T90 minus T50) and (e) dose differences (T30–T70 minus T50). The inner yellow line shows the clinical target volume (CTV). (f) Dose-volume histogram with respective gating windows.

receptor distance are 170 and 240 cm, respectively. Fluoroscopy imaging conditions are a tube voltage of 100 kV, tube current of 20–80 mA, exposure time of 4 ms per frame and 15 frames per second (fps).

EVALUATION METHODOLOGY

The following two metrics were evaluated with various gating windows.

Dose assessment

Certified radiation oncologists delineated the gross tumour volume (GTV) manually on the 4DCT at the reference phase (T50). GTV contours at other phases were warped by applying B-spline-based deformable image registration (DIR).¹⁵ Radiation oncologists and medical physicists checked the GTV contours at respective phases, and if necessary, modified the contours manually. The clinical target volume (CTV) was calculated by adding a uniform 6-mm margin for lung case and 10-mm margin for liver case (except Patient 7) to the GTV. To compensate for intrafractional range variation, we defined the range-adapted internal target volume (range-ITV) using 4DCT within the gating window.¹⁶ We then calculated the planning target volume (PTV) by adding a setup margin of 2-mm water-equivalent pathlength to the range-ITV.

The treatment beam was delivered using C-PBS with eight times the isoenergy-layered PCR.² The isoenergy layer was changed by synchrotron energy (30-mm range step) and multiple range

shifters to achieve 3-mm range steps.¹⁷ Beam spots were optimized using the relative biological effectiveness (RBE)-weighted absorbed dose.¹⁸ A single uniform field optimization was selected. We did not consider the interplay effect because our previous study reported that PCR four or more times improves dose conformation to a moving target.^{1,9} Accumulated dose distribution was calculated by registering the dose distribution in the gating window to that in the reference phase using DIR. This is a different situation from DIR for contouring, because nobody knows the correct answer for the accumulated dose, therefore oncologists cannot modify it. Also, since DIR-related dose calculation can have a significant impact on treatment accuracy, DIR accuracy was quantified (Appendix A). If DIR accuracy was >2 mm (Euclidian distance), we changed DIR parameters until the accuracy was <2 mm. By doing this, the accuracy of the accumulated dose calculation was improved without manual modifications. These processes were performed by our in-house software.¹⁹

Prescribed doses delivered to the PTV were 48–60 Gy (RBE) via two or four different beam ports from the ipsilateral rather than the contralateral side of the tumour for lung cases, and 48.0–64.8 Gy (RBE) from 0° and 90° or 270° for liver cases. The details are summarized in Table 1.

We evaluated the dose assessments using the following metrics: the lowest dose encompassing 95% of the CTV (D_{95}), the maximum dose (D_{max}) for the cord and oesophagus, and the volume of the

Table 3. Treatment time per fraction, beam efficiency per fraction and total imaging dose averaged over all patients for respective gating windows

Dose assessment metrics		Gating window				
		T00–T90 (absolute value)	T20–T80 (ratio)	T30–T70 (ratio)	T40–T60 (ratio)	T50 (ratio)
Mean $\pm$ SD (lung)	Treatment time/ fr (s)	99.1 $\pm$ 51.9	1.07 $\pm$ 0.93	1.21 $\pm$ 0.77	1.52 $\pm$ 0.97	2.14 $\pm$ 1.74
	Beam efficiency (%)	64.4 $\pm$ 20.2	0.89 $\pm$ 0.71	0.77 $\pm$ 0.81	0.57 $\pm$ 0.60	0.43 $\pm$ 0.52
	Total imaging dose (mGy)	49.2 $\pm$ 50.6	1.05 $\pm$ 1.03	1.14 $\pm$ 1.06	1.38 $\pm$ 1.24	1.96 $\pm$ 1.92
Max–min (lung)	Treatment time/ fr (s)	175.3–54.5	1.00–1.04	1.00–1.34	1.09–1.19	1.76–1.39
	Beam efficiency (%)	89.1–37.8	0.87–1.00	0.86–1.00	0.56–0.45	0.42–0.28
	Total imaging dose (mGy)	128.7–10.9	1.05–1.04	1.12–1.34	1.35–1.19	2.07–1.39
Mean $\pm$ SD (liver)	Treatment time/ fr (s)	158.3 $\pm$ 88.2	1.14 $\pm$ 1.06	1.67 $\pm$ 1.98	2.58 $\pm$ 2.75	3.64 $\pm$ 3.03
	Beam efficiency (%)	61.8 $\pm$ 18.3	0.88 $\pm$ 0.88	0.65 $\pm$ 0.88	0.40 $\pm$ 0.55	0.25 $\pm$ 0.19
	Total imaging dose (mGy)	123.0 $\pm$ 140.9	1.09 $\pm$ 1.03	1.55 $\pm$ 1.53	2.47 $\pm$ 2.31	3.21 $\pm$ 2.68
Max–min (Liver)	Treatment time/ fr (s)	307.9–86.8	1.07–1.00	1.79–1.22	2.67–2.54	3.22–3.21
	Beam efficiency (%)	91.1–41.3	0.88–0.94	0.71–0.56	0.46–0.37	0.22–0.30
	Total imaging dose (mGy)	368.1–20.4	0.22–1.90	1.52–1.40	2.33–2.16	2.74–5.49
Mean $\pm$ SD (all)	Treatment time/ fr (s)	128.7 $\pm$ 75.0	1.11 $\pm$ 1.07	1.49 $\pm$ 1.89	2.17 $\pm$ 2.85	3.06 $\pm$ 3.59
	Beam efficiency (%)	63.1 $\pm$ 18.2	0.88 $\pm$ 0.80	0.71 $\pm$ 0.88	0.49 $\pm$ 0.67	0.34 $\pm$ 0.54
	Total imaging dose (mGy)	86.1 $\pm$ 107.1	1.08 $\pm$ 1.04	1.43 $\pm$ 1.53	2.16 $\pm$ 2.37	2.86 $\pm$ 2.84
Max–min (all)	Treatment time/ fr (s)	307.9–54.5	1.07–1.04	1.79–1.34	2.67–1.19	3.22–1.39
	Beam efficiency (%)	91.1–37.8	0.88–1.00	0.85–0.61	0.55–0.41	0.41–0.28

fr, fraction; GW, gating window; max, maximum; min, minimum; SD, standard deviation.

Results for the GW(T00–T90) were expressed by the absolute values, however, those for other gating windows were expressed by the ratio to the those for the GW(T00–T90).

target irradiated with $>n$ Gy (RBE) (V_n) for the lung and liver. The International Commission on Radiation Units and Measurements suggested to report $D_{2\%}$ instead of $D_{\max}$ ²⁰ because $D_{\max}$ is the maximum dose even though it represents a single voxel, and it could be affected by statistical errors. However, the reason for use of $D_{\max}$ in this study is that these metrics were defined in our treatment protocol, and this study compared dose metrics under the same conditions except the gating window.

Treatment time and imaging dose

Fluoroscopic imaging dose from two oblique directions was estimated at the skin surface by using air kerma, which was measured at the isocentre position from two different angles. Because fluoroscopic imaging was performed using pulse X-ray exposure (=4 ms), we measured accumulated air kerma for several hundred pulses and divided them by the number of

X-ray pulses. By doing this, air kerma per image for both directions was calculated (= approximately 0.1 mGy/image for both directions). The imaging dose was calculated by the number of images multiplied by the air kerma per image. Necessary beam-on time was calculated from the treatment log file. Fluoroscopic images were obtained during actual treatment and were reused in this study. The number of images counted until a beam-on time was reached was retrospectively compared with the necessary beam-on time by the markerless tumour-tracking software. When the actual number of images exceeded the original number of images, the fluoroscopic images were repeated from the first image. We calculated the total imaging dose by summing up imaging doses at respective treatment fractions. The beam efficiency was defined by the ratio of the treatment beam “on” time to the total treatment time.

The tracking software, which is based on template-matching and machine-learning algorithms, also calculated the treatment time in the respective gating windows retrospectively.¹⁰ Because the total treatment time was strongly affected by the number of fractions throughout the treatment course, the treatment time per fraction was evaluated.

RESULTS

Dose assessment

Dose assessment metrics averaged over all patients are summarized in Table 2. For patients with lung cancer, sufficient dose conformation to the CTV was achieved ($D_{95\text{-CTV}} > 99\%$ of the prescribed dose) and independently of the gating window. The OAR doses ($V_{20\text{-lung}}$, $D_{\text{max-cord}}$ and $D_{\text{max-oesophagus}}$ values) were slightly decreased approximately 5.9% and 7.4% by shortening the gating window for GW(T20–T80) and GW(T40–T60), respectively.

When the dose assessment metrics were averaged over patients with liver cancer, the $D_{95\text{-CTV}}$ value was $98.8 \pm 0.6\%$ of the prescribed dose for GW(T00–T90) and almost the same for the respective gating windows (Table 2). Compared with liver- V_{10} value for GW(T00–T90), these values were decreased approximately 4.4%, 9.4% and 12.8% by shortening the gating window for GW(T20–T80), GW(T30–T70) and GW(T40–T60), respectively. Moreover, D_{max} values for cord and oesophagus for GW(T40–T60) were also decreased 24.6% and 29.8%, respectively. Because these values were averaged out over a number of patients, gating window dependency was small; however, some cases did show more substantial gating window dependency (Appendix B).

Accumulated dose distributions and dose–volume histograms for a liver case (Patient 8) are shown in Figure 1. The intra-fractional diaphragm displacement in 4DCT imaging was over 8 mm; however, the centre of mass for CTV was a small displacement due to 4DCT artefact. Sufficient prescribed dose was given to the CTV for respective gating windows ($D_{95\text{-CTV}} > 97\%$ of the prescribed dose), and hot and cold spots within the CTV did not occur. To better understand the dose distribution differences for the respective gating windows, we calculated dose differences for the gating windows of T00–T90 and T30–T70 minus T40–T60 (Figure 1d,e). The small gating window reduced the liver dose outside of the CTV, $V_{10\text{-liver}}$ value was minimized approximately 20% for GW(T40–T60) (Figure 1d,e). In this case, no excessive dose to the oesophagus was observed [$D_{\text{max-oesophagus}}$ was 0 Gy (RBE)]. The respective lung and liver cases are described in the Appendix B (Figure A1).

Treatment time and imaging dose

Treatment time, beam efficiency and total imaging dose averaged over all patients are summarized in Table 3. Because tumour position was always out of GW(T40–T60) and GW(T50) for two patients with lung cancer (the first fraction for Patient 4 and fourth fraction for Patient 5) and out of T50 for a liver patient (the seventh and eighth fractions for Patient 10) due to inter-fractional positional variation, the treatment time and imaging dose could not be calculated.

The treatment time per fraction averaged over all patients was 128.7 s for GW(T00–T90), these were increased 11.1% [GW(T20–T80)], 49.5% [GW(T30–T70)] and 117.4% [GW

Figure 2. Tumour position (superior-inferior direction) measured by markerless tumour-tracking software at the (a) first and (b) seventh treatment fractions (Patient 8). The horizontal bands are the treatment beam irradiation positions (=gating window).

(T40–T60)] times longer than that for GW(T00–T90). The treatment time for the liver cases was approximately 1.6 times longer than that for the lung cases at the large GW(T00–T90) and GW(T20–T80) vs approximately 2.7 times longer at the small GW(T40–T60) and GW(T50). This is because the interfractional tumour positional variation reduced the probability that the tumour would be located inside the irradiation region defined by the treatment planning and because the target volume for the liver cases was larger than that for lung cases.

Although beam efficiency for liver cases was almost the same as that for lung cases at the large gating window [ratio (liver/lung) = 0.95 for GW(T00–T90) and GW(T20–T80)], beam efficiency for the liver cases was decreased with shortening of the gating window, with ratios (liver/lung) = 0.81 for GW(T30–T70), 0.68 for GW(T40–T60) and 0.56 for GW(T50). Compared with the imaging dose for GW(T00–T90), these were increased 8.2%, 43.5% and 115.8% for GW(T20–T80), GW(T30–T70) and GW(T40–T60), respectively.

Tumour positions measured by fluoroscopic images at the first and seventh treatment fractions are shown in Figure 2 (Patient 8). Since tumour position at the first treatment fraction was interfractionally shifted to the inferior direction from that at the planning CT position, tumour position at inhale was located within GW(T50) (Figure 2a). Beam efficiency was therefore closely similar for respective gating windows. However, because the tumour position at the seventh treatment fraction was shifted slightly in the inferior direction relative to the first treatment fraction (Figure 2b), the tumour position was located within the gating window except for exhale, and the beam efficiency was decreased as the gating window shortened [the ratios to GW(T00–T90) were 0.53 and 0.40 for GW(T30–T70) and GW(T40–T60), respectively]. This case had the longest treatment time because the target volume was the largest ($=720\text{ cm}^3$). The total imaging doses in GW(T40–T60) ($=859.0\text{ mGy}$) and GW(T50) ($=1009.1\text{ mGy}$) were 2.3 and 2.7 times higher than that in GW(T00–T90) ($=368.1\text{ mGy}$). The results for the respective patients averaged over all fractions are summarized in the Appendix B (Figure A2).

DISCUSSION

In this study, we evaluated dose assessment, treatment time and imaging dose in radiographic fluoroscopic imaging and determined optimum gating windows for individual patients by reusing the accrual treatment data retrospectively. Our results show that doses to OARs were decreased as the gating window was shortened but that treatment time and imaging dose were increased. The skin dose from imaging might not be counterbalanced to the OAR dose; however, imaging dose is a particularly important factor because it can increase radiation damage to the patient directly. Longer treatment times are uncomfortable for the patient and limit the number of patients who can be treated.

In most cases, treatment time and imaging dose showed large changes between GW(T40–T60) and GW(T30–T70), followed by small changes between [GW(T30–T70) and GW(T00–T90)]. This is explained as follows. The magnitude of intrafractional tumour displacement was larger at both mid-inhale and mid-

exhale than at other phases. 4DCT images at T30 and T70 therefore include relative larger tumour displacement. As a result, the PTV size increased from GW(T40–T60) to GW(T30–T70).

Although evaluation metrics were dependent on patient characteristics, in some cases the metrics above were closely similar in respective gating windows. When OAR doses were less than the tolerance level or showed small variation in the respective gating windows, imaging dose could be reduced by extending the gating window. An example of this is Patient 8, in whom $D_{\text{max-cord}}$ and $V_{10\text{-liver}}$ values were approximately 25 Gy (RBE) and 38% at GW(T40–T60), respectively. These values increased with increasing gating window over T40–T60. The total imaging dose for GW(T40–T60) was close to 900 mGy, which is unacceptable from a radiation protection point of view. The imaging dose was minimized to 559.6 mGy for GW(T30–T70), when a $V_{10\text{-liver}}$ value of 40.8% at GW(T30–T70) was clinically acceptable. Other cases are summarized in Appendix B.

The use of amplitude-based gating allows the treatment beam to be targeted to the tumour position as defined in treatment planning even though the respiratory pattern varies during treatment. However, this gating method cannot fully cover interfractional positional change. A small gating window might not capture the tumour inside the irradiation region due to interfractional changes between planning CT and treatment. We observed three cases (Patients 4, 5 and 10) in which the beam was not always “on” at certain treatment fractions for GW(T50). Even in this situation, the patient should not be shifted to superimpose the tumour position onto the irradiation location because the particle beam is strongly affected by tissue density variations, especially bone, therefore the beam range from the patient surface to the tumour might change, resulting in incorrect delivery of the beam to the tumour. One solution to compensate for interfractional tumour positional change is to expand the gating window.

In this study, we used constant imaging frame rate ($=15\text{ fps}$) and did not optimize it for respective patients because the respiratory pattern was varied during treatment, and it is hard to optimize before treatment. However, our imaging system has been integrated to the dose reduction function by changing high frame rate when tumour moved close to the gating window.

We quantified the evaluation metrics at GW(T50) as a baseline, however, the gating window of T50 was not preferred in actual treatment. This is because beam-on time was so short, and because when the gating window was selected for T50 only, the range-ITV was equal to the CTV. This is a similar situation to treatment planning without the use of range-ITV.

Finally, our treatment protocol used hypofractionation for lung and liver treatments. Although this might affect on dose distribution due to the interplay effect, which often results into underdosage and overdosage, we did not consider the interplay effect. This is because we have found that adequate frequency PCR preserves dose distribution even though it was hypofractionated treatment.^{1,21}

CONCLUSION

This study evaluated dose assessment and fluoroscopic imaging dose in various gating windows. Minimizing gating windows reduced OAR doses; V_{20} -lung/ V_{10} -liver values were 0.0%/4.4% for GW(T20–T80), 2.5%/9.4% for GW(T30–T70) and 6.0%/12.8% for GW(T40–T60). Imaging doses were increased 8.2%, 43.5% and 115.8% for GW(T20–T80), GW(T30–T70) and GW(T40–T60), respectively. However, our results showed that when OAR doses are less than the tolerance

level, the gating window should be expanded to cover inter-fractional tumour positional changes and minimize imaging dose and treatment time. Fluoroscopic gating systems will be widely adopted if the major barrier of imaging dose is overcome.

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APPENDIX A

DEFORMABLE IMAGE REGISTRATION
ACCURACY ASSESSMENT

A point-landmark matching is one of the image registration accuracy assessments to obtain quantitative results. However, it is time consuming and not practical in clinical routine procedure. We quantified the DIR accuracy from the CT image at exhale to that at inhale as follows:

DIR software calculated deformable vector field (DVF) using CT images at exhale and inhale.

$$\text{DVF} : \Omega_{\text{exhale}} \rightarrow \Omega_{\text{inhale}} \quad (\text{A1})$$

where Ω_{exhale} and Ω_{inhale} are discrete domains of CT images at exhale and inhale.

A warped CT image at inhale is derived by applying DVF to the CT image at exhale. However, the DIR cannot remove registration error completely using patient images.

$$x_{\text{inhale}} \neq \text{DVF}(x_{\text{exhale}}) \quad (\text{A2})$$

Figure A1. The ratios of the dose assessment metrics as a function of gating window to those at the gating window of T00-T90. (a) D_{95} -clinical target volume (CTV), (c) V_{20} -lung and (e) D_{max} -cord for a lung case. (b) D_{95} -CTV, (d) V_{10} -liver and (f) D_{max} -cord for a liver case. No doses were irradiated to the cord for the Patients 2, 6, 7 and 9. Pt.no., patient number.

Figure A2. Ratios of (a), (b) the treatment time per fraction; (c), (d) the beam efficiency; and (d), (e) the imaging dose throughout the treatment course to those at the gating window GW(T00-T90). Tumour position was always out of the planning target volume region at the first (Patient 4) and fourth (Patient 5) treatment fractions for GW(T40-T60) and GW(T50), and the seventh/eighth (Patient 10) treatment fractions for GW(T50). Pt.no., patient number.

where x_{exhale} and x_{inhale} are position vectors on CT images at exhale and inhale, respectively.

We calculated another DVF (DVF') by using the warped CT image and CT image at inhale.

$$\text{DVF}' : \Omega_{\text{exhale}}^{\text{DVF}} \rightarrow \Omega_{\text{inhale}} \quad (\text{A3})$$

Then DVF' is applied to the warped CT at exhale.

$$x'_{\text{exhale}} = \text{DVF}'[\text{DVF}(x_{\text{exhale}})] \quad (\text{A4})$$

DIR accuracy is quantitatively analyzed by the following calculation:

$$\|\text{DVF}'(x_{\text{exhale}}) - x_{\text{inhale}}\|_2 \quad (\text{A5})$$

where $\|\cdot\|$ represents a norm.

To understand the DIR accuracy, we visualized the norm in colour map overlaid to CT image. As an example of this, we showed DIR error map in Figure A3.

Figure A3. The main screen of our in-house software. The upper panel shows accumulated carbon-ion beam dose distribution overlaid on the CT image at the reference phase (Patient 8). The lower panel shows deformable image registration (DIR) error (magnitude of the deformed vector field) colour map between CT images at exhale and mid-inhale overlaid on the CT image at mid-inhale. Red, green and blue colours are the DIR error of 2, 1 and 0 mm, respectively.

APPENDIX B

RESULTS FOR INDIVIDUAL PATIENTS

In this section, we summarize the results for dose assessment (Figure A1) and treatment time, beam efficiency and total imaging dose (Figure A2) for individual patients. To clearly understand the gating window dependency, these results were expressed by the ratios to those at GW(T00–T90). By doing this, the ratios of the treatment time, total treatment time, total imaging dose and imaging dose per fraction were the same values, because the imaging dose was in proportion to the treatment time. And the ratio of the beam efficiency was approximately calculated by a reciprocal number of the ratio of the treatment time or imaging dose.

Lung cases

For the first lung case, dose conformation to the CTV was sufficiently prescribed ($=99.3\%$), and the V_{20} -lung value was 8.3% and $D_{\max}$ -cord value was 11.2 Gy (RBE) at GW(T00–T90). The metrics of both D_{95} -CTV and V_{20} -lung were independent of the gating window; however, $D_{\max}$ -cord values were slightly decreased to the ratio of 0.86 by shortening of the gating window to GW(T40–T60). Because the magnitude of tumour motion was small (Table 1), the treatment time per fraction, beam efficiency and total imaging dose for GW(T00–T90) were 175.3 s, 37.8% and 70.1 mGy for all gating windows, respectively. Therefore, GW(T00–T90) was acceptable in this case.

The second lung case showed good dose conformation (D_{95} -CTV $>99\%$ for respective gating windows). V_{20} -lung was

17.3% for GW(T00–T90), it slightly decreased to the ratio of 0.95 for GW(T40–T60). $D_{\max}$ -cord [$=17.2$ Gy (RBE)] and $D_{\max}$ -oesophagus [$=13.6$ Gy (RBE)] were almost the same in the respective gating windows. With regard to the treatment time per fraction, beam efficiency and total imaging dose were 126.9 s, 57.1% and 128.7 mGy for GW(T00–T90), respectively. The treatment time and the total imaging dose were increased to the ratio of 1.35 for GW(T40–T60) and 2.09 for GW(T50). Beam efficiency was decreased to the ratio of 0.74 for GW(T40–T60) and 0.48 for GW(T50). Since dose assessment results in this case were not affected by the gating window, a large gating window such as GW(T00–T90) was preferred.

For the third lung case (Patient 3), total imaging dose and treatment time per fraction for GW(T00–T90) were 25.1 mGy and 83.8 s, respectively. Those longer than GW(T30–T70) showed a small change, but thereafter increased to the ratio of 1.79 for GW(T40–T60) and to the ratio of 2.77 for GW(T50). Although OAR doses were decreased by gradually decreasing GW (the ratios of 0.97 , 0.91 and 0.85 for V_{20} -lung, $D_{\max}$ -cord and $D_{\max}$ -oesophagus, respectively), all were at clinically acceptable levels [V_{20} -lung $=10.5\%$, $D_{\max}$ -cord $=17.2$ Gy (RBE), $D_{\max}$ -oesophagus $=13.6$ Gy (RBE) for GW(T00–T90)]. D_{95} -CTV value was 99.3% for all gating windows. A window larger than GW(T30–T70) was preferred in this case.

For Patient 4, the total imaging dose was 10.9 mGy for GW(T00–T90), and it was sharply increased to the ratio of 2.09 and 3.50 for GW(T30–T70) and GW(T40–T60), respectively. The beam efficiency for GW(T40–T60) was significantly decreased to

the ratio of 0.21 from that for GW(T00–T90) (=79.2%). Dose to the oesophagus was not excessive. $D_{\max}$ -cord and V_{20} -lung were small [1.6 Gy (RBE) and 3.6% for GW(T00–T90), respectively]; these values were decreased to the ratio of 0.78 and 0.25 for V_{20} -lung and $D_{\max}$ -cord, respectively. Since imaging dose is the priority metric, GW(T00–T90) could be selected.

For Patient 5, dose assessment metrics for D_{95} -CTV and $D_{\max}$ -cord values were not dependent on the gating window [D_{95} -CTV = 99.3% and $D_{\max}$ -cord = 17.2 Gy (RBE)]. The V_{20} -lung value was decreased to the ratio of 0.85 for GW(T40–T60) from that for GW(T00–T90) (=3.5%). $D_{\max}$ -oesophagus value was 0 Gy (RBE) for all gating windows.

Total imaging dose [=11.0 mGy for GW(T00–T90)] and treatment time [=54.9 s/fr for GW(T00–T90)] were also slightly increased to the ratio of 1.18 for GW(T40–T60). Beam efficiency [=58.8% for GW(T00–T90)] was decreased to the ratio of 0.63 for GW(T40–T60). A long gating window was preferred in this case.

Liver cases

With regard to the first liver case (Patient 6), dose to the cord was zero and V_{10} -liver value was 10.0% for GW(T00–T90), and these were decreased to the ratio of 0.83 and 0.82 for GW(T40–T60) and GW(T50), respectively. The treatment time per fraction and total imaging dose for GW(T00–T90) were 86.8 s and 69.4 mGy, respectively. The ratios of the treatment time and total imaging dose were increased to 2.78 and 3.21 for GW(T40–T60) and GW(T50), respectively. Beam efficiency for GW(T00–T90) (=57.6%) was decreased to the ratio of 0.36 and 0.31 for GW(T40–T60) and GW(T50), respectively. A gating window of T00–T90 was clinical acceptable.

For Patient 7, $D_{\max}$ -cord values for respective gating windows were zero. By increasing the gating window from T40–T60 to T30–T70, the ratios of the total imaging doses were minimized from 2.81 (=308.0 mGy) to 1.82 (=199.0 mGy). The beam efficiency for GW(T00–T90) was 41.3%, and the ratios of them

were significantly decreased to 0.36 and 0.22 for GW(T40–T60) and GW(R50), respectively. However, the tumour size was so large in this case that the ratio of the V_{10} -liver value was 0.84 (=47.3%), even though the gating window was T50 only. Moreover, the ratio of V_{10} -liver values for GW(T40–T60) (=0.85) did not substantially differ from that for GW(T50) (=0.84). To maintain liver function, we preferred GW(T40–T60) over GW(T30–T70).

Details for Patient 8 are provided in the Discussion section.

For Patient 9, dose to the cord were not excessive [$D_{\max}$ = 0 Gy (RBE)]. The ratios of V_{10} -liver values were slightly decreased to 0.84 and 0.82 for GW(T40–T60) and GW(T50), respectively. However, these differences in absolute value showed small variation from GW(T50) (=24.3%) to GW(T30–T70) (=26.2%) but reached almost 30% for GW(T20–T80) and GW(T00–T90). Moreover, the ratio of the total imaging dose showed small variation (=1.25) between GW(T20–T80) and GW(T00–T90) (=47.4 mGy). GW(T30–T70) was therefore a suitable trade-off between treatment planning dose assessment and imaging dose.

For the last liver case (Patient 10), the total imaging dose and the treatment time for GW(T00–T90) were 20.4 mGy and 101.8 s/fr, respectively. These values increased significantly for GW(T40–T60) (=2.16) rather than for GW(T30–T70) (=1.40). The beam efficiency for GW(T00–T90) was 91.1%. These for GW(T20–T80) and GW(T30–T70) were slightly differences, however, those for GW(T40–T60) were significantly decreased from that for GW(T30–T70).

V_{10} -liver value was markedly high (=41.5%) and independent of the gating window. $D_{\max}$ -cord values increased linearly with expansion of the gating window; the ratio of 0.66 and 0.57 for GW(T40–T60) and GW(T50), respectively, achieving 23.2 Gy (RBE) for GW(T00–T90). Since the number of treatment fractions was four, the cord dose should be minimized to <20 Gy (RBE). The preferred gating window was T30–T70.