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ORIGINAL ARTICLE

Factors affecting the accuracy of respiratory tracking of the image-guided robotic radiosurgery system

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Abstract

Purpose To analyze the factors affecting the tracking accuracy of the CyberKnife Synchrony Respiratory Tracking System (SRTS).

Materials and methods A dynamic motion phantom (motion phantom) reproduced the respiratory motions of each patient treated with the SRTS using a ball as the target. CyberKnife tracked the ball using the SRTS, and this process was recorded by a video camera mounted on the linear accelerator head. The tracking error was evaluated from the images captured by the video camera. Multiple regression analysis was used to identify factors affecting tracking accuracy from 91 cases.

Results The median tracking error was 1.9 mm (range 0.9–5.3 mm). Four factors affected the tracking accuracy: the average absolute amplitude of the tumor motion in the cranio-caudal (CC) direction ($p = 0.007$), average position gap due to the phase shift between the internal tumor and external marker positions in the CC direction ($p < 0.001$), and average velocity of the tumor in the CC ($p < 0.001$) and anterior–posterior directions ($p = 0.033$).

Conclusion We identified factors that affected tracking accuracy. This information may assist the identification of suitable margins that should be added to each patient's clinical target volume.

Keywords Stereotactic radiotherapy · Lung · Respiratory tracking · Accuracy · Margin

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Introduction

Stereotactic radiosurgery (SRS) or stereotactic radiotherapy (SRT) using multiple cross-fired radiation beams has enabled the delivery of high doses of radiation to a tumor while protecting critical surrounding structures from radiation injury. Initially, this technique was mainly utilized for intracranial lesions; however, it is now available to irradiate tumors that move with respiratory motion, such as lung tumors [1-5].

Precise treatment using external beam radiotherapy is challenging to achieve when irradiating tumors that move during respiration. Common strategies to compensate for respiratory motion include enlargement of the clinical target volume (CTV), reduction of motion by abdominal compression, breath-holding techniques, respiratory gating, and real-time tracking [6]. The CyberKnife Synchrony Respiratory Tracking System (SRTS, Accuracy Inc., Sunnyvale, CA, USA) has adopted a real-time tracking approach to motion management [7, 8]. Because the SRTS continuously synchronizes the beam delivery to tumor movement, patients can breathe normally during treatment and treatment margins can be reduced as a result of precise tracking.

The functions are based on the relationship between the internal tumor position (ITP) and the external marker position (EMP). ITPs are measured at multiple discrete time points using orthogonal X-ray images and EMPs are continuously monitored using optical light-emitting diodes. The SRTS estimates the ITP from the EMP using a correlation model and delivers beams to the moving tumor. Additionally, the SRTS uses the prediction model to compensate the time delay caused while adjusting the linear accelerator position [8-10]. A poor correlation between the ITP and EMP and/or irregular breathing patterns may have adverse effects on the precision of dose delivery because the SRTS utilizes both correlation and prediction models.

Several previous studies have demonstrated the tracking accuracy of the SRTS [9-18]. In addition, Sumida et al. [16] and Inoue et al. [17] showed that the tracking accuracy of the SRTS is patient-dependent. Thus, a suitable margin determined according to the tracking accuracy of each patient is necessary, as a poor margin increases the probability of tumor recurrence. In order to determine a suitable margin for each patient, factors that affect the tracking error should be identified. To our knowledge, there have been few reports that discuss these factors.

This study aimed to identify factors that affect the tracking accuracy of the SRTS, using multiple regression analysis. In addition, we assessed the tracking error caused by each factor that may be used as a reference when determining the appropriate margin for individual patients.

Materials and methods

Patient characteristics

We analyzed 91 lung cancer patients who were treated with the SRTS between March 2012 and May 2017 and for whom respiratory motion data from cine magnetic resonance (MR) images could be obtained. The median age of the patients was 76 years (range 44–89 years; 56 males, 35 females). All study participants provided informed consent and the institutional review board approved the study design.

Respiratory motion data

A cine MR scan was performed with a 1.5 Tesla (Magnetom Symphony Syngo, Siemens Medical Solutions, Munich, Germany) or 3 Tesla whole-body clinical MR scanner (Magnetom Skyra 3 T, Siemens Medical Solutions, Munich, Germany). A test tube containing a contrast agent was placed on the patient's abdomen as an external marker. The sagittal image was set to the plane that passed through the center of the tumor and test tube, and images were acquired every 0.2–0.3 s.

Respiratory motion data were collected from the cine MR images using a template matching method based on a zero mean normalized cross-correlation function. The position of the lung tumor in the cranio-caudal (CC) and antero-posterior (AP) directions and the motion of the test tube in the AP direction were yielded simultaneously from the cine MR images. To reduce noise, smoothing was applied to all respiratory motion data using a simple moving average, which was defined as the unweighted mean of two points. This method of collecting respiratory motion data has been described in a previous study [17]. The average length of the respiratory motion data was 259.0 s (range 157.3–430.7 s).

Tumor motion amplitude, velocity of the tumor, respiratory cycle, time lag due to the phase shift between ITP and EMP (phase shift), phase shift ratio, and position gap due to the phase shift between ITP and EMP (position gap) were measured in the breathing cycles of each patient using the respiratory motion data (Fig. 1). Figure 1b shows a sample breathing pattern. There were also cases where the EMP was earlier than the ITP. Tumor motion amplitude was defined as the tumor position from the beginning of the expiratory ITP of one breath to the beginning of the inspiratory ITP for the same breath. The velocity of the tumor was defined as the velocity of the intermediate position between the end-expiratory ITP and the beginning of the inspiratory ITP. Respiratory cycle was defined as the period from the beginning of the expiratory phase of one breath to the beginning of the expiratory phase for the next breath. Phase shift was defined as the period from the beginning of the expiratory internal tumor phase of one breath to the beginning of the expiratory external marker phase for the same breath. Phase shift ratio was defined by the following equation:

$$\text{Phase shift ratio} = \text{Phase shift} \div \text{Respiratory cycle}.$$

The position gap was defined as the positional difference between the peak of the tumor motion and that of the external marker motion at the beginning of expiration for a single breath.

Dynamic motion phantom

We used the CIRS Dynamic Thorax Phantom Model 008A (Computerized Imaging Reference Systems, Inc., Norfolk, VA) as a dynamic motion phantom (motion phantom). This motion phantom consists of two separate platforms, a target motion simulator and a body surface motion simulator that are independently controlled by the CIRS motion-control software. The motion phantom generates three-dimensional target motion and has a manufacturer-stated absolute position accuracy of 0.1 mm. The motion phantom was used to apply different waveforms to CC, AP, and left–right (LR)

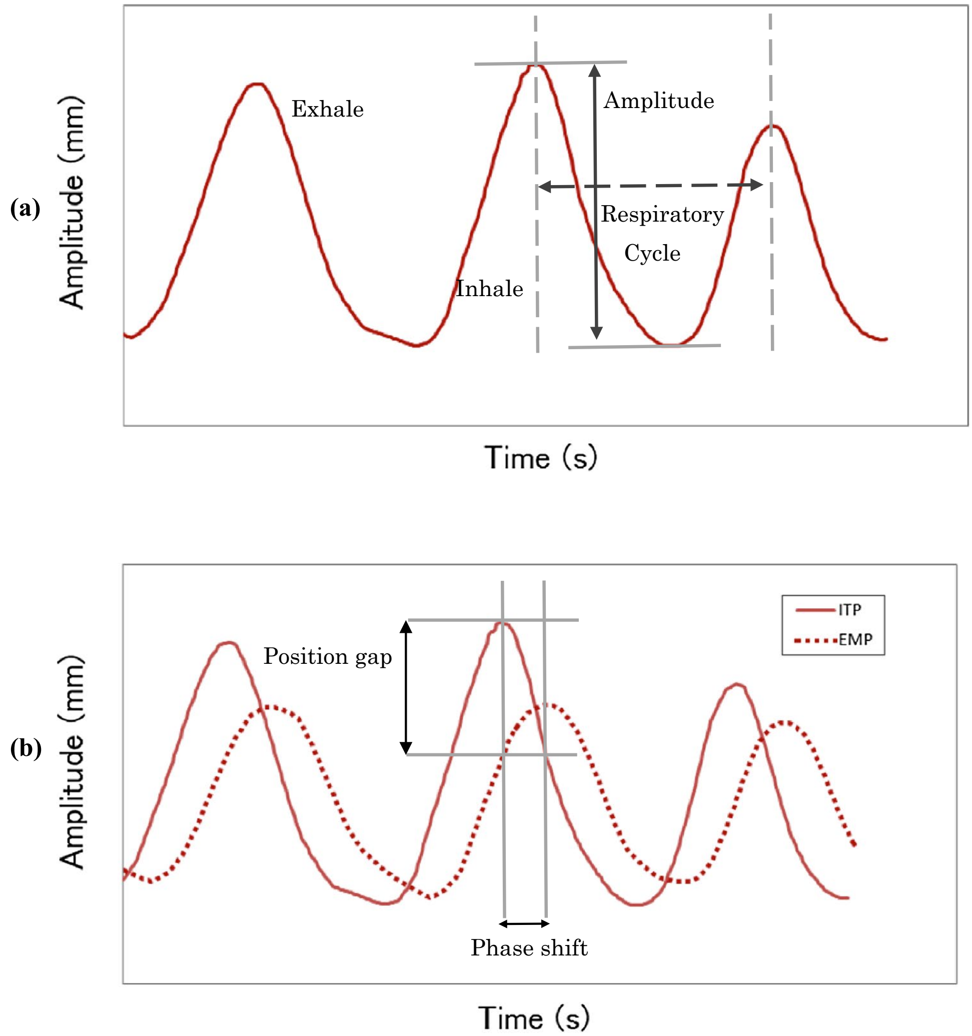

Fig. 1 **a** Tumor motion amplitude was defined as the position from the beginning of the expiratory internal tumor position (ITP) of one breath to the beginning of the inspiratory ITP for the same breath. Respiratory cycle was defined as the period from the beginning of the expiratory phase of one breath to the beginning of the expiratory phase for the next breath; **b** the phase shift between the ITP and external marker position (EMP) was defined as the period from the beginning of the expiratory internal tumor phase of one breath to the beginning of the expiratory external marker phase for the same breath. Position gap was defined as the positional difference between the peak of the tumor motion and that of the external marker motion at the beginning of expiration for a single breath

directions. In addition, the amplitudes and phase shift for the CC, AP, and LR directions were adjusted independently.

A plastic ball of 20 mm in diameter with a gold marker inserted at its center was used as the target. The ball was set on the target motion simulator and three optical markers were set on the body surface motion simulator.

SRTS tracking accuracy

The treatment plan utilized 10 beams with several different source positions. All beams were aimed at the center of the ball and were set to 200 MU for 15 s of data acquisition.

The motion phantom reproduced the motion of the tumor and the surface of the patient's abdomen using each patient's respiratory motion data. The respiratory motion pattern was repeated for 2–4 cycles during measurement, including setup time. The CyberKnife was subsequently operated with the delivery system in a demonstration mode and a video camera (GC-XA2; JVCKENWOOD Corporation, Yokohama, Japan) mounted on the head of the linear accelerator (LINAC). The image center of the video camera was matched to the central axis of the LINAC beam using a custom-built jig. The video recordings were performed while the LINAC tracked the ball. Under ideal tracking, the ball was stationary at the image center of the video camera. Conversely, if the SRTS had tracking error, the ball shifted away from the image center of the video camera. The deviations between the image center of the video camera and the center of the ball were measured at 30 Hz. Although we used a different video camera compared with a previous study, the precision of the ball position detection was equivalent.

Previously, tracking error was defined as the median value of the deviations tracked with a probability greater than 95% from 10 beams [17]. In the present study, tracking error was defined as the deviations tracked with a probability greater than 95% from all images obtained from the video camera.

Multiple regression analysis

Multiple regression analysis was employed to estimate the factors affecting tracking accuracy. The tracking error was assigned as the dependent variable. Twelve items extracted from the respiratory motion data were assigned as independent variables. The multiple regression model was created using the minimum Akaike Information Criterion (AIC) procedure. All analyses were conducted using R version 3.3.1 (R Foundation for Statistical Computing, Vienna, Austria). We used a variance inflation factor (VIF) to quantify the degree of multicollinearity for each individual independent variable in the model. The 14 independent variables were as follows:

- average tumor motion amplitude in the CC direction,
- coefficient of variation (CV) of the tumor motion amplitude in the CC direction,
- average tumor motion amplitude in the AP direction,
- CV of the tumor motion amplitude in the AP direction,
- average velocity of the tumor in the CC direction,
- average velocity of the tumor in the AP direction,
- average respiratory cycle,
- CV of the respiratory cycle,
- average phase shift in the CC direction,
- average phase shift in the AP direction,
- average phase shift ratio in the CC direction,
- average phase shift ratio in the AP direction,
- average position gap in the CC direction,
- average position gap in the AP direction,

Results

Table 1 shows the median and the range of the average tumor motion amplitude, the CV of the tumor motion amplitude, the average velocity of the tumor, the average respiratory cycle, the CV of the respiratory cycle, the average phase shift, and the average position gap extracted from the respiratory motion data. The average tumor motion amplitude ranged from 0.5 to 6.2 mm in the AP direction and 0.6to 26.7 mm in the CC direction. The average velocity of the tumor ranged from 0.6to 7.0 mm/s in the AP direction and 0.8to 23.1 mm/s in the CC direction. The average respiratory cycle ranged from 1.8 to 9.1 s. The average phase shift ranged from 0.0 to 1.1 s (median 0.2 s) in the AP direction and 0.0to 0.3 s in the CC direction. The average phase shift ratio ranged from 0.00 to 0.24 in the AP direction and 0.00to 0.07 in the CC direction. The average position gap ranged from 0.0 to 2.1 mm in the AP direction and from 0.0 to 0.5 mm in the CC direction.

Four of the 14 independent variables (CV of the tumor motion amplitude in CC, average position gap in CC, average velocity of the tumor in CC, and average velocity of the tumor in AP) were selected by the AIC as the model selection criteria. To evaluate the multicollinearity of the multiple regression model, we calculated the VIF from the four independent variables. We determined that the multiple regression analysis was not affected by multicollinearity because the VIF of each independent variable was < 2.

Table 1 Median and range of amplitude, CV of amplitude, velocity, cycle, CV of cycle, phase shift, and position gap

	Median	Range	
		Minimum	Maximum
Amplitude in AP (mm)	2.3	0.5	6.2
CV of amplitude in AP	0.20	0.03	0.76
Amplitude in CC (mm)	8.1	0.6	26.7
CV of amplitude in CC	0.16	0.02	0.74
Velocity in AP (mm/s)	2.5	0.6	7.0
Velocity in CC (mm/s)	7.0	0.8	23.1
Cycle (s)	3.9	1.8	9.1
CV of cycle	0.10	0.01	0.82
Phase shift in AP (s)	0.2	0.0	1.1
Phase shift in CC (s)	0.1	0.0	0.3
Phase shift ratio in AP	0.05	0.00	0.24
Phase shift ratio in CC	0.01	0.00	0.07
Position gap in AP (mm)	0.2	0.0	2.1
Position gap in CC (mm)	0.1	0.0	0.5

AP antero-posterior, *CC* cranio-caudal, *Amplitude* average of the tumor motion amplitude, *CV of amplitude*, coefficient of variation in the tumor motion amplitude, *Velocity* average velocity of the tumor, *Cycle* average of the respiratory cycle, *CV of cycle* coefficient of variation for the respiratory cycle, *Phase shift* average phase shift between the internal tumor position and external marker position, *Phase shift ratio* average phase shift ratio between the internal tumor position and external marker position, *Position gap* average position gap due to the phase shift between the internal tumor position and external marker position

Figure 2 shows the frequency distribution of tracking errors. The median value of the tracking errors of all the patients was 1.9 mm (range 0.9–5.3 mm).

Table 2 shows the results of the multiple regression analysis for the factors affecting tracking accuracy. The average absolute amplitude of the tumor motion in the CC direction, average position gap due to the phase shift between the internal tumor and external marker positions in the CC direction, and average velocity of the tumor in the CC and antero–posterior directions affected tracking accuracy. Among the four factors, the average velocity of the tumor in CC and the average position gap in CC were large for β.

Conversely, three independent variables,the average position gap in CC ($p < 0.001$), the average velocity of the tumor in CC ($p < 0.001$), and the average velocity of the tumor in AP ($p < 0.001$)were significant in the univariate analysis, while the CV of the tumor motion amplitude in CC

Fig. 2 Frequency distribution of the tracking errors. The median value of the tracking errors was 1.9 mm (range 0.9–5.3 mm)

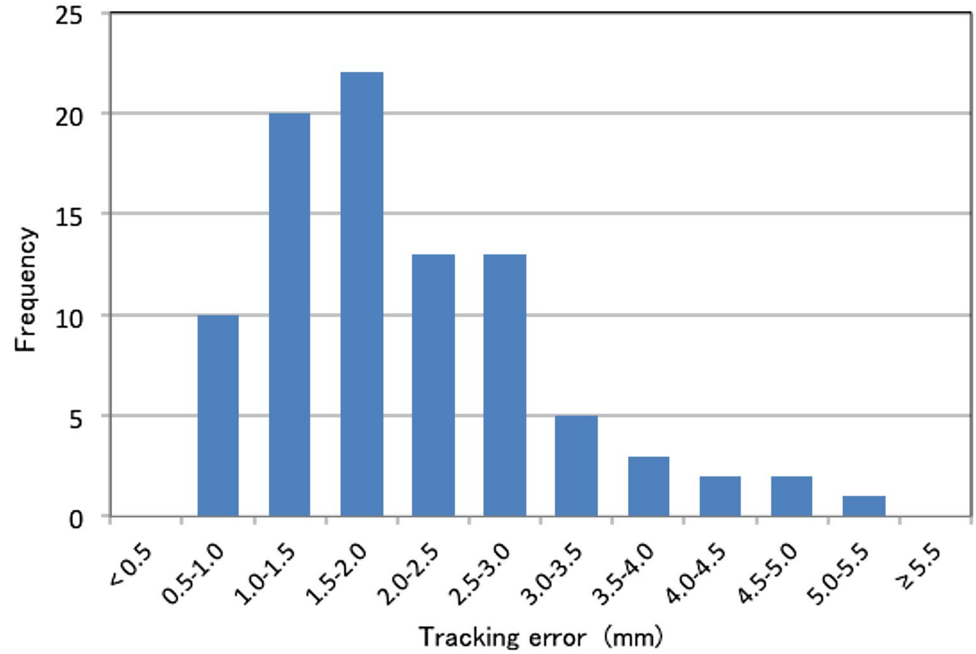

Table 2 Results of the multiple regression analysis with four independent variables selected by the minimum Akaike Information Criterion procedure

	β	*t* value	*p* value
CV of amplitude in CC	0.193	2.740	0.007
Position gap in CC	0.284	3.809	< 0.001
Velocity in CC	0.608	7.419	< 0.001
Velocity in AP	0.150	2.166	0.033

β standard partial regression coefficients, *CC* cranio-caudal, *AP* antero-posterior, *CV of amplitude* coefficient of variation of the tumor motion amplitude, *Position gap* average position gap due to the phase shift between the internal tumor position and external marker position, *Velocity* average velocity of the tumor motion

Table 3 Average and standard deviation of the tracking error for each range of velocity in CC

Velocity in CC (mm/s)	Tracking error (mm)
< 5.0	1.5 ± 0.5
5.0–10.0	2.0 ± 0.7
10.0–15.0	2.5 ± 0.9
15.0–20.0	3.5 ± 0.9
≧ 20	4.0 ± 0.8

Velocity average velocity of the tumor, *CC* cranio-caudal

($p = 0.406$) was not. Table 3 shows the average and standard deviation of the tracking error for each range of the average velocity of the tumor in CC. When the average velocity of the tumor in CC was large, the tracking error also increased.

Discussion

Seppenwoolde et al. [19] described the amplitude of lung tumor motion and the length of the breathing period. They reported that the mean amplitude of tumor motion was 0.2–8.2 mm in the AP direction and 0.2–24.6 mm in the CC direction, with an average breathing cycle length of 3.6 s. Similarly, our results showed an average of the tumor motion amplitude ranging from 0.5 to 6.2 mm in the AP direction and from 0.6 to 26.7 mm in the CC direction, with an average respiratory cycle of 3.9 s. Regarding the velocity of the target with respiratory motion under normal breathing, Schweikard et al. [7] reported that the velocity of the target ranged from 5 to 10 mm/s. Similarly, in our study, the average velocity of the tumor was 2.5 mm/s in the AP direction and 7.1 mm/s in the CC direction. Tsunashima et al. [20] previously showed using a respiratory sensor that the phase shift between the respiratory waveform and tumor motion were generally in the range of 0.0–0.3 s. They also observed a phase shift > 1.0 s. Similarly, our observed average phase shift was 0.2 s in the AP direction and 0.1 s in the CC direction. As described above, the respiratory motion data described in our findings are consistent with those in the literature.

Sumida et al. [16] reported tracking errors between 1.4 and 3.7 mm in six volunteers' breathing patterns. The difference between the minimum and maximum tracking error was > 2 mm. In the present study, the tracking errors were 0.9 and 5.3 mm, with the difference between the minimum and maximum tracking error being > 4 mm. These trends indicate that the accuracy of the SRTS is patient-dependent, necessitating a need for addition of a suitable margin related to the tracking accuracy for each patient.

The average of the tumor motion amplitude and the average respiratory cycle were not significantly related to the tracking error. However, the average velocity of the tumor correlated with the tracking error. In many cases, a large tumor amplitude and a short respiratory cycle resulted in faster tumor motion. However, in general, even if the tumor amplitude was high, the velocity of the tumor did not increase if the respiratory cycle was long. Similarly, when the respiratory cycle was short and the tumor amplitude was low, the velocity of the tumor did not increase. Therefore, we can conclude that the average tumor motion amplitude and the average respiratory cycle are not related to the tracking error. The significant correlation between the CV of the tumor motion amplitude and the tracking error suggests that the prediction model may not be applicable to a patient who has a large CV of the tumor motion amplitude (Fig. 3).

The average phase shift and the average phase shift ratio were not significantly related to the tracking error. However, Akino et al. [18] showed that the phase shift between the target motion and LED marker motion resulted in a large tracking error. Their measurement was performed with the extra stage delayed by 0.4 s (10% of the respiration frequency) with the motion amplitude of 10 mm. In this study, the maximum phase shift and the phase shift ratio in the CC direction were 0.3 s and 7%, respectively. In addition, the motion amplitude was different in each case, unlike the observations we made in our study.

The current software version of the SRTS can use linear, single quadratic, and dual quadratic models as the correlation model. The dual quadratic model reduces the tracking error caused by hysteresis due to the phase shift between the ITP and EMP. The parameters of each correlation model type are calculated using a least-square fit of all available positional relationships between the ITP and the EMP, and the optimal model is selected automatically. If the amplitude of the tumor motion is not constant, the least-square fit of the dual quadratic model will be less accurate than the linear model. This makes the linear model a more reasonable choice in many clinical situations. Since the linear model is more commonly used, we hypothesized that the average position gap in CC was related to tracking error. Conversely, when the amplitude of the tumor motion is constant, selecting the dual quadratic model will decrease the tracking error. Although the average position gap in AP was larger than the average position gap in CC, the former does not significantly affect the tracking accuracy because the average tumor motion amplitude and the average velocity of the tumor in the AP direction are smaller than those in the CC direction.

Akino et al. [18] plotted tracking errors against phantom velocity in their study to show significant linearity between the two variables. Similarly, the relationship between the average velocity of the tumor in the CC direction and the tracking error was significant in the univariate analysis (Table 3) in the present study. When the average velocity of the tumor in CC was > 20 mm/s, the tracking error was approximately 2 mm larger than the median tracking error. The tracking error became greater in response to an increase in the average velocity of the tumor in CC. In consideration of the results shown in Table 3, it is possible to add a suitable margin to the clinical target volume for each patient. We hypothesized that Table 3 can be used to determine the average velocity of the tumor in AP, when this value is large. The tracking error exceeded the median tracking error by approximately 1.3 mm when the average position gap in CC was > 0.2 mm. Therefore, the average position gap in CC must be considered when adding a margin to a patient's clinical target volume.

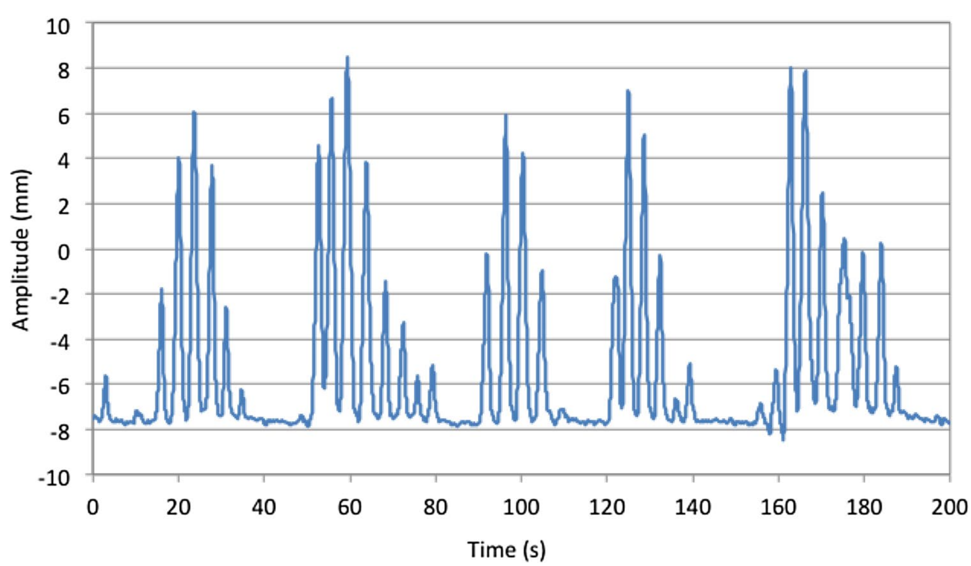

Fig. 3 Sample respiratory motion data for a patient with a large coefficient of variation of the absolute amplitude of the tumor motion in the cranio-caudal direction

The CV of the tumor motion amplitude in CC was not significant in the univariate analysis, although it significantly affected the tracking accuracy according to the multiple regression analysis. Therefore, the relationship between the tracking error and the CV of the tumor motion amplitude in CC is inconclusive. In contrast, the tracking error correlated with the average velocity of the tumor in CC and the average position gap in CC. In determining a suitable margin, the observations summarized in Table 3 may be useful. For example, one may set the standard velocity of the tumor in the CC direction to 5–10 mm/s, given the average value of 7.0 mm/s. If the velocity of the tumor in the CC direction was 15–20 mm/s, a margin of 1.5 mm may be added to standard margin. Furthermore, Table 3 may also be used to consider the margin for the velocity of the tumor in the AP direction. Similarly, if the average position gap in CC was > 0.2 mm, a margin of 1 mm may be added to the standard margin. Depending on the facility, cine MR scan may not be available, in which case it may be possible to obtain the velocity of the tumor from 4D-CT.

This study has some notable limitations. We could not account for tumor motion in the LR direction because we used the sagittal plane, which was obtained simultaneously during motion of the tumor and the body surface. However, Seppenwoodle et al. [19] assessed three-dimensional tumor motion and found that the amplitude of the overall tumor motion was the smallest in the LR direction. Therefore, we believe this limitation had a minimal effect on our results. Next, the temporal resolution of cine MR was 0.2–0.3 s. However, the relationship between ITP and EMP was well maintained. When the tracking error is large, vibration of the LINAC head was often observed. Such robotic movement was the same at the treatment and this measurement. Therefore, we considered that the temporal resolution does not affect the result so much. Finally, the correlation model of SRTS could not be updated during the measurements. The average length of respiratory motion data was 259.0 s and baseline drift was observed in some of these data. Respiratory motion data with baseline drift may result in a large tracking error. Although the result lacks accuracy, this may be negligible because, in many cases, consideration of the margin is considered safer.

The results of the multiple regression analysis showed that the factors affecting the tracking accuracy were the CV of the tumor motion amplitude in CC, the average position gap in CC, the average velocity of the tumor in CC, and the average velocity of the tumor in AP. The results indicate that the tracking accuracy of the SRTS is patient-dependent. Therefore, the four factors should be employed to verify tracking accuracy at each clinical facility. Additionally, we showed a significant relationship between the tracking error and the average velocity of the tumor in CC and the average position gap in CC. These factors may be used to determine an appropriate margin for treatment of the target tumor to enhance clinical outcomes.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical statement All study participants provided informed consent and the study design was approved by the appropriate ethics review board.

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