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Abstract. Use of four-dimensional cone-beam CT (4D-CBCT) and fiducial markers for image guidance during radiation therapy (RT) of mobile tumors is challenging due to the trade-off among image quality, imaging dose, and scanning time. This study aimed to investigate different 4D-CBCT acquisition settings for good visibility of fiducial markers in 4D-CBCT. Using these 4D-CBCTs, the feasibility of marker-based 4D registration for RT setup verification and manual respiration-induced motion quantification was investigated. For this, we applied a dynamic phantom with three different breathing motion amplitudes and included two patients with implanted markers. Irrespective of the motion amplitude, for a medium field of view (FOV), marker visibility was improved by reducing the imaging dose per projection and increasing the number of projection images; however, the scanning time was 4 to 8 min. For a small FOV, the total imaging dose and the scanning time were reduced (62.5% of the dose using a medium FOV, 2.5 min) without losing marker visibility. However, the body contour could be missing for a small FOV, which is not preferred in RT. The marker-based 4D setup verification was feasible for both the phantom and patient data. Moreover, manual marker motion quantification can achieve a high accuracy with a mean error of <1.4 mm. © 2018 Society of Photo-Optical Instrumentation Engineers (SPIE) [DOI: [10.1117/1.JMI.5.2.021207](https://doi.org/10.1117/1.JMI.5.2.021207)]

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1 Introduction

Fractionation is commonly used in radiation therapy (RT), meaning that the total dose of radiation is divided into several smaller doses delivered over a period of several treatment days (i.e., fractions).^{1,2} It is important to reproduce the patient and tumor positions in each treatment fraction as they are in the planned treatment setup, which is usually represented by the computed tomography (CT) scan acquired prior to the treatment course for treatment planning purposes (the so-called planning CT scan). The kilovoltage (kV) cone-beam CT (CBCT) scanner mounted on the gantry of a linear accelerator (linac) for RT allows the acquisition of fractional CBCT scans of patients directly prior to each dose delivery.^{3–5} By registering the planning CT scan to the fractional CBCT scan with respect to (for instance) bony anatomy or tumor, the patient setup position can be verified and, if necessary, corrected.^{6–9} The use of tumor volume as the region of interest for CT-CBCT registration for setup verification is preferable, but it is often hindered by poor visibility of the tumor in the CT and CBCT scans due to the limited soft-tissue contrast, especially for mediastinal and abdominal tumors.¹⁰ Implantation of fiducial markers in the tumor (e.g., esophageal, pancreatic, hepatic, and prostate tumors) has been used in RT to aid delineation of tumor volume and quantification of the variation in tumor position, as well as for tumor-based setup verification.^{11–18}

Four-dimensional CBCT (4D-CBCT), i.e., respiration-correlated CBCT, was introduced to facilitate patient setup in RT for tumors prone to respiration-induced motion.¹⁹ The current use

of 4D-CBCT is mainly limited to the stereotactic body RT (SBRT) for lung cancer, where the contrast in 4D-CBCT between the lung tumor and surrounding lung tissue is adequate. Specifically, the position of the lung tumor in different breathing phases of the 4D-CBCT is registered to the midposition of the tumor derived from the 10 phases of the planning 4D-CT to yield the tumor trajectory. Next, the measured tumor trajectory is averaged (time weighted) to quantify displacement of the mean tumor motion for a baseline shift correction.^{20,21} Using 4D-CBCT in combination with fiducial markers may be suitable for RT of other mobile tumors (e.g., esophageal, pancreatic, and hepatic tumors) to take into account respiration-induced tumor motion during setup verification.²² However, the feasibility of using fiducial markers in the 4D-CBCT scans for setup verification (i.e., registration of the planning CT to the 4D-CBCT) has not yet been assessed.

For SBRT of lung tumors, the 4D-CBCT scan is usually acquired with a small scanning field of view (FOV), which can image the tumor region with a radius of 120 to 135 mm in the axial plane (depending on the vendor of the linac). However, for RT of mobile tumors with standard fractionation (especially for mediastinal and abdominal tumors), a slightly larger FOV (410 × 410 or 450 × 450 mm²) for CBCT acquisition is clinically preferred. During a 4 to 5-week treatment, this enables inspection of anatomical change (e.g., variation in the gastrointestinal gas volume and variation in body contour) to evaluate whether or not re-planning for the remaining treatment fractions is needed. Irrespective of the FOV, if the 4D-CBCT is used for marker-based setup verification in the standard

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Fig. 1 (a) Dynamic thorax phantom on the linear accelerator couch. (b) In-house manufactured silicone insert with two gold markers in the dynamic moving cylinder.

fractionated RT of these above-mentioned mobile tumors, it is necessary to first investigate the trade-off between the image quality in terms of marker visibility and acquisition parameters, such as imaging dose, scanning FOV, and gantry rotation speed, before assessing the marker-based 4D registration.

In addition to using the markers for 4D registration, quantification of the respiration-induced motion by manually registering individual markers in a chosen reference breathing phase of the 4D-CBCT to the corresponding markers in the remaining breathing phases of the 4D-CBCT is of interest. This is a simple approach to analyzing the interfractional (i.e., day-to-day) variability of respiration-induced tumor motion, which is important for selecting an appropriate way to cope with respiration-induced tumor motion.^{23,24} Although 4D-CT can also be used for this purpose, it is not common practice to acquire daily 4D-CT due to the high imaging dose. Alternatively, the respiration-induced motion amplitude can be estimated using the markers in the CBCT projection images;²⁵ however, this requires a reliable marker segmentation tool, which remains a challenge. Therefore, it is necessary to assess the accuracy of manual respiration-induced motion quantification using markers and 4D-CBCT.

The present study aimed to find suitable settings of 4D-CBCT acquisition to ensure good visibility of the markers in 4D-CBCT. Also assessed were the feasibility and accuracy of marker-based 4D registration and manual quantification of respiration-induced motion using markers and 4D-CBCT. For this, we applied a dynamic phantom and included two patients with esophageal cancer.

2 Materials and Methods

2.1 Phantom

This study used a dynamic thorax phantom (Model 008A; CIRS, Norfolk, Virginia). The materials in this anthropomorphic phantom have electron densities similar to those in human tissue. A detachable cylinder in the left lung can move along and rotate around the longitudinal axis, i.e., the cranial–caudal (CC) direction of the phantom, driven by an external engine [Fig. 1(a)]. A cylindrical silicone insert containing two gold markers was manufactured in house and inserted in the dynamic moving cylinder [Fig. 1(b)]. On the 3D-CT scan, the CT values of the silicone insert [mean $\pm$ standard deviation (SD)] measured in Hounsfield units (HU) were 227 ± 33 , which was higher than that of soft tissue (range -130 to 77).²⁶ Two types of gold markers were tested: (1) a rigid straight marker (RSM) with length 5 mm and diameter ranging from 0.43 to 0.64 mm

(Cook Medical, Limerick, Ireland), and (2) a flexible coil-shaped marker (FCM) with length 12 mm and diameter 0.35 mm (Visicoil; IBA dosimetry, Bartlett, Tennessee). After positioning the silicone insert, the two markers were positioned parallel to the longitudinal axis of the phantom [Fig. 1(b)].

Three motion signals were applied to the cylinder with the silicone insert containing the two gold markers. Two of the motion signals were created based on the respiration-induced tumor motion (i.e., mean and maximum amplitude) in one breathing cycle, quantified using the 4D-CT scans of 14 patients with esophageal cancer who were investigated in an earlier study.²⁷ The two motion signals are periodical and the period was set at 4 s, corresponding to the average breathing cycle found in the 14 patients. The amplitudes of these two signals are 5.3 mm (representing medium motion) and 14.0 mm (representing large motion) in the CC direction, respectively. Because the motion of the insert in the left–right (LR) and anterior–posterior (AP) directions can only be simulated by rotating the cylinder around the longitudinal axis, the motion signals actually applied in these two directions were correlated and different from the signals generated from the patient data. Therefore, the motion of the two markers in the LR and AP directions was limited to <2 mm.

In addition, one 6-min long nonperiodic motion signal [Fig. 2(a)] was applied to the phantom, of which the mean amplitude over the breathing cycles is 9.4 mm [Fig. 2(b)]. This signal represents the respiratory diaphragm motion of a patient with esophageal cancer in the CC direction, which was extracted from the 4D magnetic resonance imaging scans. In this scenario, no motion signal was applied to the LR and AP directions.

Since respiration-induced motion is usually dominant in the CC direction, in the present study, motion in the CC direction only was evaluated.

2.2 Patient Data

Two patients with esophageal cancer were also included to investigate whether the phantom-based results are representative for the clinical setting. Both patients gave informed consent and received endoscopic ultrasound-guided implantation of two 10-mm-long FCM at the cranial and caudal borders of the primary tumor. This procedure of marker implantation was approved by the local medical ethics review committee (METC) and is currently standard clinical practice for esophageal cancer RT in our clinic.¹⁵ However, in one of these patients, one marker was lost before the start of treatment; thus, only three of the four markers were included for assessment of the patient data.

Fig. 2 (a) Amplitude of the nonperiodic 6-min motion signal in the CC direction. (b) Mean motion signal (red line) of motion signals per breathing cycle (gray line) with standard deviation (SD, bars).

Table 1 Specifications of CBCT acquisition and reconstruction settings.

Setting	Collimator	Gantry rotation arc (deg)	Gantry speed (deg/min)	Approx. number of projections	Current (mA)	Exposure time (ms)	Approx. scanning time (min)	Reconstruction option	Total imaging dose relative to setting 1 (%)
1	M20	360	180	660	32	40	2	3D	100
2	M20	360	180	660	32	40	2	4D	100
3	M20	360	90	1320	20	32	4	4D	100
4	M20	360	45	2640	16	20	8	4D	100
5	S20	200	50	1320	20	32	4	4D	100
6	S20	360	90	1320	20	32	4	4D	100
7	S20	200	80	825	20	32	2.5	4D	62.5
8	S20	200	50	1320	20	20	4	4D	62.5

2.3 CT Imaging

For the phantom, three “snapshot” 3D-CT scans were acquired as the planning CT scans (i.e., reference): one for each motion signal. The scans were acquired with an in-plane resolution of 0.7 mm and a slice thickness of 2.5 mm. In addition to the 3D-CT, a 4D-CT of the phantom was acquired for each motion signal. Since, in most studies, manual respiration-induced motion quantification is usually done using 4D-CT, in the present study, the 4D-CT scans were used for comparison with the 4D-CBCT in terms of the marker-based motion quantification accuracy.^{27,28} The breathing motion signal for 4D-CT reconstruction was monitored and acquired by the real-time position management system (Varian Medical System, Palo Alto, California). The sorting and binning of the 4D-CT data into 10 breathing phases was done using the Advantage 4D software (General Electric, Waukesha, Wisconsin).

For the patients, a 3D-CT scan was also acquired as the planning CT. The in-plane pixel size is 1.3 mm and a slice thickness is 2.5 mm. All 3D-CT and 4D-CT scans were acquired with the LightSpeed RT 16 CT scanner (General Electric).

2.4 Cone-Beam CT Imaging

All CBCT scans were acquired using the CBCT scanner mounted on the Elekta Synergy linac (Elekta AB, Stockholm,

Sweden). With the dynamic phantom, we tested eight settings with different CBCT scanning and reconstruction parameters (Table 1). The beam energy for all eight settings was 120 kVp. Setting 1 used the M20 collimator in combination with a required shifted detector and full arc rotation, resulting in a medium FOV of 410×410 mm² in the axial plane. This setting is routinely applied in the setup verification procedures in the standard fractionated RT of most thoracic, mediastinal, and abdominal tumors. However, the standard 4D-CBCT setting for lung cancer SBRT often needs a S20 collimator with no shift of the detector, giving a small FOV of 270×270 mm² in the axial plane. Therefore, in our experiments, we tested both the M20 (settings 2 to 4) and S20 (settings 5 to 8) collimator.

Settings 2 to 8 were designed on the basis of setting 1 due to the clinically used scanning parameters in setting 1. Setting 2 employed the same scanning parameters as in setting 1, but with a 4D volume reconstruction. For settings 3 to 8, we mainly adjusted the gantry rotation arc and speed, current, and exposure time. Meanwhile, we aimed to retain (settings 3 to 6) or reduce (settings 7 and 8) the total nominal imaging dose compared with setting 1. The scanning rate remained at the default rate of 5.5 projection images per second. Therefore, when the gantry rotation speed was increased or decreased, the scanning time and total number of projection images (for the same rotation arc) were correspondingly decreased or increased.

All CBCT scans were reconstructed using the x-ray volume imaging software (XVI 4.5.0; Elekta AB, Stockholm, Sweden), which sorted the projection images into 10 breathing phases²⁹ and reconstructed the CBCT using the high-speed Feldkamp–Davis–Kress (FDK) algorithm.³⁰ The spatial resolution was isotropic and set at 1.0 mm for both the 3D and 4D reconstructions. The eight settings were applied to acquire CBCT scans for the phantom with both the medium and large motion periodic signals, as well as the 6-min long nonperiodic motion signal. In total, three 3D-CBCT and 21 4D-CBCT scans of the phantom were obtained.

For the two patients, only settings 1 to 3 were tested because of the current clinical requirement of a medium FOV and acceptable acquisition time. For CBCT acquisition, setting 1 (the same as setting 2) was used on the first treatment fraction and setting 3 was used on the second treatment fraction. All 4D-CBCTs were retrospectively reconstructed. The requirement of additional ethical approval for human subject involvement was waived by the local METC. Therefore, for each patient, one 3D-CBCT and two 4D-CBCT scans were included for assessment.

2.5 Marker Visibility

For each of the 24 CBCT scans of the phantom, the visibility of the two gold markers was quantitatively assessed by calculating the contrast-to-noise ratio (CNR), which was defined as

$$\text{CNR} = \frac{|\mu(I_m) - \mu(I_s)|}{\sigma(I_s)}, \quad (1)$$

where $\mu(I_m)$ refers to the mean intensity of 30 voxels with highest intensity within a cubic volume of interest (VOI) containing the marker; $\mu(I_s)$ refers to the mean voxel intensity of the silicone insert within a cubic VOI centered in the insert; and the denominator, $\sigma(I_s)$, is the SD of the voxel intensity of the silicone insert within the VOI (Fig. 3). For the two markers (i.e., the RSM and FCM), the CNR was calculated separately. The CNRs for the patient data were also calculated by Eq. (1), but with I_s referring to the voxel intensity in a cubic VOI in the surrounding tissue of the marker. All the VOIs have the size $11 \times 11 \times 11 \text{ mm}^3$.

Fig. 3 Example of VOI for markers (top/yellow and bottom/green squares) and silicone insert (middle/red square) on one transverse slice of 4D-CBCT phase 0 acquired with setting 3. Note: WL, window level and WW, window width.

2.6 Marker-Based Four-Dimensional Registration

The feasibility of marker-based 4D rigid registration was tested for the 4D-CBCT scans of both the phantom and the patients. For each 4D-CBCT, using the XVI software, the reference CT was first registered to the average CBCT scan of all 10 breathing phases with respect to bony anatomy. Next, for each breathing phase a marker-based registration to the reference CT was performed using a manually created 3D mask (i.e., VOI) consisting of the marker(s) and the peripheral volume. The applied automatic rigid gray-value-matching technique in XVI uses the correlation ratio of all the voxels in the mask as a cost function.³¹ For the phantom, the translations in the CC direction derived from the marker-based 4D registration were compared with the periodic input motion signal or the mean of the nonperiodic input motion signal in one cycle, by calculating the mean absolute error (MAE) and the root mean square error (RMSE). For the patient data, the marker-based 4D registration was only visually assessed due to the lack of a “true” motion signal.

2.7 Manual Motion Quantification

For the 21 4D-CBCT scans of the phantom, the quantification of respiration-induced marker motion was manually performed and assessed. Specifically, first, the reference CT was registered to the average CBCT of all 10 breathing phases based on the bony anatomy. Subsequently, per marker, the 10 breathing phases of the 4D-CBCT were manually registered to the reference CT by visually aligning the markers. Thus, the derived translations in the CC direction represented the marker motion. For settings 2 to 8, the 10 translations were compared with the periodic input motion signal, or the mean signal of the nonperiodic input motion signal in one cycle, by calculating the MAE and RMSE in the CC direction. Moreover, for the 4D-CT, the motion was quantified in the same way and was also compared with the input motion signal.

For the patient data, there was no “true” motion signal with which to compare the 4D-CBCT-based quantified motion. Further, since the motion on the two treatment fractions differs, there is no rationale to compare these motions; therefore, in these two patients, we did not assess manual quantification of the marker motion.

3 Results

3.1 Marker Visibility in the Phantom

Irrespective of the motion signal used in the phantom, both investigated markers (FCM and RSM) were sufficiently visible in all 14 CBCT scans of the phantom when the window level and width were adjusted (Fig. 4). Figure 5 presents the CNRs of the two markers for each CBCT acquisition setting associated with the three motion signals (i.e., the periodic medium and large motion signals and the nonperiodic 6-min motion signal). The distribution of CNRs for settings 2 to 8 indicates the variation in CNR between the 10 breathing phases of the 4D-CBCT. Compared with the FCM, in these CBCT scans, it was easier to visually identify the RSM, which might also reflect the larger CNRs found for the RSM (Fig. 5). This could be due to the larger diameter of the RSM compared with that of the FCM.

Figure 5 shows that, when an M20 collimator was used (i.e., of settings 2 to 4), setting 4 gave the best marker visibility (i.e., the largest CNR). This was due to the use of a reduced gantry speed leading to a larger number of projection images,

Fig. 4 One transverse slice of the 3D/4D-CBCT scans acquired with settings 1 to 8 for the phantom controlled with (a) the periodic medium motion signals, (b) large motion signals, and (c) nonperiodic 6-min motion signal. Note: WL, window level and WW, window width.

Fig. 5 CNR calculated using the 3D/4D-CBCT scans acquired with the eight settings for the RSM and FCM in the phantom in (a-c) three motion scenarios.

which contributed to less streak artifacts. However, the scanning time of setting 4 (~ 8 min) is too long for a daily treatment fraction compared with setting 2 (~ 2 min) and setting 3 (~ 4 min). Although the marker visibility for setting 2 was acceptable, the limited number of projection images in each breathing phase resulted in an overall inferior CBCT image quality. This hampers the use of the 4D-CBCT scans for daily inspection of anatomical changes, such as body contour and volume changes of gastrointestinal gas pockets during RT.

When an S20 collimator with a small FOV was used (i.e., of settings 5 to 8), setting 5 was best in terms of image quality and marker visibility quantified by the highest CNR (Figs. 4 and 5). This is due to the use of a higher dose (compared with settings 7 and 8) and smaller sampling angle (compared with settings 6 and 7). Although settings 6 to 8 were inferior in CNR compared with setting 5, the difference between them was relatively small and, visually, the marker visibility and image quality of these 4D-CBCT scans was acceptable (Fig. 4). This suggests that it is possible to visualize the markers in the 4D-CBCT while retaining or reducing the total imaging dose. Moreover, in terms of scanning time, setting 7 was superior to settings 5, 6, and 8 (i.e., setting 7 was 1.5-min shorter).

According to Fig. 5, for settings 5 to 8, the CNR did not vary substantially among the three motion scenarios (i.e., the two periodic motion signals and the nonperiodic motion signal). This implies that the amplitude and regularity of the motion are unlikely to have a strong influence on marker visibility, especially when the S20 collimator is used.

3.2 Marker Visibility in the Patients

In the four 4D-CBCT scans of the two patients acquired using settings 2 and 3, all markers were identified without difficulty (Fig. 6). Furthermore, there was no substantial difference between the CNRs of the two 4D-CBCT scans acquired using settings 2 and 3 (Fig. 7). The CNRs in the patients were slightly smaller than those in the phantom. This is probably due to the additional cardiac-induced motion of the marker. Moreover, in the first patient, a slight difference in CNR was found between the two FCMs. Since respiration-induced marker motion amplitude has been found to correlate with marker location,^{18,24} this difference in CNR might be due to different marker locations resulting in different motion amplitudes.

Fig. 6 One marker (arrow) in the three orthogonal planes of the first breathing phase of the 4D-CBCT acquired using settings 2 (a–c and h–j) and 3 (d–f and k–m) for the two patients. Note: WL, window level and WW, window width.

Fig. 7 CNR of the FCMs in (a) patient 1 and (b) patient 2 with CBCT acquisition settings 1 to 3.

3.3 Marker-Based Four-Dimensional Registration

As shown in Fig. 8, most of the outcomes of automatic marker-based 4D registration did not deviate substantially from the periodic or nonperiodic input motion signals. Figure 9 shows the MAE and RMSE in each scenario for settings 2 to 8.

The MAE and RMSE are similar, implying the absence of outliers in the 10 errors associated with the 10 breathing phases. The MAE and RMSE for periodic large and nonperiodic 6-min

motion were larger than those for the periodic medium motion. This can probably be attributed to the elongated shape of the markers induced by the large amplitude, or nonperiodic irregularity during acquisition of the reference 3D-CT and 4D-CBCT scans.

By visually inspecting the patient data, the marker-based 4D registration was performed properly (Fig. 10); however, due to the lack of a “true” motion signal, the accuracy cannot be calculated.

Fig. 8 Translation in the CC direction assessed using marker-based 4D registration of the reference CT to the 4D-CBCTs associated with 10 breathing phases for acquisition settings 2 to 8 in (a–c) the three scenarios.

Fig. 9 MAE and RMSE of the marker-based 4D registration in (a–c) the three motion scenarios for settings 2 to 8 of 4D-CBCT acquisition.

Fig. 10 Marker-based 4D registration examples showing the coronal plane of the 4D-CBCT acquired using setting 3 for patient 1 and setting 2 for patient 2. The reference 3D-CT is illustrated in purple, the 10 breathing phases (0 to 9) of the 4D-CBCT are shown in green. After registration, perfect alignment results in a white spot at the marker position. Note: WL, window level and WW, window width.

3.4 Manual Motion Quantification

Figure 11 shows the manually quantified motion translations using the 4D-CT and the 4D-CBCTs, as well as the input motion signals for the RSM and FCM in the phantom for the three motion scenarios. Figure 12 shows the MAE and RMSE between the manual registration results and the input or average input motion signals. For settings 2 to 8, the mean MAE was <1.4 mm and the SD of the MAEs was <0.3 mm. The MAE and RMSE associated with using 4D-CT for motion quantification were even slightly larger than those associated with using 4D-CBCT when the periodic motion signals were applied. These results suggest that it is feasible to accurately quantify the respiration-induced marker motion using manual registration of 4D-CBCT, irrespective of the investigated setting of 4D-CBCT acquisition.

4 Discussion

To our knowledge, this is the first study to assess the feasibility of using 4D-CBCT in combination with implanted fiducial markers for setup verification in RT. Also, it is the first experience with and accuracy assessment of the use of fiducial markers and 4D-CBCT to quantify respiration-induced motion. Our experiments with both phantom and patient data demonstrate that it is feasible to visualize and identify implanted gold markers in 4D-CBCT for a variety of acquisition settings. Altering the 4D-CBCT acquisition settings allowed for acquisition of 4D-CBCTs of sufficient image quality while retaining or reducing the total imaging dose that is currently routinely used for 3D-CBCT acquisition. Also, we have shown the feasibility of using 4D-CBCT scans with markers to perform the marker-based 4D registration in setup verification of RT of mobile

Fig. 11 Comparison of the manually quantified motions with the input motion signals for the RSM and FCM in (a–c) the three motion scenarios.

Fig. 12 MAE and RMSE of the manual 4D registration for the RSM and FCM in (a–c) the three motion scenarios for settings 2 to 8 of 4D-CBCT acquisition and 4D-CT.

tumors. Moreover, irrespective of the investigated 4D-CBCT acquisition settings, manual quantification of respiration-induced motion using markers and 4D-CBCT can be performed with an accuracy similar to that when markers are used in combination with 4D-CT scans.

For marker visibility, it is inappropriate to compare the CNRs between settings 2 to 4 and 5 to 8 because the CT values of these 4D-CBCT scans were not perfectly calibrated, and the filtering of the projection image in the FDK volume reconstruction was different for the two tested collimators (i.e., S20 and M20). Despite that motion amplitude and motion regularity are expected to have an impact on the CNR of markers, in the three tested scenarios, the CNRs did not differ substantially, implying that these factors may not have a strong influence on the visibility of the markers. However, these factors did affect the marker-based 4D registration results obtained with the XVI software; irregular motion, as well as motion with a larger amplitude, resulted in less accurate registration outcomes.

The use of low spatial resolution in the 4D-CBCT reconstruction (e.g., 2.0 mm) might help smooth the streak artifacts induced by the large sampling angle of the projection images. However, this might also blur the marker in the transverse plane because of the small diameter of the markers. The isotropic spatial resolution of 1.0 mm (as used in the 3D-CBCT reconstruction) resulted in good marker visibility for both the phantom and patients. However, the memory consumption needed to reconstruct the 4D-CBCT scans with a medium FOV was exponentially increased compared with the low-resolution 4D-CBCT. Therefore, the trade-off between marker visibility, image quality, and memory consumption should be taken into consideration when applying 4D-CBCT in the clinic.

Compared with setting 2, settings 3 and 5 to 8 were preferred to achieve improved marker visibility and image quality for the marker-based 4D registration, as well as a reasonable scanning time. When a medium FOV is needed to inspect anatomical changes during conventional RT for mobile tumors, setting 3 would be appropriate. When a small FOV fulfills the need of daily image guidance, 4D-CBCTs acquired with setting 5 for

the best image quality, or with setting 7 for reduced imaging dose and shorter scanning time, are preferred.

Accurate manual quantification of respiration-induced marker motion using 4D-CBCT enables analysis of interfractional variation in respiration-induced tumor motion when markers are implanted, even though no repeat 4D-CT scan is available.^{23,24} In the present study, although motion was quantified only in the CC direction, accuracy of the quantification in the LR and AP directions would not differ from that found in the CC direction, since the scan resolution was isotropic.

5 Conclusions

Using the phantom and patient data, we investigated which 4D-CBCT acquisition setting is suitable for visualizing the markers for setup verification during RT and motion quantification for mobile tumors. If a medium FOV is required, an acquisition setting with 1320 projection images, 20-mA current, and 32-ms exposure time can balance the scanning time and the image quality for sufficient marker visualization and marker-based 4D registration. If a small FOV can be used, it is possible to reduce the imaging dose of the most commonly used setting by 37.5% and achieve a scanning time of 2.5 min with sufficient image quality for marker-based 4D registration. Further, it is feasible to estimate the respiration-induced marker motion by means of manually registering the markers, irrespective of the 4D-CBCT acquisition setting, with an accuracy comparable with that of 4D-CT.

Disclosures

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