4D registration and 4D verification of lung tumor position for stereotactic volumetric modulated arc therapy using respiratory-correlated cone-beam CT

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We propose a clinical workflow of stereotactic volumetric modulated arc therapy (VMAT) for a lung tumor from planning to tumor position verification using 4D planning computed tomography (CT) and 4D cone-beam CT (CBCT). A 4D CT scanner, an Anzai belt and a BodyFix were employed to obtain 10-phase respiratory-correlated CT data for a lung patient under constrained breathing conditions. A planning target volume (PTV) was defined by adding a 5-mm margin to an internal target volume created from 10 clinical target volumes, each of which was delineated on each of the 10-phase planning CT data. A single-arc VMAT plan was created with a D95 prescription dose of 50 Gy in four fractions on the maximum exhalation phase CT images. The PTV contours were exported to a kilovoltage CBCT X-ray Volume Imaging (XVI) equipped with a linear accelerator (linac). Immediately before treatment, 10-phase 4D CBCT images were reconstructed leading to animated lung tumor imaging. Initial bone matching was performed between frame-averaged 4D planning CT and frame-averaged 4D CBCT datasets. Subsequently, the imported PTV contours and the animated moving tumor were simultaneously displayed on the XVI monitor, and a manual 4D registration was interactively performed on the monitor until the moving tumor was symmetrically positioned inside the PTV. A VMAT beam was delivered to the patient and during the delivery further 4D CBCT projection data were acquired to verify the tumor position. The entire process was repeated for each fraction. It was confirmed that the moving tumor was positioned inside the PTV during the VMAT delivery.

Keywords: 4D registration; 4D verification; lung volumetric modulated arc therapy (lung VMAT)

INTRODUCTION

Radiotherapy has a long history of use in treating lung tumors. Many techniques have been proposed to manage respiratory motion during treatment. Of these, passive breath-hold is the simplest but the least accurate approach. An alternative approach is active breath-hold, which is a temporary suspension of breathing at a desired respiratory phase [1]. However, it is argued that the suspension mechanism facilitates the protection of the heart better in breast cancer patients than in lung cancer patients who tend to have a smaller breathing capacity.

Gating was initially proposed in proton therapy for liver tumors using a pressure sensor on the abdominal wall [2]. Gated radiotherapy using an external respiratory signal has been clinically implemented using commercially available systems. However, it has been reported that respiratory-gated beam delivery cannot result in margin reduction without respiratory-correlated image guidance [3]. For more accurate gated radiotherapy, a gold fiducial marker can be implanted near a lung tumor for real-time diagnostic X-ray fluoroscopy [4]. However, a major problem of any gating technique is longer delivery time leading to lower patient throughput as well as the possibility of reduced tumor control [5].
Another approach is dynamic tumor tracking with a gimbaled treatment head that allows continuous beam delivery, where the moving target may be located by an implanted fiducial marker and diagnostic X-ray fluoroscopy in real time [6]. Although it is assumed that the spatial relationship between tumor volume and a point marker remains unchanged, this may not always be true due to the mobility of the marker. In addition, accuracy of treatment may ultimately be defined as a volumetric relationship between the tumor and the dose distribution during the entire beam delivery. The marker-based approach does not always comply with this definition.

Still another method for managing respiratory motion is the use of an internal target volume (ITV) determined by contouring clinical target volumes (CTVs) on 10-phase 4D planning CT images. In this case, the problem of respiratory motion management can be reduced to a tumor registration problem with a larger, but virtually still, target volume on the treatment couch. By constraining the breathing amplitude with the aid of abdominal compression, the ITV approach may decrease the target volume and thus the dose to normal lung. Using 4D cone-beam CT (CBCT), a respiratory-correlated lung tumor volume can be visualized immediately before treatment [7–9]. An advantage of the 4D-CBCT-based ITV approach is that the above-mentioned volumetric accuracy can be directly confirmed on a CBCT workstation prior to each fractionated treatment.

To the authors’ knowledge, a clinical workflow using 4D CBCT for lung treatment has not previously been established. The purpose of this study was to propose a clinical workflow of stereotactic volumetric modulated arc therapy (VMAT) for lung tumors from planning to tumor position verification.

MATERIALS AND METHODS

A large bore 16-multislice CT scanner, Aquillion LB (Toshiba, Japan), an Anzai belt (Anzai Medical, Japan) and a body fixation device, BodyFix (Elekta, Germany), were employed to obtain 10-phase respiratory-correlated CT data for a lung patient under constrained breathing conditions induced by an abdominal compression plate. The patient was diagnosed with stage IV metastatic lung tumor (squamous cell carcinoma) from an anal cancer. The lung tumor had a major diameter of 15 mm and a minor diameter of 8 mm. The amplitude of the tumor motion was 11.7 mm in the craniocaudal direction, 1.8 mm in the lateral direction and 0.8 mm in the anteroposterior direction. A planning target volume (PTV) was defined by adding a 5-mm margin to an ITV created by 10 clinical target volumes, each of which was delineated on each of the 10-phase 4D planning CT images. A single-arc VMAT plan was created with a $D_{95}$ prescription dose of 50 Gy in four fractions on the maximum exhalation phase CT images [10] where the photon energy was 6 MV with a maximum dose rate of 580 MU/min.

The PTV contours were exported to a kilovoltage CBCT X-ray Volume Imaging (XVI) version 4.5, equipped with a Synergy linear accelerator (linac) (Elekta, UK). Immediately before treatment, 10-phase 4D CBCT data were reconstructed with an acquisition time of 4 min, generating animated lung tumor imaging. Initial bone matching was performed between frame-averaged 4D planning CT and frame-averaged 4D CBCT datasets, where the frame-averaged 4D planning CT data were calculated by in-house software and the frame-averaged 4D CBCT data were provided by XVI built-in functionality. Subsequently, the imported PTV contours and the animated moving tumor were simultaneously demonstrated on the XVI display monitor, and a manual 4D registration was interactively performed by moving the imported ITV and PTV contours using a mouse on the axial, coronal and sagittal views until the moving tumor was symmetrically positioned inside the PTV. After confirmation of the registration results on the display monitor, the patient couch was repositioned and stereotactic VMAT beams were delivered.

During the delivery, another set of 4D CBCT projection data was acquired to verify the tumor position, and phase-sorted volumetric reconstruction was performed using in-house software [11]. This in-house program was needed because the current XVI version does not provide CBCT imaging during treatment. The entire process was repeated in each of the four fractions.

The current study is in compliance with ethical guidelines of the hospital and written informed consent was obtained before the treatment was initiated.

RESULTS

Manual 4D registration using the PTV contours and the animated lung tumor required only a few seconds. Figure 1a–e show 4D CBCT images on the first day overlaid with the PTV (in sky blue) and ITV (in yellow) contours after the 4D lung tumor registration. Registration required a couch translation of 3.2 mm toward the patient’s right, 1.5 mm toward the caudal direction, and 4.4 mm toward the anterior direction, respectively. The figures show images for five consecutive respiratory phases that cover half a breathing cycle, in which the tumor moves from cranial to caudal direction during the half cycle.

Figure 2a–d shows 4D CBCT images acquired during VMAT delivery on the first day and reconstructed afterwards to verify the in-treatment moving tumor position in reference to the PTV and ITV contours. The VMAT
delivery time was 210 s. For the in-treatment CBCT, the number of phase bins was four, which covered an entire breathing cycle. It was confirmed that during the VMAT delivery on the first day the moving tumor was also located inside the PTV. Similar satisfactory results were obtained on the other three days.

**DISCUSSION**

It is assumed that the lung tumor has a periodic motion. This assumption is most likely valid if the beam delivery time is short. It is known that VMAT delivery is faster than any other intensity-modulated treatment. In addition, in-treatment CBCT can be acquired during VMAT delivery for 4D tumor position verification. Thus, VMAT may be a logical choice for lung tumor treatment. The CBCT images in Fig. 2 a–d show some blurring, possibly due to the smaller number of phase bins, which may be improved by providing 10-phase in-treatment 4D CBCT datasets. A limitation of this technique would be that the amplitude of tumor motion may not be sufficiently reduced by abdominal compression in the case of some tumors having a large breathing motion, possibly leading to a prohibitively large ITV volume. The measured respiratory movement in this study was relatively large and could have been reduced by increasing the compression of the plate to the abdominal surface. Whereas the dose calculation in this study was based on maximum exhalation phase CT images, the authors are currently updating their procedure using mid-ventilation CT data.

**CONCLUSION**

We have proposed a clinical workflow of stereotactic lung VMAT capable of 4D registration and 4D verification of the tumor position, and initial promising results have been obtained. The authors believe that the proposed 4D workflow for stereotactic lung VMAT is valid for respiratory motion management because the VMAT delivery is sufficiently fast to maintain respiratory periodicity, but much longer than the patient breathing cycle for obtaining 4D CBCT. Our lung VMAT delivery employs a sequence with a maximum leaf speed of 1 mm/degree [10], and therefore it is anticipated that doubling the dose rate using flattening filter free techniques [12], combined with doubled leaf speeds, may reduce the treatment time down to an order of 100 seconds for delivering a prescribed dose of 50 Gy in four fractions.
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Fig. 2. 4D CBCT images acquired during VMAT delivery on the first day to verify the in-treatment moving tumor position in reference to the PTV and ITV contours. In this case, the number of phase bins was four, which covered an entire breathing cycle.

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