Technical note: Comparison of the internal target volume (ITV) contours and dose calculations on 4DCT, average CBCT, and 4DCBCT imaging for lung stereotactic body radiation therapy (SBRT)

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Technical Note: Comparison of the internal target volume (ITV) contours and dose calculations on 4DCT, average CBCT, and 4DCBCT imaging for lung stereotactic body radiation therapy (SBRT)

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Abstract
Purpose: To investigate the differences between internal target volumes (ITVs) contoured on the simulation 4DCT and daily 4DCBCT images for lung cancer patients treated with stereotactic body radiation therapy (SBRT) and determine the dose delivered on 4D planning technique.

Methods: For nine patients, 4DCBCTs were acquired before each fraction to assess tumor motion. An ITV was contoured on each phase of the 4DCBCT and a union of the 10 ITVs was used to create a composite ITV. Another ITV was drawn on the average 3DCBCT (avgCBCT) to compare with current clinical practice. The Dice coefficient, Hausdorff distance, and center of mass (COM) were averaged over four fractions to compare the ITVs contoured on the 4DCT, avgCBCT, and 4DCBCT for each patient. Planning was done on the average CT, and using the online registration, plans were calculated on each phase of the 4DCBCT and on the avgCBCT. Plan calculations were tested by measuring ion chamber dose in the CRS lung phantom.

Results: The Dice coefficients were similar for all three comparisons: avgCBCT-to-4DCBCT (0.7 ± 0.1), 4DCT-to-avgCBCT (0.7 ± 0.1), and 4DCT-to-4DCBCT (0.7 ± 0.1); while the mean COM differences were also comparable (2.6 ± 2.2mm, 2.3 ± 1.4mm, and 3.1 ± 1.1mm, respectively). The Hausdorff distances for the comparisons with 4DCBCT (8.2 ± 2.9mm and 8.1 ± 3.2mm) were larger than the comparison without (6.5 ± 2.5mm). The differences in ITV D95% between the treatment plans and avgCBCT calculations were 4.3 ± 3.0% and 4.5 ± 4.6%, between treatment plan and 4DCBCT plans, respectively, while the ITV V100% coverages were 99.0 ± 1.9% and 93.1 ± 8.0% for avgCBCT and 4DCBCT, respectively.

Conclusion: There is great potential for 4DCBCT to evaluate the extent of tumor motion before treatment, but image quality challenges the clinician to consistently delineate lung target volumes.

Key Words
4DCBCT, 4DCT, lung SBRT, respiratory motion
1 | INTRODUCTION

For early-stage lung cancer patients, stereotactic body radiotherapy (SBRT) has become one of the primary treatment options. Improvements in patient localization using on-board imaging and cone-beam computed tomography (CBCT) and the ability to account for tumor motion have led to the increase in long SBRT treatments. One strategy for tumor motion management is the use of four-dimensional CT (4DCT) simulations to determine the total extent of motion for planning purposes. Then a 3D CBCT is used for online patient setup and the patient is treated free breathing. This strategy, however, does not take into account potential variations in a patient’s breathing pattern from simulation to treatment.

The four-dimensional CBCT is now becoming a clinically feasible tool in the treatment room. The advantage is the ability to visualize the motion of the tumor at the time of treatment. While a phantom study suggested image guidance with 3D CBCT has similar accuracy to 4D CBCT image guidance, a clinical study showed improved target localization with 4D CBCT as tumor motion increased. Several investigators have looked at 3D CBCT for dose accumulation and adaptive planning of SBRT lung treatment. Even so, the issue of calculating dose on a moving target exists. Similar to the advent of 4DCT, 4D CBCT can be employed to determine dose delivered to a moving tumor at the time of treatment.

This study evaluated the internal target volume (ITV) of clinically treated patients by comparing the contours on 10 phases of the 4DCBCT with the treatment planning ITV based on the 4DCT. Dose to the moving tumor was calculated on each phase of the 4DCBCT, and ITV coverage was compared to the treatment plan. Eclipse 4D CBCT dose calculations were checked with ion chamber measurements in a CIRS anthropomorphic lung phantom.

2 | METHODS

Nine patients with non-small-cell lung cancer underwent a 4DCT with a Philips Big Bore Brilliance 16 CT Simulator (Philips Healthcare, Massachusetts, USA). Patients were immobilized in an Elekta BodyFix (Stockholm, Sweden). The Philips Brilliance 16 CT was used to capture the breathing trajectory. Projections were retrospectively binned and reconstructed into four phases based on the phase breathing trace. Clinically, four phases are utilized for planning: Average CT (avgCT) and maximum intensity projection (MIP) datasets were generated from the phases. The ITV was contoured on the 4DCT MIP (4D CT ITV), and evaluated on each breathing phase. A 3-mm isotropic margin was placed around the ITV to create the planning target volume (PTV). Treatment plans were generated for a Varian EDG linear accelerator (Varian, Palo Alto, CA) with a 6 MeV flattening filter free beam. Treatment plans were compared using the avgCT using Eclipse’s AAA algorithm version 15, with prescription doses of 40Gy in four fractions. Planning criteria were based on RTDG 0915, such that at least 95% of the PTV is covered by the prescription dose. Key plan metrics evaluated include V100% (percent of target covered by the prescription dose) and D95% (dose covering 95% of the target).

For each fraction, a free-breathing 4DCBCT was acquired. Varian Real-time Position Management (RPM) was used to track patient breathing. The RPM block was placed on the patient between the xiphoid and umbilicus for diaphragmatic displacement tracking. A total of 1500 projections were acquired over a full 360° rotation at a speed of 3 degrees per second. For patient localization 3D CBCT (avgCBCT) was reconstructed (filtered back-projection) online using every projection. The same projections used for localization were binned into 10 phases based on the RPM breathing trace and reconstituted online. A radiation oncologist contoured the target volume on the avgCBCT (avgCBCT ITV) and each 4D CBCT phase (Fig. 1).

The 4D CBCT ITV was formed by the union of the 10 contours. The Dice coefficient, Hausdorff distance, and center of mass distance between the 4D ITV, avgCBCT ITV, and 4D CBCT ITV were computed with in-house software. The Dice coefficient quantifies the overlap between two contours by the ratio of twice the intersection divided by the sum of the contour volumes. The Hausdorff distance is the greatest minimum distance between all vertices of the two contours. Mean values for each patient (over four fractions) as well as mean of the means over nine patients (group systematic error) and standard deviation of means (SD of the systematic error) were calculated.

Using the online registration, the treatment plans were calculated on each phase of the 4D CBCT and the avgCBCT for each fraction of nine patients. The average treatment metrics over four fractions, D95%, and V100%, were compared with the contours achieved in the original treatment plans. It was assumed that the length of each of the 10 phases was the same, thus treatment field contributed 1/10 of the MUs to each phase. A plan sum of all the phases verified the single fraction dose delivered to the target.

Patient-specific calculations and measurements were acquired for each plan using a CIRS lung phantom. A 10 phase 4D CBCT of the phantom was acquired (Fig. 2) and patient plans were mapped to and calculated on each phase of the phantom’s scan. The interphase average coefficient of variation (CV) was determined using all 76 treatment fields to quantify how uncertainty created from CBCT imaging noise affects the dose calculation accuracy. The interphase average CV was found by comparing the standard deviation in calculated dose over the 10 phases of the 4D CBCT in each treatment field and averaging all treatment fields together. Point dose measurements were acquired with an IBA CCD set at isocenter to test the calculation algorithm’s precision for 4D CBCT based dose calculations. The ion chamber was calibrated in solid water against the treatment-planning system the day of the plan measurements.

3 | RESULTS

3A | Contouring

Table 1 shows the three contour comparisons performed over the four treatment fractions: 4DCT ITV against avgCBCT ITV, 4D CT ITV
in slightly larger contours on the daily CBCTs, which did not match well with the planning CT. Compared to contouring in 2D, the 3D approach has shown improvements in accuracy and consistency.

**CONFLICTS OF INTEREST**
None.

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**Fig. 1.** Four-dimension CBCT ITV.

**Fig. 2.** A single 4D CBCT phase of the CIRS lung phantom used for dose measurements. Note the streaking artifacts and overall uniformity of the image.

**Table 2.** Shows the dose coverage comparisons for the four fractions of the treatment. The overall prescription dose coverage of the 4D CBCT ITV and 4D CBCT ITV was 99.0 ± 1.9% and 93.1 ± 8.0% for tumor motion of 5 cm. The coverage dropped to 90.2 ± 2.9 cm and 81.1 ± 3.2 cm for tumor motion of 1 cm. **Fig. 3.** A single 4D CBCT phase of the CIRS lung phantom used for dose measurements. Note the streaking artifacts and overall uniformity of the image.
TABLE 1  
Comparison of 4DCT, average CBCT, and 4DCBCT ITV contours using the following evaluation metrics: Hausdorff distance, center of mass difference, and dice coefficient.

| Patient | 4DCT - Average CBCT (1) | 4DCT - 4DCBCT (2) | Average CBCT - 4DCBCT (3) |
|---------|-------------------------|-------------------|--------------------------|
|         | Hausdorff distance (mm) | COM (mm) | dice coefficent | Hausdorff distance (mm) | COM (mm) | dice coefficent | Hausdorff distance (mm) | COM (mm) | dice coefficent |
|         | mean | SD | mean | SD | mean | SD | mean | SD | mean | SD | mean | SD | mean | SD | mean | SD |
| 1       | 3.5  | 0.4 | 1.2  | 0.3 | 0.8  | 0.8 | 0.0  | 0.0 | 4.9  | 0.7 | 1.2  | 0.3 | 0.9  | 0.1 |
| 2       | 3.1  | 0.5 | 0.9  | 0.4 | 0.8  | 0.8 | 0.1  | 0.1 | 2.8  | 0.5 | 1.5  | 0.6 | 0.8  | 0.0 |
| 3       | 5.3  | 0.5 | 1.5  | 0.7 | 0.8  | 0.8 | 0.0  | 0.0 | 7.0  | 0.6 | 1.5  | 0.4 | 0.8  | 0.0 |
| 4       | 3.8  | 0.8 | 1.2  | 0.6 | 0.8  | 0.8 | 0.1  | 0.1 | 7.3  | 1.1 | 1.9  | 0.9 | 0.6  | 0.1 |
| 5       | 3.7  | 0.8 | 1.8  | 0.5 | 0.8  | 0.1 | 4.3  | 0.3 | 1.9  | 0.6 | 0.7  | 0.3 | 0.9  | 0.1 |
| 6       | 8.6  | 0.9 | 2.5  | 1.6 | 0.6  | 0.1 | 11.6 | 1.2 | 3.2  | 0.4 | 0.4  | 0.1 | 7.7  | 0.8 |
| 7       | 9.9  | 1.2 | 2.3  | 0.6 | 0.6  | 0.0 | 11.8 | 1.1 | 2.1  | 0.2 | 0.0  | 0.0 | 0.0  | 0.0 |
| 8       | 9.2  | 1.1 | 4.3  | 0.6 | 0.0  | 9.0 | 17.0 | 0.3 | 2.0  | 0.0 | 0.0  | 0.0 | 2.0  | 0.0 |
| 9       | 9.1  | 0.7 | 6.5  | 1.5 | 0.8  | 0.8 | 0.0  | 0.0 | 15.8 | 2.2 | 2.2  | 0.6 | 0.1  | 0.1 |
| Mean Group Error [mm] | 6.5  | 2.3 | 0.7 | 8.2 | 3.1 | 0.7 | 8.1 | 2.6 |
| Systematic Error (D) | 2.5  | 1.2 | 0.1 | 2.9 | 1.6 | 0.1 | 3.2 | 2.1 |
| Random Error (r) | 0.8  | 1.3 | 0.0 | 1.0 | 1.3 | 0.0 | 1.4 | 0.7 |

The increase in Hausdorff distances for 4DCBCT ITV results from the presence of streak artifacts that limit the ability to visualize the complete tumor motion. As seen in Fig. 3, streak artifacts decreased the conspicuity of the lesion borders. In a single 4DCBCT phase, the border of the tumor and chest wall is hardly distinguishable. This led to the 4DCBCT ITV expanding posteriorly and laterally into the chest wall compared to the average CBCT. While a larger Hausdorff distance difference between average CBCT and 4DCBCT may be expected, since the full extent of the motion is being contoured compared to an average intensity, a similar distance was also observed for the 4DCT ITV and 4DCBCT ITV comparison. This is due to the registration, image quality, and difference in breathing patterns. Another consideration is the difference between the 4- phase 4DCT and 10-phase 4DCBCT. Previous publications have shown that the ITV may be underestimated when contoured on two extreme phases or when the tumor motion is greater than 1.6 cm.14 The work by Cao et al. demonstrated that ITVs contoured on the 4-phase scans encompassed 94.4% of the 10-phase ITVs.18

The advantage of 4DCBCT is the ability to capture the full range of tumor motion.31 Shlimovich et al.30 showed that increasing the scanning intervals on a phantom, 4DCBCT had improved target localization over average CBCT. Sweaney et al. used an Edge Synergy to evaluate patient setup using online 4DCBCT. They showed improved localization compared to 3D with increasing tumor motion and especially with tumors adjacent to the diaphragm. Two patients (7 and 9) patients with tumors located adjacent to the diaphragm had tumor motion ≥1 cm. These contour differences were notably greater, suggesting 4DCBCT localization may have improved setup accuracy. This is backed up by the Table 1 comparison of average CBCT to 4DCBCT. The COM and Dice coefficients for the two patients (7 and 9) are much worse than the other seven patients. If the average CBCT is used for online patient setup, an appropriately sized ITV margin should be applied to encompass the diaphragmatic tumor motion uncertainty not captured in the average motion envelope.

For Patient 6, low Dice coefficients and COM calculations between simulation 4DCBCT and treatment CBCTs can be explained by the development of scar tissue adjacent to the tumor. This resulted

FIG. 3  
Single phase ITV (red) from patient 4 where tumor (red) is indistinguishable due to significant streak artifacts in the 4DCBCT (A). Resulting 4DCBCT ITV (blue) moves posteriorly and laterally into the chest wall compared to the avgCBCT ITV (orange) and yields lower dose coverage reported to 4DCT ITV. This can be seen by the low Dice coefficient between avgCBCT and 4DCBCT in Table 1.

98.3 ± 1.0% and 98.1 ± 3.8% respectively. The aggregate difference in D95% between the treatment plan versus avgCBCT and treatment plan versus 4DCBCT were 4.3 ± 3.0% and −5.5 ± 4.4%, respectively. For tumors with <1 cm of motion, D95% increased 3.4% for 4DCBCT. While tumors with 21-31 cm of motion, D95% decrease by approximately 2.6%. Tumor motion did not affect D95% for the average CBCT.

The overall interface CV was 3.8 ± 1.4% over 10 phases. Point dose measurements per patient showed excellent agreement with 4DCBCT dose calculations with an average dose difference of 0.1 ± 1.0%. Over all 76 treatment beams the average dose difference was 0.1 ± 2.7%. Per field calculation versus measured dose differences did not exceed 10% for any patient. These measurements provide a basis for 4DCBCT dose calculations.

4 DISCUSSION

This study sought to quantify the capability to contour on 4DCBCTs and determine the dose delivered to patients receiving SBRT. The 4DCBCT image quality affected the physician’s ability to identify the tumor volume. Streak artifacts, as well as lesions adjacent to high intensity anatomy (blood vessels, the diaphragm, and the chest wall), reduced tumor contrast. Additionally, tumor size and composition may change over the course of treatment.12

Contrast to noise ratio for CBCT has been shown to decrease linearly with faster gantry speed and fewer projections.33 For this study a compromise was made between scan time and number of projections per phase on the 4DCBCT. A scan speed of 2 seconds was selected to improve image quality, while doubling the typical avgCBCT scan time. Due to phase blurring, 4DCBCT image quality per phase is inferior to avgCBCT.33 The projections are split into 10 phases, reducing the number of projections per phase approximately 10-fold, relative to a standard avgCBCT using a standard CBCT speed (1.8 RPM).

On average the Dice coefficients had similar values across all three comparisons. The similarity of the datasets in regard to the avgCBCT ITV versus the 4DCT ITV and 4DCBCT ITV is due to the overlap of the time-average dose envelope captured by the avgCBCT and the full motion envelope estimated by 4DCT and 4DCBCT.14-16 Similar Dice coefficients for 4DCT and 4DCBCT ITV comparisons show that although the 4D images are acquired differently (slice based vs. planar based, and daily breathing pattern variations), the ITV contours largely overlap (Dice coefficient of 0.7).

The COM differences were smallest between the 4DCT versus avgCBCT comparison (2.3 mm), which is due to the physician performing online registration with these two image sets. A larger difference was found with the avgCBCT versus 4DCBCT comparison (2.6 mm), including a systematic error of 2.1 mm. For tumor motion greater than 1 cm, the systematic shift increases to 2.4 mm. This stems from the time-average motion envelope compared to the full motion envelope, these differences become more pronounced with greater tumor motion. This explains how the 4DCT versus 4DCBCT comparison has a higher COM difference (3.1 mm) relative to the 4DCT versus avgCBCT comparison. When the systematic shift between average and 4D acquisitions methods is factored in, 4DCT versus 4DCBCT has the lowest COM difference. Therefore, online 4DCBCT patient localization would improve the targeting accuracy as tumor motion increases.