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CLINICAL INVESTIGATION **Lung**

FOUR-DIMENSIONAL COMPUTED TOMOGRAPHY–BASED INTERFRACTIONAL REPRODUCIBILITY STUDY OF LUNG TUMOR INTRAFRACTIONAL MOTION

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Purpose: To evaluate the interfractional reproducibility of respiration-induced lung tumors motion, defined by their centroids and the intrafractional target motion range.

Methods and Materials: Twentythree pairs of four-dimensional/computed tomography scans were acquired for 22 patients. Gross tumor volumes were contoured, Clinical target volumes (CTVs) were generated. Geometric data for CTVs and lung volumes were extracted. The motion tracks of CTV centroids, and CTV edges along the cranio–caudal, anterior–posterior, and lateral directions were evaluated. The Pearson correlation coefficient for motion tracks along the cranio–caudal direction was determined for the entire respiratory cycle and for five phases about the end of expiration.

Results: The largest motion extent was along the cranio–caudal direction. The intrafractional motion extent for five CTVs was <0.5 cm, the largest motion range was 3.59 cm. Three CTVs with respiration-induced displacement >0.5 cm did not exhibit the similarity of motion, and for 16 CTVs with motion >0.5 cm the correlation coefficient was >0.8. The lung volumes in corresponding phases for cases that demonstrated CTVs motion similarity were reproducible. No correlation between tumor size and mobility was found.

Conclusion: Target motion reproducibility seems to be present in 87% of cases in our dataset. Three cases with dissimilar motion indicate that it is advisable to verify target motion during treatment. The adaptive adjustment to compensate the possible interfractional shifts in a target position should be incorporated as a routine policy for lung cancer radiotherapy. © 2008 Elsevier Inc.

Lung cancer, Respiration-induced tumor motion, Four-dimensional computed tomography, Radiotherapy.

INTRODUCTION

Advances in radiation delivery technology allow us to administer a precise, conformal dose to almost any target. However, the dose-shaping ability works best for static targets. Inaccuracies arise from perturbation of our idealized static anatomic architecture by physiologically induced motion and/or changes in the course of treatment (1–6). The extent of this variability may be clinically insignificant or considerable. These factors of nuisance, as they might be perceived, affect the entire treatment-planning process. During treatment administration there are usually two time scales of effects considered: intrafractional and interfractional. The former is affected by structure motion and variability and the latter by technical setup inaccuracies and possible internal changes due to therapy and/or disease progress. This might result in the loss of reproducibility originally assumed for the plan.

It is still most common to deal with the problem of organ motion and setup errors by placing sufficient planning target volume (PTV) margins around the static clinical target volume (CTV). However, recent advances in imaging allow for the procurement of data with specificity designed for a tailored dose delivery and the refinement of the PTV margins. Organ motion measurement is indispensable in a current treatment-planning methodology. In the majority of reported studies the extent of target motion associated with the intrafractional time span was of interest. A question of equal importance concerns the validity of these data throughout the course of radiation treatment—In other words, the issue of the reproducibility of the motion that is evaluated for the plan. Tumors in the thoracic cavity are especially susceptible to the deleterious influence of motion. Insight into target mobility is crucial to guarantee the quality of each plan because lung cancer radiation therapy might extend beyond 6 weeks (4, 6).

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Table 1. Patient characteristics and anatomic tumor locations.

Case no.	Stage	Sex	Age (y)	Anatomic site	Modality
1	IIIb	M	60	L-L-I-S	3D
2	IIIa	M	46	L-R-M-M	3D
3	LS	F	74	M-L—	IMRT
4	IIIb	F	81	L-R-S-P	3D
5	IV	F	66	L-R-S-P	IMRT
6	ES	M	48	L-R-I-B	3D
7	IIIa	F	64	L-L-I-S	3D
8	IV	M	79	L-R-S-A	3D
9	I(LR)	M	74	L-R-S-P	3D
10	IV	F	71	L-R-I-S	3D
11	LS	F	59	L-R-S-P	3D
12	IIIa(LR)	M	56	M-R—	3D
13	LS	F	68	M-R—	3D
14	IIa(LR)	F	67	L-L-I-S	IMRT
15	I	F	78	L-L-S-P	IMRT
16	IIIa	F	79	L-L-I-PB	3D
17	IIIa	F	66	L-L-I-AB	3D
18	I	M	61	L-L-I-LB	SRS
19	IIIb	F	80	L-R-S-C	IMRT
20	IIIa	F	82	L-R-I-LB	IMRT
21	IV(LR)	M	69	L-L-I-S	IMRT
22	IIIb	M	74	L-L-S-P	IMRT
23	IIIb	M	74	L-L-S-P	IMRT

Abbreviations: M = male; F = female; 3D = three-dimensional conformal radiotherapy; LR = locoregional recurrence; IMRT = intensity modulated radiotherapy; SRS = stereotactic radiosurgery; LS = limited stage; ES = extensive stage.

Case no. denotes the ordinal number of a given four-dimensional CT (4D-CT) scan pair.

Anatomic site of the tumor is denoted by the string *a-b-c-d*, where *a* is mediastinum (M) or lung (L); *b* is right (R) or left (L) lung; *c* is the lobe where, the tumor is located: inferior (I), medial (M), or superior (S); and *d* is the segment of the lobe: superior (S), medial (M), basal (B), posterior (P), inferior (I), anterior (A), lateral (L), or apical (C).

Patients 3,6, and 11 were diagnosed with small-cell lung carcinoma, patient 10 with metastatic breast cancer, and the rest with non–small-cell lung carcinoma.

Lung cancer motion management relies mainly on data provided by various CT-based imaging approaches (7–9). Recently, four-dimensional (4D) -CT technology has become a primary imaging technique used for the evaluation of tumor mobility. We have used two retrospective 4D-CT scans to assess respiration-induced motion and its reproducibility. A tacit assumption is that the range or more generally the pattern of motion is maintained for the entire duration of treatment (e.g., respiratory gating, with a duty cycle strictly determined at the outset, relies on this supposition). The magnitude of the motion concerns the margins and the duty cycle. The change of the motion pattern affects the latter. This work reports the results of an evaluation of the reproducibility of respiration-induced intrafractional motion of lung tumors in the interfractional frame time, the determination of the correlation between the motion tracks acquired at two dates along the cranio–caudal (CC) direction, and the evaluation of the intrafractional target motion range for different sections of lungs.

METHODS AND MATERIALS

This study was conducted under an institutional review board–approved process. Table 1 shows patient characteristics and the tumors' anatomic locations. Nine men and thirteen women participated; 21 patients had two and 1 patient had three 4D-CT scans (the last two entries in Table 1). Patient ages ranged from 46 to 82 years, with a median age of 68 years. Three tumors were located in the mediastinum, and 19 were in the lung parenchyma. According to clinical examination and radiologic findings, none of the patients presented with diaphragmatic paralysis.

For the mobility classification, the pulmonary topographic location, as used by van Sörnsen de Koste et al. (9), was ascribed to each tumor centroid. Although not anatomic, the lungs were halved into dorsal–ventral and medial–lateral sections. The superior–inferior parts were demarcated by the fifth thoracic vertebra. There were 18 dorsal, 4 ventral, 4 superior, and 18 inferior tumors. In addition, the apical (3 tumors within 6 cm below the tip of the lung), supradiaphragmatic (4 tumors within 3 cm above the diaphragm), and central (the rest of the lung) sections of the lungs were also differentiated because the kinematics of the lungs and the resulting mobility of the tumors in those parts differ greatly. The sections' schematic is shown in Fig. 1.

Four-dimensional CT

For each patient, two scans were acquired: one before treatment and the second during or shortly after treatment (Table 2). Images were obtained with a four-slice GE LightSpeed CT scanner (GE Medical Systems, Milwaukee, WI) coupled with a real-time position management respiratory gating system (Varian Medical Systems, Palo Alto, CA). Slice thickness was 2.5 mm. All patients were immobilized in a supine position with their arms extended above their heads. Patients were coached using an audio directive (''breathe in'') that matched their normal respiratory period. The CT images were sorted (Advantage4D software; GE Medical

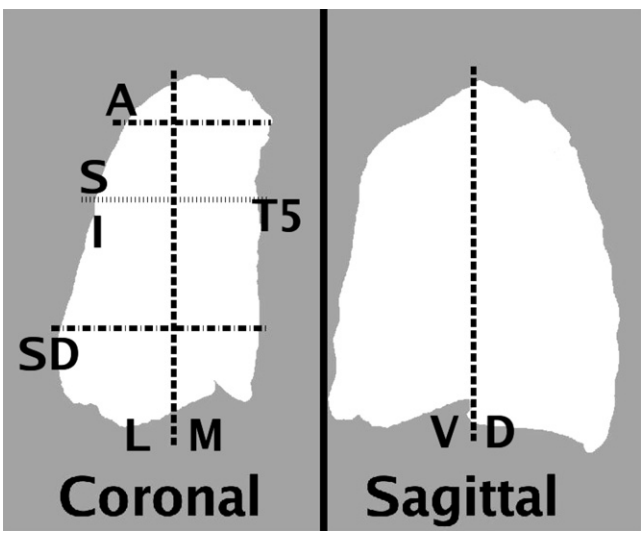

Fig. 1. Lung partitioning into sections depicted on the schematic of the structure's coronal and sagittal view. The vertical dashed line separates a lateral(L) and a medial(M) section on the coronal view and a ventral(V) and a dorsal(D) section on the sagittal view. The dotted line corresponding to T5 separates a superior(S) and an inferior(I) section. An apical(A) section is above the dash–dot line, and a supradiaphragmatic(SD) section is below the other dash–dotted line.