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CLINICAL INVESTIGATION **Lung**

DAILY ALIGNMENT RESULTS OF IN-ROOM COMPUTED TOMOGRAPHY–GUIDED STEREOTACTIC BODY RADIATION THERAPY FOR LUNG CANCER

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Purpose: To determine the extent of interfractional setup errors and day-to-day organ motion errors by assessing daily bone alignment results and changes in soft tissue tumor position during hypofractionated, in-room computed tomography (CT)-guided stereotactic body radiation therapy (SBRT) of lung cancer.
Methods and Materials: Daily alignment results during SBRT were analyzed for 117 tumors in 112 patients. Patients received 40–50 Gy of SBRT in four to five fractions using an integrated CT-LINAC system. The free-breathing CT scans acquired during treatment setup were retrospectively realigned to match with each of the bony references and the gross tumor volume (GTV) defined on the reference CT by rigid-body registration, and the daily deviations were calculated.
Results: The mean magnitude (± SD) three-dimensional shift from the initial skin marks to the final bone-aligned positions was 9.4 ± 5.7 mm. The mean daily GTV deviation from the bone position was 0.1 ± 3.8 mm in the anterior–posterior direction, −0.01 ± 4.2 mm in the superior–inferior direction, and 0.2 ± 2.5 mm in the lateral direction. A clinically noteworthy trend (net change >5 mm in any direction) in GTV position relative to the bone was observed in 23 cases (20%).
Conclusions: Soft tissue target position can change significantly beyond the motion envelope defined in the original internal target volume in four-dimensional CT-based treatment planning for SBRT of lung cancer. Additional margin should be considered for adequate coverage of interfractional changes. **© 2011 Elsevier Inc.**

Stereotactic body radiation therapy, Computed tomography on-rail system, Lung cancer, Image-guided radiation therapy, Adaptive radiation therapy.

INTRODUCTION

Stereotactic body radiation therapy (SBRT) can deliver a high dose of radiation to the target, with rapid dose–falloff gradients (1). Over the past decade, numerous studies have evaluated the efficacy and feasibility of hypofractionated SBRT for lung cancer using a variety of fractionation regimens; in study cohorts of 10 to 71 patients, with a median follow-up period of 10 to 36 months, crude local control rates of 80–100% and minimal toxicity were reported (2–8). Therefore, SBRT is an appealing alternative to an aggressive surgical approach for the treatment of early non–small-cell lung cancer (NSCLC) and solitary lung metastases from selected primary tumors.

However, SBRT requires a high degree of precision for each treatment in the series. Patient position is verified in various ways before every treatment to reduce interfractional setup error, and a stereotactic body frame (9) is used for rigid immobilization during treatment to reduce intrafractional setup error. The organ motion error in SBRT for lung tumors is mainly caused by respiratory motion, so internal target volumes (ITVs) are determined on the basis of the individualized assessment of respiratory motion. In addition, interfractional shifts in the target position can be caused by changes in breathing patterns and changes in tumor position over the course of treatment resulting from the physiologic or structural effects of high-dose radiation therapy. Determining the extent of inter- and intrafractional setup errors and organ motion errors is crucial to defining a safe margin for planning target volumes (PTVs), and both the optimization of the daily setup accuracy and adaptive strategies against the interfractional shifts of soft tissue targets are warranted to decrease the amount of normal tissue volume irradiated while maintaining adequate target coverage.

In this study, we summarized the daily alignment results for hypofractionated in-room computed tomography (CT)-guided SBRT for lung cancer, and the differences in gross

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tumor volume (GTV) position and bony position were further analyzed to see if there was a statistically significant time trend in the position of the GTV relative to the bone over 4 or 5 consecutive treatment days. The range of soft tissue target position relative to bony reference was assessed against the predicted target motion when using four-dimensional (4D) CT to design the ITV for treatment planning.

METHODS AND MATERIALS

Patients

This study was a retrospective analysis that was approved by the institutional review board, with patient informed consent waived. Medical records and CT images for 112 patients with 117 tumors who underwent SBRT for lung tumor at M. D. Anderson Cancer Center between September 2004 and February 2007 were retrospectively collected and reviewed for this study. Of these patients, 70% had Stage I non–small-cell lung cancer (NSCLC), 17% had a metastatic lung tumor, and 8.9% had local recurrence of lung cancer. Details of the patient characteristics are given in Table 1.

Treatment planning

Treatment simulation was performed on a commercial scanner (Discovery ST, GE Healthcare, Waukesha, WI). Patients were immobilized using a cradle and body shell. The imaging protocol consisted of obtaining a scout view of the patient before CT scanning, a session of fast helical CT of the entire thoracic and abdominal region, and then a 4DCT scan. Both the free-breathing helical CT scan and the 4DCT scan were performed with the patient supine and breathing freely. The 4DCT images were used to evaluate respiratory motion and determine the ITV. The 4DCT process has been previously described in detail (10, 11). Computed tomography images corresponding to 10 phases of the full breathing cycle were acquired. When a patient's breathing was not regular for physiologic or other clinical reasons, breathing instruction and training were given. When an intervention was deemed necessary, the patients were provided with video goggles, which displayed real-time video of their breathing traces, allowing them to assess and regulate their breathing during the 4DCT scanning.

Acquired CT scans were imported into the Pinnacle[3] treatment planning system (Philips Medical System, Andover, MA). Heterogeneity dose calculations were used by the collapsed-cone convolution superposition algorithm. On the basis of the International Commission on Radiation Units and Measurements (ICRU 62) guidelines, the ITVs were manually contoured on the single maximum-intensity projection CT set by the physicians. The clinical target volumes (CTVs) were generated by adding an isotropic margin of 8 mm to the ITVs, and PTVs were generated by adding an isotropic margin of 3 mm to the CTVs. The treatment plan was designed to deliver a prescription dose to 98% of the PTV.

Verification of reproducibility of set-up and radiation therapy

All patients were treated using a commercially available integrated CT-LINAC system (ExaCT, Varian Oncology Systems, Palo Alto, CA), which allows for convenient CT imaging during radiation treatment while the patient remains immobilized in the treatment position (12, 13). Before CT scanning, patients were aligned using the skin marks tattooed and cradle marks during the treatment simulation, and radiopaque fiducial markers were placed on the patient at the laser intersections. The CT scans, without contrast enhancement, were performed just before every treatment using 2.5-mm axial slices throughout. The matrix size was 512 × 512, and the pixel size was approximately 1 mm. Acquired CT scans were imported into an image registration program (computer-assisted targeting [CAT]) developed at M. D. Anderson Cancer Center to calculate the daily shifts of bony structures or GTVs from the bony reference region of interest (ROI) defined on the reference CT. This software incorporates a rigid-body image registration algorithm that has been optimized to match the image intensity and patterns of the GTVs in thoracic regions between corresponding image pairs in this specific application. As a reference of original position, the average CT scans derived from 4DCT datasets were used in 36 patients, and free-breathing CT scans performed on a commercial scanner for

Table 1. Characteristics of patient cohort and lung tumors (n = 112)

Factor	No. of cases	Cases (%)
Gender		
M	68	58.1
F	44	37.6
Lung tumor		
Primary lung cancer	82	73.2
Clinical stage		
IA	65	
IB	14	
IIIB	1	
IV	2	
Local recurrence of lung cancer	10	8.9
Metastatic lung tumor	19	17.0
Original organ site		
Lung	14	
Colon	2	
Oral cavity	1	
Bone	1	
Unspecified	1	
Unspecified	1	0.9
Histologic classification		
Adenocarcinoma	49	43.8
Squamous cell carcinoma	36	32.1
Poorly differentiated carcinoma	21	18.8
Bronchioloalveolar carcinoma	2	1.8
Large cell carcinoma	2	1.8
Adenosquamous cell carcinoma	1	0.9
Ewing sarcoma	1	0.9
Left/right lung		
Left	47	42.0
Right	63	56.3
Both	2	1.8
Tumor location		
Upper lobe	61	54.5
Lower lobe	44	39.3
Middle lobe	3	2.7
Upper/lower lobe	2	1.8
Middle/lower lobe	2	1.8
No. of tumors		
Single	107	95.5
Two lesions	5	4.5
Previous treatment		
Surgery		
Yes	11	9.8
No	101	90.2
Radiation therapy		
Yes	21	18.8
No	91	81.3