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Physics Contribution

Interfraction Displacement of Primary Tumor and Involved Lymph Nodes Relative to Anatomic Landmarks in Image Guided Radiation Therapy of Locally Advanced Lung Cancer

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Summary

In 12 patients with locally advanced non-small cell lung cancer, displacements of primary tumor (PT), involved lymph nodes (LN), carina, and 1 thoracic vertebra were investigated on weekly 4D fan beam CTs. Carina-based setup resulted in a more reproducible alignment of PT and LN than bony anatomy setup. Displacements were significantly correlated with PT and LN volume regression.

Purpose: To analyze primary tumor (PT) and lymph node (LN) position changes relative to each other and relative to anatomic landmarks during conventionally fractionated radiation therapy for patients with locally advanced lung cancer.

Methods and Materials: In 12 patients with locally advanced non-small cell lung cancer PT, LN, carina, and 1 thoracic vertebra were manually contoured on weekly 4-dimensional fan-beam CT scans. Systematic and random interfraction displacements of all contoured structures were identified in the 3 cardinal directions, and resulting setup margins were calculated. Time trends and the effect of volume changes on displacements were analyzed.

Results: Three-dimensional displacement vectors and systematic/random interfraction displacements were smaller for carina than for vertebra both for PT and LN. For PT, mean (SD) 3-dimensional displacement vectors with carina-based alignment were 7 (4) mm versus 9 (5) mm with bony anatomy ($P<.0001$). For LN, smaller displacements were found with carina- (5 [3] mm, $P<.0001$) and vertebra-based (6 [3] mm, $P=.002$) alignment compared with using PT for setup (8 [5] mm). Primary tumor and LN displacements relative to bone and carina were independent ($P>.05$). Displacements between PT and bone ($P=.04$) and between PT and LN ($P=.01$) were significantly correlated with PT volume regression. Displacements between LN and carina were correlated with LN volume change ($P=.03$).

Conclusions: Carina-based setup results in a more reproducible PT and LN alignment than bony anatomy setup. Considering the independence of PT and LN displacement and the impact of volume regression on displacements over time, repeated CT imaging even with PT-based alignment is recommended in locally advanced disease. © 2014 Elsevier Inc.

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Introduction

Image guided radiation therapy for patients with locally advanced lung cancer relies on anatomic landmarks or—if clearly defined—the primary tumor (PT) for patient setup. Current onboard imaging with planar x-rays or cone beam computed tomography (CBCT) often allows satisfactory identification of the PT but fails to clearly visualize involved mediastinal lymph nodes (LNs), resulting in potential misalignment of LN volumes. Accurate patient alignment during radiation therapy is also complicated by interfraction variations in position (1-5) and regression of both PT and LN volumes (6-8).

Various landmarks, such as skin tattoos, bony anatomy, and carina (7, 9, 10) or implanted fiducials (11-13) have been investigated as surrogates for lung cancer positioning in image guided radiation therapy. In general, bony anatomy- and carina-based setup resulted in less uncertainty than tattoos. Carina and fiducials were found to be more reliable than bone for tumor localization.

Only a few reports specifically analyze positional variations of involved LNs as part of the gross tumor volume. Recent publications either investigated LNs over a short time period at the beginning of radiation therapy only (5, 6, 14), used suboptimal imaging for LN assessment with CBCT (10), or used respiration management techniques that are not widely used, such as gating or active breathing control (7, 8).

This study analyzed PT and LN position changes relative to each other and relative to anatomic landmarks during conventionally fractionated radiation therapy using state-of-the-art imaging with weekly free-breathing 4-dimensional computed fan-beam tomography (4D CT) with good detectability of PT and LN soft-tissue boundaries. Different from other studies (15), time trends of the positional variations and the influence of PT and LN volume regression and PT location on the observed positional variations were evaluated. In addition, safety margins were calculated for the different setup scenarios.

Methods and Materials

Patient characteristics

In a prospective, institutional review board-approved image acquisition study 12 consecutive patients with stage 3A locally advanced non-small cell lung cancer were enrolled. All patients were treated according to department protocol with definitive conventional radiation therapy (1.8-2 Gy per fraction for 5 days per week to total dose between 64.8 and 70 Gy) combined with concurrent chemotherapy. Table 1 shows patient-specific clinical data.

Image acquisition and contouring

All patients underwent a 4D planning CT scan and weekly 4D CTs (Brilliance Big Bore; Philips Medical Systems, Andover, MA) with audiovisual biofeedback during their course of radiation therapy (16). Four to eight 4D CTs per patient (total of 65) with a slice thickness of 3 mm and 512 × 512 axial resolution (approximately 1-mm pixel size) were acquired. Primary tumor, involved LNs, a thoracic vertebra, and carina were manually contoured by 1 physician on the 10 respiratory phases of each 4D CT (total of 650 3-dimensional [3D] CT scans) using a commercial treatment planning system (Pinnacle, version 8.1; Phillips, Fitchburg, WI). The vertebra selected for contouring was in the central thoracic spine, close to the involved LNs and the carina. Because no contrast was used, only well-identifiable mediastinal LNs (total 17) were contoured. To minimize any contouring variation, contours were copied between phases and manually corrected. In addition, templates of PT and LNs were created from each patient's initial 4D CT scan as contouring guidelines to reduce contouring variability between weekly scans. Although all LNs and the parts of the PTs next to mediastinum, diaphragm, and chest wall were contoured in the default mediastinal window, PTs neighboring lung tissue were delineated in the lung window. The carina landmark was defined as a point at the most superior tip of the cartilaginous ridge between the main bronchi in the lung window. All contours were reviewed by a second physician.

Data analysis

Three-dimensional displacement vectors, systematic/random displacements, and resulting margins

To analyze the interfractional positional variability of contoured structures for each patient, first the average centroid positions of PT, LNs, and vertebra were calculated for each 4D CT by determining the geometric center of each structure for each breathing phase in the 3 cardinal directions and averaging these positions over the 10 breathing phases. Similarly, for calculating the average carina position, the carina point coordinates were averaged over the 10 breathing phases for each 4D CT. After assessing the distances between the average centroid positions of PT/LN, PT/vertebra, PT/carina, LN/vertebra, and LN/carina per 4D CT of each patient, variations in the distances between these centroid positions between the initial planning scan (reference) and the subsequent scans during therapy were determined for lateral (x), anteroposterior (y), and craniocaudal (z) directions by subtracting the distance between 2 average centroids for each weekly 4D CT from the distance measured on the reference planning scan. From these results, 3D displacement vectors were calculated as the square roots of the summed squared displacements in the 3 directions for each 4D CT and each patient. Displacements for all 3 directions and for 3D displacement vectors were averaged over all scans of each patient and over all patients. The dependence of displacements on PT location was analyzed.

Systematic and random displacements were calculated according to Van Herk (17). Systematic displacements were defined as the standard deviations of the individual patients' mean centroid displacements averaged over all 4D CTs per patient in the 3 cardinal directions. Random displacements were calculated as the square root of all patients' average variances that were derived from the individual patients' standard deviations of the average centroid displacements per 4D CT in the 3 cardinal directions averaged over all 4D CT scans. Systematic and random displacements were used to calculate setup margins for PT-, vetebra-, and carina-based image guidance according to Van Herk et al's formula corrected for penumbra in lung tissue (18). The setup margins do not include variations in respiratory motion or contouring variability. Both are presumed to be small, assuming motion-inclusive planning (19) and having 1 observer