Int. J. Radiation Oncology Biol. Phys., Vol. 74, No. 1, pp. 290–296, 2009

0360-3016/09/$–see front matter

ELSEVIER

doi:10.1016/j.ijrobp.2008.12.060

**PHYSICS CONTRIBUTION**

# IMPLICATIONS OF RESPIRATORY MOTION AS MEASURED BY FOUR-DIMENSIONAL COMPUTED TOMOGRAPHY FOR RADIATION TREATMENT PLANNING OF ESOPHAGEAL CANCER

Abhijit A. Patel, M.D., Ph.D., John A. Wolfgang, Ph.D., Andrzej Niemierko, Ph.D., Theodore S. Hong, M.D., Torunn Yock, M.D., and Noah C. Choi, M.D.

Department of Radiation Oncology, Massachusetts General Hospital, Boston, MA

**Purpose: To evaluate the respiratory motion of primary esophageal cancers and pathologic celiac-region lymph nodes using time-resolved four-dimensional computed tomography (4D CT).**

**Methods and Materials: Respiration-synchronized 4D CT scans were obtained to quantify the motion of primary tumors located in the proximal, mid-, or distal thoracic esophagus, as well as any involved celiac-region lymph nodes. Respiratory motion was measured in the superior–inferior (SI), anterior–posterior (AP), and left–right (LR) directions and was analyzed for correlation with anatomic location. Recommended margin expansions were determined for both primary and nodal targets.**

**Results: Thirty patients underwent 4D CT scans at Massachusetts General Hospital for planned curative treatment of esophageal cancer. Measurements of respiratory tumor motion were obtained for 1 proximal, 4 mid-, and 25 distal esophageal tumors, as well as 12 involved celiac-region lymph nodes. The mean (SD) peak-to-peak displacements of all primary tumors in the SI, AP, and LR dimensions were 0.80 (0.45) cm, 0.28 (0.20) cm, and 0.22 (0.23) cm, respectively. Distal tumors were found to have significantly greater SI and AP motion than proximal or mid-esophageal tumors. The mean (SD) SI, AP, and LR peak-to-peak displacements of the celiac-region lymph nodes were 0.92 (0.56) cm, 0.46 (0.27) cm, and 0.19 (0.26) cm, respectively.**

**Conclusions: Margins of 1.5 cm SI, 0.75 cm AP, and 0.75 cm LR would account for respiratory tumor motion of >95% of esophageal primary tumors in the dataset. All celiac-region lymph nodes would be adequately covered with SI, AP, and LR margins of 2.25 cm, 1.0 cm, and 0.75 cm, respectively.** 

**Esophageal cancer, Tumor motion, Four-dimensional CT, Lymph nodes, Internal target volume.**

## INTRODUCTION

Radiotherapy is commonly used with concurrent chemotherapy as either definitive or preoperative treatment for esophageal cancer (1–5). The radiation fields are typically defined on the basis of structures identified in a helical CT scan obtained while the patient is freely breathing. Motion of thoracic and abdominal contents with respiration has been shown to introduce significant artifacts and inaccuracies in the CT images (6) and has raised concern about the possibility of underdosing part of a moving tumor. To adequately cover the moving target within the radiation field without irradiating excessive surrounding normal tissue, precise information about the magnitude and direction of tumor motion should ideally be obtained for individual patients.

The International Commission on Radiation Units and Measurements Report 62 (7) modified the definition of the planning target volume to include two distinct components: (1) the setup margin to account for uncertainties in beam alignment and patient position, and (2) the internal target volume (ITV) to account for variations in size, shape, and position of the tumor. Respiration-synchronized four-dimensional (4D) CT has enabled more accurate, patient-specific measurement of the ITV for tumors that move with respiration, permitting customization of target volumes to minimize dose to normal tissues while avoiding a geographic miss.

If 4D CT is unavailable or impractical for routine patient simulations, margins to account for tumor motion must be applied to helical CT volumes on the basis of knowledge of measurements taken from a population of patients. Although several studies have examined the respiratory motion of tumors in the lung (8–12) and infradiaphragmatic organs (13–15), the literature describing esophageal tumor motion

Reprint requests to: Noah C. Choi, M.D., Department of Radiation Oncology, Massachusetts General Hospital, Harvard Medical School, 100 Blossom Street, Boston MA 02114. Tel: (617) 726-5184; Fax: (617) 726-3603; E-mail: nchoi@partners.org

A.A.P.'s present address is: Department of Therapeutic Radiology, Yale University School of Medicine, New Haven, CT.

Conflict of interest: none.

*Acknowledgments*—The authors thank Dr. Brian Alexander for assistance with statistical analysis.

Received Nov 17, 2008, and in revised form Dec 14, 2008. Accepted for publication Dec 15, 2008.

is limited. Lorchel *et al.* (16) have reported measurements of esophageal tumor motion by acquiring CT scans during inspiratory and expiratory breath-hold for a series of 8 patients (16). Dieleman *et al.* (17) analyzed healthy esophageal motion using normal-breathing 4D CT in 29 patients with non-esophageal thoracic malignancies (17). Two recently published studies from the M.D. Anderson Cancer Center by Zhao *et al.* (18) and Yaremko *et al.* (19) have used normal-breathing 4D CT to characterize the motion of tumors at the gastroesophageal junction in 25 and 31 patients, respectively. To our knowledge, there are no published studies using normal-breathing 4D CT to evaluate the motion of malignancies in the upper, mid-, and lower esophagus. Moreover, measurement of the motion of pathologically enlarged or positron emission tomography (PET)-positive celiac region lymph nodes has not been previously reported. Because the craniocaudal radiation field margins typically used for celiac region nodes (approximately 2 cm) are not as generous as those used for esophageal primary tumors (approximately 5 cm) (20), it is particularly important to characterize their motion.

In the present study, we retrospectively evaluated the respiratory motion of esophageal tumors and involved celiac-region lymph nodes using 4D CT during quiet breathing in 30 patients. We aimed to determine adequate radiation field expansion margins to account for motion of primary tumors in the upper, mid-, and lower esophagus, as well as involved celiac-region lymph nodes. We also examined the association between primary tumor location and magnitude of motion.

## METHODS AND MATERIALS

### *Patients*

Thirty-five patients with pathologically confirmed squamous cell carcinoma or adenocarcinoma of the thoracic esophagus underwent 4D CT scanning for radiation treatment planning at Massachusetts General Hospital between July 2004 and September 2007. Patients with cervical esophageal malignancies were excluded. Scans of 5 patients could not be un-archived for technical reasons. Therefore, the 4D CT simulations of 30 patients constitute the dataset for this study. Eligible patients had tumors of Stages I–IVA, defined as T1–4, N0–1, M0–1a according to the American Joint Committee on Cancer staging guidelines. Six patients were found to have distant metastatic disease (M1b) after the treatment-planning CT had already been performed (their scans were not excluded from the analysis). All patients were planned to be candidates for either definitive or neoadjuvant radiotherapy at the time of CT scanning. Inclusion in the study required the ability to follow instructions during the acquisition of 4D CT images. All scans were performed without spirometry.

### *CT Scanning*

Four-dimensional CT scans were performed on patients with esophageal cancer using a GE Lightspeed QX/i four-slice CT scanner (GE Medical Systems, Milwaukee, WI). Patients were positioned supine with their arms above their head, with a standard wingboard used for immobilization. The Varian Real-time Position Management (RPM) system (Varian Medical Systems, Palo Alto, CA) was used to monitor the breathing cycle. The RPM system uses infrared beams from stationary sources mounted in the room to measure the displacement of infrared-reflecting markers placed on the epigastric region of the patient's abdomen. Motion of the external markers on the abdomen is correlated with motion of the intrathoracic and intra-abdominal structures. A standard, helical, free-breathing CT scan was obtained first for all patients. Patients were instructed to continue quiet free breathing during scanning, defined as normal, unlabored breathing without deep inspiratory or expiratory efforts. For 4D CT scans, up to 1500 CT slices were acquired for each patient, and the images were then sorted by respiratory phase to generate 10 complete CT datasets using Advantage 4D software (GE Medical Systems).

### *Measurements of tumor motion*

The CT datasets were loaded into a commercial treatment-planning system (Fusion; GE Medical Systems), and each of the 10 respiratory phases were fused to the standard free-breathing scan. Rigid body fusions were performed using the vertebral spine as the reference for alignment because this was judged to be the structure most likely to be stationary during the respiratory and cardiac cycles. Software was developed in-house to permit visualization of the 10 respiratory phases as a cycling movie in the axial, coronal, and sagittal planes. The CT phases representing maximal inspiration and maximal expiration during quiet breathing were identified by visual inspection. A single physician (A.A.P.) measured the motion of the primary esophageal tumors, as well as any pathologically enlarged or PET-positive celiac-region lymph nodes that were well circumscribed. The software enabled overlaying of a stationary grid with 0.5-cm spacing to facilitate accurate quantification of target motion. Maximal displacements of the superior, inferior, anterior, posterior, and lateral edges of the tumors and lymph nodes were measured. The measurements were rounded to the nearest 2.5 mm, which was thought to be the smallest distance that was reliably discernible. Because of the possibility of tumor deformation, the maximal displacement of the superior edge of the target did not necessarily equal that of the inferior edge of the target. To account for this possibility, we measured motion according to the peak-to-peak convention (21). The peak-to-peak motion in the craniocaudal (superior–inferior [SI]) dimension was defined as the average (arithmetic mean) of the displacements of the superior and inferior tumor edges. Peak-to-peak motion was similarly recorded for each tumor in the anterior–posterior (AP) and left–right (LR) dimensions. Total three-dimensional motion was estimated by calculating the square root of the sum of the squares of peak-to-peak motion in each dimension.

### *Margin expansions for ITV coverage*

Because it is not always possible or practical to obtain patient-specific measurements of target motion, it is important to determine adequate field margin expansions that would account for expected motion on the basis of knowledge of such motion in a population of patients. To avoid a partial geographic miss, the ITV expansion in a particular direction would have to be at least as large as the maximum displacement of the edge of the tumor in that dimension. Because tumor deformation was judged to be unpredictable, if the maximal displacement of the one edge differed from that of the opposite edge, the larger of the two values was used. We determined the minimum expansion necessary to cover the ITVs of 95% of the tumors in the SI, LR, and AP dimensions. A similar calculation was performed to determine the expansion necessary to cover 100% of the tumors in our dataset. Because we did not presume a Gaussian