Fiducial Marker Placement Using Endobronchial Ultrasound and Navigational Bronchoscopy for Stereotactic Radiosurgery: An Alternative Strategy

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Background. **Stereotactic radiosurgery is being increasingly used to treat patients with early-stage non-small cell lung cancers (NSCLC) who are not candidates for surgical resection. Stereotactic radiosurgery usually needs fiducial markers (FMs) for the tracking process. FMs have generally been placed using percutaneous computed axial tomography scan guidance. We report the results of FM placement using endobronchial ultrasound (EBUS) in 43 patients.**

Methods. **A multidisciplinary tumor board evaluates NSCLC patients before they are offered stereotactic radiosurgery. In patients selected for stereotactic radiosurgery, FMs were inserted into peripheral, central, and mediastinal tumors using EBUS and, in selected patients, navigational bronchoscopy. Patients underwent repeat computed axial tomography chest scans 2 weeks later to ensure stability of the FMs before beginning stereotactic radiosurgery.**

Results. **Included were 43 consecutive patients (21 men, 22 women; mean age, 74.4 years). Forty-two (98%) had NSC carcinomas (5 recurrences); 1 had a carcinoid tumor. Twenty-two tumors were located in the left lung, 19 in the right lung, 1 at the carina, and 1 pretracheal. Two to 5 FMs were placed in and around all tumor masses using EBUS and, for peripheral lesions, EBUS combined with navigational bronchoscopy. Thirty patients had no displacement of FMs. In the 13 who had displaced 1 or more FMs, the ability to use the remaining FMs for stereotactic radiosurgery was unimpaired.**

Conclusions. **EBUS and navigational bronchoscopy are safe and effective methods to position FMs for preparing patients with both central and peripheral lung cancers for stereotactic radiosurgery.**

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Lung cancer is a global epidemic. In 2002 there were 1.35 million new cases of lung cancer causing 1.18 million deaths [1]. The United States has been a major contributor to these statistics. In 2004 an estimated 358,128 Americans were living with lung cancer. In 2007 an estimated 213,380 new cases were diagnosed, and about 160,392 Americans were expected to die of lung cancer. Approximately 16% of the patients are diagnosed with early-stage lung cancer [2], and theoretically, most of these patients would be candidates for a potentially curative resection.

Many of patients with lung cancer are afflicted with severe smoking-induced morbidities such as chronic obstructive pulmonary disease (COPD), and arteriosclerotic heart disease that will preclude any attempts at curative resection. Some will have severe age-related disabilities, and some who would be physiologically able to tolerate the operation will refuse despite impartial presentation of evidence that surgical resection of lung cancer is the optimal method for achieving long-term survivorship [3].

The evolution of newer radiosurgical and bronchoscopic technologies is offering alternatives for the diagnosis and treatment of thoracic malignancies. Stereotactic radiosurgery (SRS) was originally designed as a neurosurgical tool in the 1950s [4], but because of the need for a rigid compression device to limit respiration and a rigid immobilization frame for the thorax [5, 6], it was not used for treatment of lung tumors.

The Cyberknife with Synchrony (Accuray Robotic Radiosurgery Systems, Accuray Inc, Sunnyvale, Ca) overcame these difficulties. It did not need an immobilizing frame and allowed for real time respiratory tracking [7, 8]. However, small metallic markers called fiducials (FMs) need to be inserted in or near the target tumor to ensure the accuracy of the delivered radiation dose [9, 10].

The insertion of FMs with minimal morbidity has been problematic. They have been inserted percutaneously using computed tomography (CT) guidance, which has resulted in a pneumothorax rate of at least 13% [11]. This percentage may be low, because CT-guided biopsies have reported pneumothorax rates of 23% to 38% [12, 13],

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Abbreviations and Acronyms

ASHD = arteriosclerotic heart disease
CKS = cyberknife with synchrony
COPD = chronic obstructive pulmonary disease
CT = computerized tomography
DICOM = digital imaging and communications in medicine
EBUS = endobronchial ultrasound
ENB = electromagnetic navigational bronchoscopy
FFB = flexible fiberoptic bronchoscopy
FM = fiducial markers
NSCLC = non-small cell lung cancer
SRS = stereotactic radiosurgery

and a more recent series of FM placements using CT guidance reported an incidence of 48% needing pigtail catheter treatment of the pneumothoraces [14].

Flexible fiberoptic bronchoscopy has been used for the placement of FMs, but can result in FM embolization or inadvertent early deployment of the FM [15]. Although flexible fiberoptic bronchoscopy is useful in accessing central lung lesions, it has severe limitations in accessing lesions at the periphery of the lung [16, 17]. At the onset of developing our SRS program, we elected to use endobronchial ultrasound (EBUS) and electromagnetic navigational bronchoscopy (ENB) to minimize the morbidity associated with positioning FMs while simultaneously increasing the number of usable FMs.

Between February 2007 and June 2008, 391 patients with histologically proven bronchogenic carcinomas were evaluated for treatment at the Franklin Square Hospital Center in Baltimore, Maryland. The patients were reviewed at multidisciplinary thoracic tumor board before being considered for thoracic SRS. Patients with a forced expiratory volume in one second of less than 40% and a diffusion capacity of the lung of less than 40% were considered to have severe chronic obstructive pulmonary disease (COPD) and in most instances were not considered candidates for surgical resection. The Institutional Review Board of MedStar Inc, the parent corporation of the Franklin Square Hospital Center, approved the data collection and analysis of these patients and waived patient consent for this review.

Material and Methods

All procedures were performed by 2 interventional pulmonologists trained in both EBUS and ENB. The methodology used was developed by one of the interventional pulmonologists (W.S.K.) and was followed by both physicians. The success rate for FM placement did not differ between these 2 pulmonologists.

All patients had noncontrast CT scans of the chest configured with slices of 0.6-mm thickness at 1-mm intervals in the Digital Imaging and Communications in Medicine (DICOM) format. All FM placements were done with the patient under general anesthesia using the oral route. Before the start of each procedure, the patient was positioned on the electromagnetic location board (superDimension Inc, Plymouth, MN) in anticipation of the possible need for ENB. The bronchoscope was an Olympus BF-1T180, 3.0-mm working channel, adult therapeutic bronchoscope (Olympus, Tokyo, Japan). EBUS was used in all of the patients and ENB was used selectively for peripheral tumors that were difficult to access using EBUS alone. Mean time for procedures was 44 $\pm$ 11 minutes.

EBUS Procedure

A 20-MHz radial EBUS probe (UM-S20–20R; Olympus) was used. The miniature probe was inserted into a guide sheath and was advanced as a unit into the working channel of the bronchoscope. This was guided into the bronchus of interest. The probe was extended until the operator sensed resistance and then slowly withdrawn while scanning. Ultrasound imaging of normal air-filled alveolar tissue produces a "snowstorm-like" whitish appearance. In contrast, in FM placement using EBUS, solid peripheral lesions are darker and more homogeneous.

When such images were seen, the target was considered to have been reached. After the peripheral lesion was localized, the probe was withdrawn, leaving the sheath either within or close to the target lesion. The FMs were then deployed through the guide sheath using fluoroscopy, if needed. In selected cases, if a peripheral lesion was difficult to reach, ENB was performed before the FMs were deployed.

ENB Procedure

The superDimension inReach System (superDimension Inc) was used for the ENB component of the procedures. The initial planning phase involved importing the CT scan into the software (superDimension) using the standard format. Registration points were marked by identifying five or six prominent anatomic landmarks on the virtual bronchoscopic images. The multiplanar images were used to plan a target pathway, starting from the target lesion and working toward a central airway. Endobronchial mapping was conducted, and the software generated a registration error that represents the radius of the expected difference in location between the tip of the sensor probe in the actual patient and where the tip is expected to be. The registration error could then be reduced by repositioning a misplaced landmark or by eliminating the landmarks with the greatest deviation. Navigation was completed by wedging the bronchoscope in the suspected bronchial segment and steering the sensor probe, together with the extended working channel, to the lesion using the multiplanar CT scan images and the "tip-view" orientation. The target was considered located when a minimum distance (< 1 cm) between the steerable probe tip and the target lesion was achieved. When navigation was completed, the steerable probe was removed.