Multimodality Guidance for Accurate Bronchoscopic Insertion of Fiducial Markers

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Introduction: Fiducial markers act as visible surrogates of tumor position during image-guided radiotherapy. Marker placement has been attempted percutaneously but is associated with high rates of pneumothorax and chest drain placement.

Methods: Patients undergoing radical radiation treatment for non–small-cell lung cancer underwent bronchoscopic implantation of gold fiducials using radial probe endobronchial ultrasound (EBUS) with virtual bronchoscopy and fluoroscopic guidance to achieve tumor localization and placement within/adjacent to peripheral lung tumors. For tumors not localized using radial EBUS, fiducial placement was achieved by electromagnetic navigation to the vicinity of the tumor.

Results: Eighteen fiducials were placed to mark 16 lesions in 15 patients. In nine patients (60%), fiducials were implanted at the time of diagnostic bronchoscopy. No procedural complications occurred. EBUS localization allowed marker implantation within the target lesion in 12 cases. In four lesions, electromagnetic navigation bronchoscopy-guided implantation achieved a median fiducial–lesion distance of 6 mm (mean 12 mm). No marker migration occurred after the implantation of two-band markers; however, early migration was observed in two of eight (25%) of the smaller linear fiducials. No migration during the course of radiation therapy was observed.

Conclusion: Fiducial marker placement is easily and safely performed bronchoscopically, including at the time of diagnostic bronchoscopy. Marker geometry appears important in stability of bronchoscopically inserted fiducials. Future studies are required to confirm the optimal marker size, geometry, and spatial relationship with the target lesion.

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The authors declare no conflict of interest.

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DOI: 10.1097/JTO.0000000000000389

ISSN: 1556-0864/15/1002-0324

Key Words: Stereotactic radiotherapy, Lung cancer, Endobronchial ultrasound.

(*J Thorac Oncol.* 2015;10: 324–330)

Fiducial markers are frequently used in management of pulmonary lesions to either aid localization of pulmonary lesions during minimally invasive surgery,[1,2] or precisely identify the location of pulmonary lesions being targeted with external beam radiotherapy.[3] Failure to locate small nodules at thoracoscopic surgery may result in incomplete resection or conversion to open thoracotomy. Peripheral lung tumors may demonstrate significant respiratory-induced motion, with large variations in magnitude and direction from patient to patient, fraction to fraction, and importantly, cycle to cycle.[4] The ensuing suboptimal targeting of radiation can result in excess toxicity and geographic tumor miss. There has particularly been an increasing interest in fiducial markers for image guidance for stereotactic ablative body radiotherapy.[5,6] Markers allowing reliable and accurate determination of lung lesion position have the potential to significantly improve treatment safety and outcomes.

Marker insertion through a percutaneous route has been associated with a high rate of complications.[7–9] Bronchoscopic placement is feasible but requires guidance tools to achieve accurate localization as lesions are not visible at bronchoscopy. Previous reports suggest that electromagnetic navigation guidance may allow marker placement in the vicinity of parenchymal lesions[10,11] though accuracy of placement remains poorly described. Only one previous study has utilized endobronchial ultrasound (EBUS), with electromagnetic navigation bronchoscopy (ENB) in selected cases, to guide marker placement. The authors reported a high degree of accuracy using the combination of guidance tools, though the exact contribution of each modality to accuracy is unclear.[12] The optimal methods to aid bronchoscopic marker implantation therefore remain uncertain, and no examination of marker features (size, shape, geometry) have been published.

Our institution utilizes numerous techniques to aid bronchoscopic localization of peripheral pulmonary lesions, including radial EBUS, virtual bronchoscopy (VB), and ENB. We have used fiducial markers to localize small pulmonary nodules, with a sequential approach to use of bronchoscopic techniques. In this report, we describe our preliminary

experience in implantation of two different types of lung fiducial markers and present our experience regarding the components of bronchoscopic fiducial marker placement and describe our preliminary experience in implantation of two different types of lung fiducial markers.

PATIENTS AND METHODS

Institutional review board approval was granted for performance of this prospective observational study. All patients provided written informed consent.

Consecutive patients referred for bronchoscopic fiducial marker placement were selected on the basis of the following:

1. Confirmed early stage peripheral lung malignancy in patients deemed medically inoperable, where fiducial marker placement was performed to aid external beam tumor irradiation, and
2. Presumed/confirmed pulmonary metastases, where marker placement was performed to aid stereotactic ablative body radiotherapy or to aid thoracoscopic resection of pulmonary metastases.

Bronchoscopic Localization of Target Lesion

Bronchoscopy was performed with a standard videobronchoscope (BF-MP160F or BF-P180; Olympus, Tokyo, Japan) under conscious sedation as previously described.[13] Guidance tools to ensure accurate marker placement were utilized in as "sequential" fashion, with VB planning and radial EBUS (described below) used to locate the target lesion in all patients. In patients where lesion position could not be confirmed by EBUS, within the same procedure ENB was used to identify the position within the bronchial tree closest to the target lesion.

Randomized trials have indicated VB significantly improves localization of small peripheral lesions.[14] We therefore completed VB preprocedure planning using multiplanar formatting of Digital Imaging and Communications in Medicine (DICOM) data from computed tomography (CT) chest (slice thickness 1.0 mm with 0.8 mm overlap). Three-dimensional reconstruction of the bronchial tree from DICOM images was performed using iLogic software (SuperDimension Inc., Plymouth, MN). A bronchoscopic pathway was determined using the iLogic software and localization of lesions was first attempted using radial EBUS as previously described,[13] based on the "virtual bronchoscopy" pathway.

If EBUS findings indicated successful localization of the lesion, the radial EBUS probe was removed, with the guide sheath remaining in situ. For lesions where preprocedure tissue diagnosis was known, we proceeded to placement of the fiducial marker. In patients where tissue diagnosis was unconfirmed, bronchial brushings from the lesion were performed and subject to rapid on-site cytologic evaluation.[15] Only when brushings confirmed the presence of diagnostic malignant material was placement of fiducial marker performed.

In patients where radial EBUS was unable to confirm the location of the target lesion, we proceeded to ENB (inReach system, SuperDimension Ltd, Minneapolis, MN). Performance of this technique has been described in detail previously.[16] Briefly, bronchoscopic direction was controlled using a steerable locator guide emits low frequency electromagnetic waves. Electromagnetic signal is detected by an electromagnetic location board which lies underneath the patient. The position of the probe within the bronchial tree is localized within a virtual bronchoscopic tree which is constructed by the iLogic software from the DICOM images, as described above. Navigation to the lesion location is undertaken and the minimum average fiducial target registration error (AFTRE) was recorded. The locator guide was withdrawn from an extended working channel (EWC) and repeat EBUS examination was performed. Subsequently, sampling (brushings, TBLB, washings) was performed under fluoroscopic vision.

Marker Placement

Markers used were determined by marker availability. Markers were either a linear fiducial 10 × 0.75 mm linear marker (Visicoil; Robertson Medical, Coffs Harbour, Australia), or a two-band 13 × 0.9 mm marker (superLock; SuperDimension Ltd, Minneapolis, MN) (Fig. 1).

Before the removal of the radial EBUS probe, or steerable locator guide, fluoroscopic imaging was used to determine the location of the lesion within the lung fields. Markers were then inserted into the guide sheath (EBUS-located lesions) or EWC (ENB procedures) and advanced to the tip of the sheath using sampling instruments. Insertion was performed under fluoroscopic vision to ensure that the location was the same as where the lesion had been located.

Postprocedure Imaging

Patients underwent chest x-ray (CXR) within 2 hours of their procedure to confirm marker position and retention. More detailed imaging was performed with 4D planning CT 7 to 12 days postprocedure. This study confirmed the positioning of the marker relative to the target lesion (marker accuracy). Confirmation of retention of the marker (marker stability) was also noted at this study. Subsequent imaging was performed according to clinical need.

The positioning of the marker relative to the target lesion (marker accuracy) was established was bas based on imaging obtained at the 4D planning CT.

RESULTS

From September 26, 2012 to February 19, 2014, 18 fiducials were placed bronchoscopically to mark 16 lesions

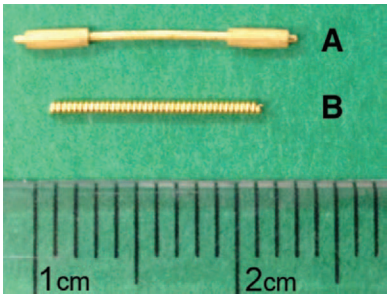

FIGURE 1. Fiducial markers used. *A,* 10 × 0.75 mm linear marker and (*B*) two-band 13 × 0.9 mm marker.

