Thoracic Fiducial Placement via Flexible Bronchoscopy

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CONTENTS

11.1 Abstract

CyberKnife® (Accuray Incorporated, Sunnyvale, CA) Frameless Image-Guided Radiosurgery [1, 2] with the Synchrony® Motion Tracking Module (Accuray Incorporated) [3, 4] is now available for the treatment of thoracic malignancies. Gold fiducial markers are required for the treatment planning and tracking of the tumor during each treatment. Fiducials have traditionally been placed percutaneously under CT-guidance. This chapter describes our center's experience placing fiducials using flexible bronchoscopy with a transbronchial aspiration needle (TBNA).

11.2 Introduction

The Synchrony Motion Tracking Module provides accurate and effective tracking of tumor movement throughout the respiratory cycle and provides compensation for the observed movement. To optimize tumor identification, the Synchrony module currently requires the placement of radio-opaque markers called fiducials, which can be visualized on plain film radiographs acquired during CyberKnife treatment. Traditionally, thoracic fiducial placement has been performed percutaneously under computed tomography (CT) guidance and has been associated with a 20–40% incidence of pneumothorax. Efforts to overcome this risk have led to increased adoption of alternative techniques, such as bronchoscopic methods of fiducial placement.

Fiducial markers are typically composed of gold and measure 3 mm in diameter (Fig. 11.1). Gold fiducials are placed either within the tumor or in close approximation to the tumor. Optimal treatment requires 3 to 5 well-placed fiducials to allow for assessment of both directional and rotational tumor movement.

Thoracic fiducial placement requires the placement of fiducial markers within the lung and thus poses significant risks to patients, such as pneumothorax, hemorrhage, hemoptysis, and migration of the markers. Patients undergoing CyberKnife stereotactic radiosurgery for thoracic malignancies are usually high-risk patients with multiple comorbidities that may exclude them from conventional therapy. Often they are not surgical candidates due to severe chronic obstructive pulmonary disease (COPD), coronary artery disease, or prior surgery

and thus are more likely to experience deleterious effects from additional risks posed to them.

At our institution the risk of pneumothorax after percutaneous CT-guided fiducial placement has been 35%. This risk is increased if a biopsy is obtained at the time of fiducial placement. Twenty-four percent of the patients who developed a pneumothorax required thoracostomy tube insertion. In addition, 24% of patients have developed hemorrhage seen on CT images, 4% have developed hemoptysis, and 5% had fiducials dropped into the pleural space during insertion [5].

Flexible bronchoscopy may be performed under conscious sedation or general anesthesia and is a common, safe, and accurate technique used to biopsy peripheral lung masses as well as mediastinal lymphadenopathy. The risks of flexible bronchoscopy include: reaction to the anesthetics, hypoxemia, bronchospasm, and bleeding (1–4%) after transbronchial biopsy. The incidence of pneumothorax with a transbronchial biopsy is 1–4%. No cases of pneumothorax following transbronchial needle aspiration (TBNA) of the mediastinum have been reported in the literature [6]. Single cases of hemomediastinum and pneumomediastinum have been reported with TBNA [7, 8].

We hypothesized that placing fiducials through flexible bronchoscopy using a modified transbronchial needle aspiration technique would be a safe, accurate, and lasting method for marking tumors in the mediastinum and larger masses in the parenchyma of the lung.

11.3 Methods

All patients referred to Georgetown University Hospital for CyberKnife stereotactic radiosurgery treatment of thoracic malignancies, were reviewed by a multidisciplinary thoracic oncology team. Patients were evaluated by a radiation oncologist, pulmonologist, and radiologist to determine if the intrathoracic tumor would be more amenable to fiducial placement via flexible bronchoscopy or CT-guided percutaneous techniques. Patients with centrally located or larger peripheral tumors (> 5 cm) were selected for fiducial placement via flexible bronchoscopy. Informed consent was obtained from all patients and collection of data was approved by the Institutional Review Board.

Video flexible bronchoscopy (Pentax Medical Company, Montvale, NJ) was performed under conscious sedation (fentanyl/midazolam or propofol) or general anesthesia at the discretion of the anesthesiologist. Patients who underwent general anesthesia were intubated with an endotracheal tube or a laryngeal mask airway. Two percent lidocaine was used for topical anesthesia of the airways.

Each sterilized gold fiducial (item no. 351-1; Best Medical International, Inc., Springfield, VA) was placed in the 19-gauge needle of a 19/21-gauge Wang transbronchial needle (C. R. Bard Inc., Billerica, MA) with the 21-gauge needle retracted (Fig. 11.2). The needle tip was then dipped in sterile surgical

Fig. 11.1 Gold fiducials.

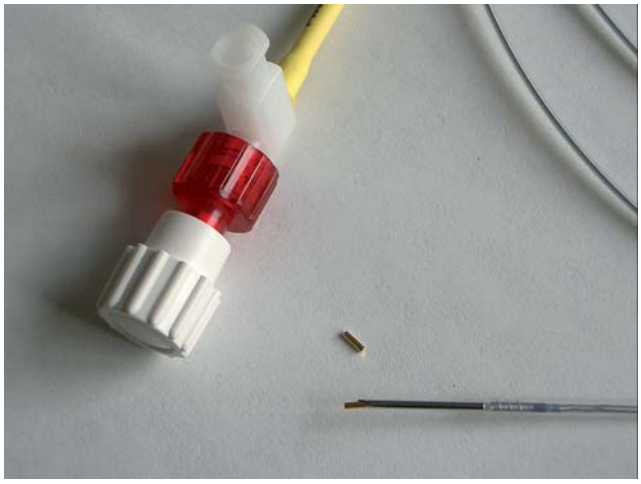

Fig. 11.2 Loading of gold fiducials into a 19/21 gauge TBNA needle.

lubricant (Surgilube; Fougera, Melville, NY) to improve the fiducial's adherence to the needle. Keeping the 21-gauge needle retracted, the 19-gauge fiducial-loaded needle was then retracted into the sheath and the sheath passed through a flexible bronchoscope. At the desired location, the 19-gauge needle was extended and inserted into the tumor through a jabbing method [7] using fluoroscopic guidance. The 21-gauge needle was tightened, deploying the fiducial (Fig. 11.3). Leaving the 21-gauge needle extended, the needle was then withdrawn from the tissue. The technique was repeated until all markers were placed.

Fiducials were positioned into or near the lung tumor. Careful planning was performed with the assistance of the radiation oncologist. Three to four markers were placed approximately 2 cm apart from each other and mindful of the 45 degree angle of the fluoroscopy units used in the CyberKnife suite. Care was taken to avoid great vessels in the mediastinum and hilum during placement. Portable chest radiographs were obtained after all procedures to rule out pneumothorax and confirm the position of the fiducials (Fig. 11.4) [9].

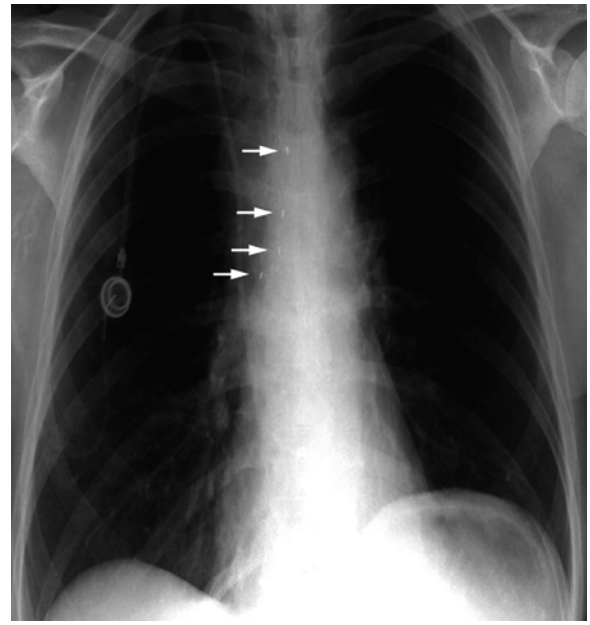

Fig. 11.4 Post procedure chest X-ray demonstrating mediastinal fiducial placement.

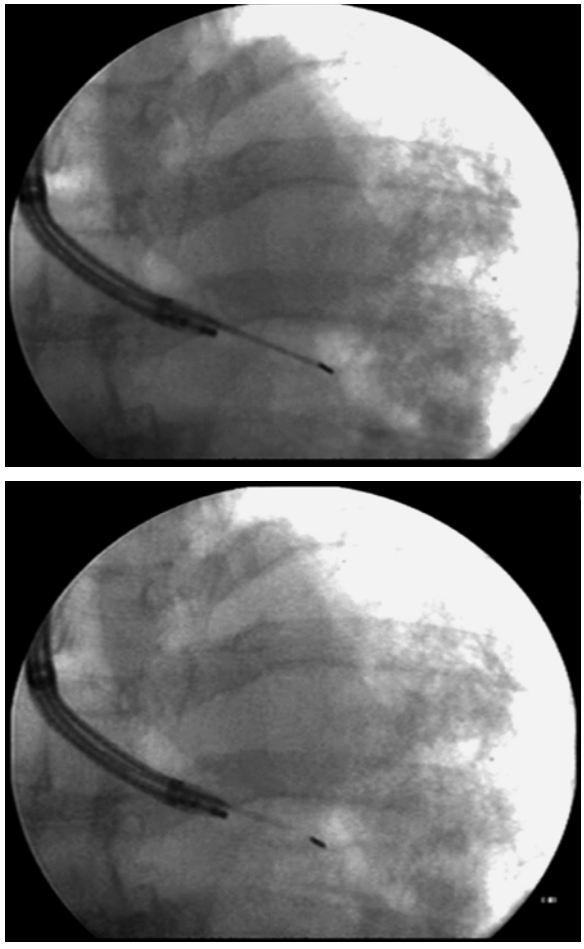

Fig. 11.3a,b. The TBNA needle is extended into the target and fluoroscopy is used to visualize deployment of the fiducial.

Patients underwent planning CT scan 7–10 days after fiducial placement to allow for fixation of fiducials. Data collected included patient demographics, number and location of fiducials placed, and complications associated with their placement.

11.4 Results

Between July 2004 and August 2006 a total of 32 patients underwent fiducial placement via flexible bronchoscopy. One patient underwent a second procedure to obtain additional tissue for pathology and because one fiducial had migrated out from a paratracheal location. Sixty-seven percent of patients were female and 87% were Caucasian. The age range was 35–81 years (mean age 59 years).

The most common diagnosis was non-small cell lung cancer (58%). Other diagnoses included metastatic disease to chest (38%) and one patient was diagnosed with small cell lung cancer at the time of bronchoscopy. The main reason for choosing CyberKnife therapy was previous radiotherapy to the chest. Other reasons included: suboptimal anatomic location of tumor for treatment by conventional irradiation because of adjacent critical structures, lack of response to prior conventional irradiation, severe COPD or coronary artery disease, and prior lung resection.

A total of 124 fiducials were successfully inserted (average of 3.9 fiducials per target lesion). Fifty-two were placed in the mediastinum, 19 in the hila, and 53 in the lung parenchyma (Table 11.1). Sixty-nine percent of patients underwent general anesthesia and 31% conscious sedation.

During the bronchoscopies 25 fiducials were dropped in the airways prior to insertion, 18 were removed with bronchopulmonary-coated disposable biopsy forceps (C. R. Bard Inc., Billerica, MA), two were suctioned, three were coughed out, and two were not retrieved. The latter were not seen on post-procedure chest X-rays (Fig. 11.5a and b).

Complications included one fiducial migration after insertion as noted above. One patient with severe COPD, who underwent endotracheal intubation, developed bronchospasm requiring mechanical ventilation for 48 hours. There were no pneumothoraces or significant bleeding.

Table 11.1 Location of Fiducials Placed via Bronchoscopy

32 Patients Average fiducials per tumor	124 Fiducials placed 3.9
Locations	
Paratracheal area	15 (station 2 and 4)
Subcarinal	21 (station 7)
Left mainstem	5
Left hilum	12 (station 11L)
Right mainstem	2
Right hilum	7
Right bronchus intermedius	9 (station 11R)
Right upper lobe (RUL)	6
Right middle lobe (RML)	4
Right lower lobe (RLL)	7
Left upper lobe (LUL)	20
Left lower lobe (LLL)	16

Three fiducials in two patients embolized during insertion via the pulmonary artery without adverse clinical consequence. The embolizations were immediately visible under fluoroscopy. The first occurred during placement of a fiducial in a subcarinal location. The other two occurred in a single patient in whom fiducials were placed in a left parahilar mass (Fig. 11.6).

11.5 Discussion

CyberKnife frameless image-guided radiosurgery with the Synchrony motion tracking module is now available for the treatment of thoracic malignancies. Gold fiducial markers are required for the treatment planning and tracking of the tumor during each treatment. Fiducials have traditionally been placed percutaneously under CT-guidance. Flexible bronchoscopy may be used to safely and accurately place fiducials for centrally located and larger peripheral tumors in the chest.

Tumors in the periphery should be greater than 1 cm in order to be visible under fluoroscopy. Peripheral lesions not visible under fluoroscopy should be considered for CT-guidance. At least three fiducials were placed in close proximity to each target lesion. Additional markers were often placed to account for any poorly positioned markers and to assure that tracking could be performed accurately. Mindful of the 45 degree orthogonal plain film imaging used in the CyberKnife suite to avoid overlap of the markers, fiducials were placed 2 cm apart from each other.

The complications of bronchoscopic fiducial placement include the risks inherent to bronchoscopy such as bronchospasm and respiratory failure. This patient population will be particularly at risk as many have severe lung disease already. Pneumothorax and hemorrhage have not occurred and should be a rare complication of bronchoscopic insertion. Placement in more peripheral locations may increase the likelihood of pneumothorax.

Fiducials dropped during the bronchoscopy may easily be removed with biopsy forceps. If not able to be located, dropped fiducials are usually coughed out immediately after the procedure. The develop-

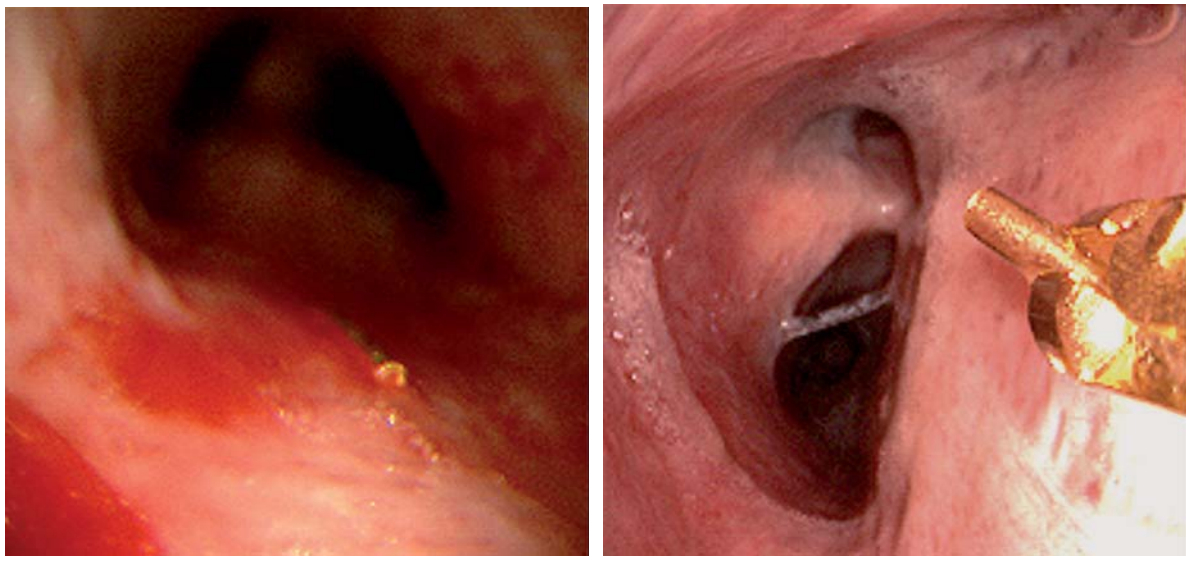

Fig. 11.5. a Dropped fiducial in left mainstem bronchus. **b** Retrieval of fiducial using biopsy forceps

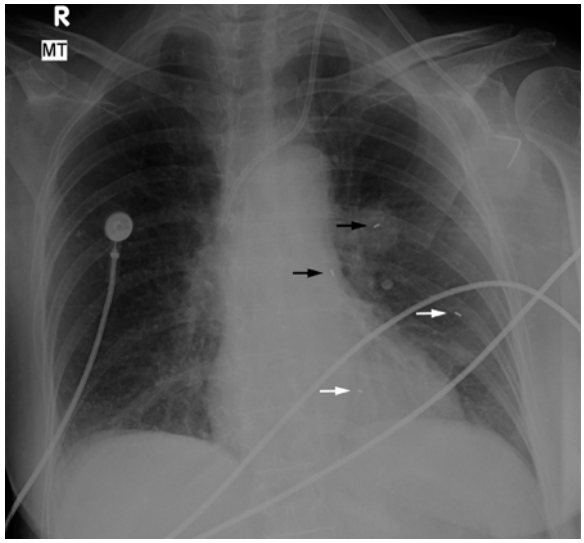

Fig. 11.6 Chest X-ray demonstrating left hilar nodule with fiducial placement. Two fiducials were observed in left lower lobe after embolization via left pulmonary artery (*white arrows*).

ment of a transbronchial needle deployment device might help decrease the incidence of this minor complication. Only a single fiducial, placed early in our experience, migrated out into the airway and was expectorated prior to treatment. It is possible that fiducials may migrate after implantation. Nevertheless, this has been infrequent and has not been a clinical problem secondary to the placement of multiple fiducials and the ability of the CyberKnife system to recognize fiducial migration.

The most important complication of bronchoscopic fiducial placement was embolization into the pulmonary artery. Unlike traditional TBNA, no blood return can be seen in the catheter if inadvertent puncture of a vessel occurs during insertion. Careful planning is essential to avoid puncture of great vessels in the mediastinum, especially those of the systemic circulation where systemic embolization could result in a cerebrovascular accident or peripheral emboli. Endobronchial ultrasound, which allows for visualization of the major vascular structures in the mediastinum at the time of bronchoscopy, may be utilized in the future to reduce the risk of such an occurrence.

Insertion of fiducials into parenchymal tumors may result in embolization as the airways run adjacent to the pulmonary vasculature. This complication has not yet been reported after CT-guided placement of fiducials, but seems possible. Embolization into the pulmonary artery, however, appears to be of low risk. Neither of our patients in whom this occurred developed late sequelae of fiducial embolization. Radioactive seeds of similar dimensions are commonly used to treat early stage prostate cancer and have been known to embolize to the pulmonary arteries. It is estimated that 1% of prostate seeds migrate to the lungs and have not been associated

with clinical symptoms. These patients did not require systemic anticoagulation and were not found to have an increased incidence of thromboembolic disease [10, 11].

An alternative method of bronchoscopic fiducial placement has been described [12–14], using a wire to push the fiducial through a plastic catheter extended through the bronchoscope working channel. In this method, however, markers were pushed into the distal airways, but not implanted into tissue. As a result, a large number (25–35%) of fiducials became dislodged prior to the planning CT scan and treatment. This complication was more common when placing fiducials in upper lobe tumors and centrally located tumors.

The use of electromagnetic guidance and virtual bronchoscopy may allow for more accurate placement of fiducials in smaller peripheral tumors. These techniques allow for CT reconstruction to plan a guided passage of the fiducial into a more precise location in the lung. Registration between the virtual bronchoscope and the video bronchoscope is accomplished and then a sheath is extended through the bronchoscope channel and positioned using a trackable probe under electromagnetic guidance. The fiducial needle may then be placed through the sheath. This technology may improve accuracy of bronchoscopic fiducial placement, especially for those lesions located in the periphery of the lung [15].

11.6 Conclusion

Flexible bronchoscopy using a modified transbronchial aspiration needle technique appears to be a safe method for placement of fiducials for mediastinal and centrally located thoracic tumors as a precursor to CyberKnife stereotactic radiosurgery. At our institution, flexible bronchoscopy is the preferred method for insertion of fiducials in mediastinal, hilar, and larger peripheral tumors. Percutaneous CT-guidance remains the preferred method of insertion for smaller peripheral nodules.

References

1. Adler JR, Jr., Murphy MJ, Chang SD, *et al.* Image-guided robotic radiosurgery. *Neurosurgery* 1999; 44:1299–1306; discussion 1306–1297.
2. Kuo JS, Yu C, Petrovich Z, *et al.* The CyberKnife stereotactic radiosurgery system: description, installation, and an initial evaluation of use and functionality. *Neurosurgery* 2003; 53:1235–1239; discussion 1239.
3. Coste-Manière È, Olender, D., Kilby, W., Schulz, R.A. Robotic Whole Body Stereotactic Radiosurgery: Clinical Advantages of the CyberKnife Integrated System. *Medical Robotics and Computer Assisted Surgery* 2005; 1:28–39.
4. Schweikard A, Shiomi H, Adler J. Respiration tracking in radiosurgery. *Med Phys* 2004; 31:2738–2741.
5. Reichner CA, Collins, B.T., Gagnon, G.J., Malik, S., Jamis-Dow, C., Anderson, E.D. Comparison of Fiducial Placement for Cyberknife Stereotactic Radiosurgery using CT-Guidance or Flexible Bronchoscopy. *Chest* 2005; 128:162–163S.
6. Wang K-P, Mehta, A., Turner,.Jr. J.F. Transbronchial Needle Aspiration for Cytology and Histology Specimens. In: Flexible Bronchoscopy: Malden: Blackwell Publishing; 2004. pp. 117–137.
7. Dasgupta A, Mehta AC. Transbronchial needle aspiration. An underused diagnostic technique. *Clin Chest Med* 1999;20:39–51.
8. Harrow EM, Oldenburg FA, Jr., Lingenfelter MS, *et al.* Transbronchial needle aspiration in clinical practice. A five-year experience. *Chest* 1989; 96:1268–1272.
9. Reichner CA, Collins, B.T., Gagnon, G.J., Malik, S., Jamis-Dow, C., Anderson, E.D. The Placement of Gold Fiducials for CyberKnife Stereotactic Radiosurgery Using a Modified Transbronchial Needle Aspiration Technique. *Journal of Bronchology* 2005; 12:193–195.
10. Ankem MK, DeCarvalho VS, Harangozo AM, *et al.* Implications of radioactive seed migration to the lungs after prostate brachytherapy. *Urology* 2002; 59:555–559.
11. Nag S, Vivekanandam S, Martinez-Monge R. Pulmonary embolization of permanently implanted radioactive palladium-103 seeds for carcinoma of the prostate. *Int J Radiat Oncol Biol Phys* 1997; 39:667–670.
12. Harada T, Shirato H, Ogura S, *et al.* Real-time tumor-tracking radiation therapy for lung carcinoma by the aid of insertion of a gold marker using bronchofiberscopy. *Cancer* 2002; 95:1720–1727.
13. Imura M, Yamazaki K, Shirato H, *et al.* Insertion and fixation of fiducial markers for setup and tracking of lung tumors in radiotherapy. *Int J Radiat Oncol Biol Phys* 2005; 63:1442–1447.
14. Morice A, Jimenez, L., Eapen, G.A., Nelson, C., Stevens, C.W., Starkschall, G. Bronchoscopic implantation of gold fiducials for estimating lung tumor motion during gated radiation therapy. *Chest* 2005; 128:163S.
15. Schwarz Y, Greif J, Becker HD, *et al.* Real-time electromagnetic navigation bronchoscopy to peripheral lung lesions using overlaid CT images: the first human study. *Chest* 2006; 129:988–994.