Preoperative Computed Tomography-Guided Pulmonary Lesion Marking in Preparation for Fluoroscopic Wedge Resection—Rates of Success, Complications, and Pathology Outcomes

Babatunde Olaiya, MD[a], Charles A. Gilliland, MD[a], Seth D. Force, MD[b], Felix G. Fernandez, MD[b], Manu S. Sancheti, MD[b], William C. Small, MD, PhD[a,*]

[a] Department of Radiology and Imaging Sciences, Emory University, Atlanta, GA
[b] Department of Cardiothoracic Surgery, Emory University, Atlanta, GA

Purpose: In this study, we describe our experience of lesion marking with fiducial markers (FM) and microcoils (MC) facilitating same-day surgical wedge resection, including success rates, pathology outcomes, and complications. We also explored patient/nodular characteristics associated with developing complications.

Materials and Methods: An IRB-approved single-institutional retrospective study of 136 patients who had 148 pulmonary nodules was conducted. All patients had CT-guided pulmonary nodule labeling with either FM (121) or MC (15) patients with plan for same-day fluoroscopic-guided wedge resection.

Results: Of 136 (98%) patients, 133 had successful same-day wedge resection as planned; 2 had delayed but successful wedge resection surgery due to complications at the time of marker placement (fiducial embolization and hemorrhage/pneumothorax, respectively). A third patient ultimately needed lobectomy due to deep lesion location. Eighty percent [118/148] of resected nodules were malignant. Further, 68% of the total group of patients [93/136] had mild complications of various types including hemorrhage [44/136, 32%], pneumothorax [35/136, 26%], a combination of both hemorrhage and pneumothorax [10/136, 7%], or migration/embolization [4/136, 3%]. Depth of nodule from skin ($P = 0.011$) and pleura ($P = 0.027$) was significantly associated with complications.

Conclusion: CT-guided marking of small or deep pulmonary lesions using either fiducial markers or microcoils provides an effective means to aid surgeons to accomplish minimally invasive wedge resection. The importance of the success of this technique is supported by the high incidence (80%) of malignant lesion etiology found at postresection pathology. Although complications occurred, the vast majority were mild and did not alter planned same-day resection.

Introduction

In many instances, solitary pulmonary nodules (SPN) are discovered as incidental findings during radiological investigations involving the neck, chest, or abdomen. These nodules are more frequently encountered in clinical practice in part due to more screening programs for high-risk patients as well as the increasingly widespread use of high-resolution computed tomography (CT) scanning during chest imaging.[1] The substantial risk and implications of malignancy necessitates prompt diagnosis and management of SPNs when discovered. Lung cancer remains the most diagnosed cancer and leading cause of cancer death worldwide.[2] Furthermore, identifying and removing early malignant lesions raises 5-year survival rates to 80% as opposed to 5% in advanced lung cancer.[3]

According to guidelines from the American College of Chest Physicians (ACCP), the approach to evaluating SPNs is based primarily on a patient's risks for malignancy and nodule characteristics.[4] Although these features can help differentiate benign from malignant lesions, definitive diagnosis of indeterminate pulmonary lesions is achieved mainly via histopathologic characterization of the lesion after biopsy or removal. Due to their small size and locations in the thorax, these lesions usually present a challenge. Although video-assisted thoracoscopic surgical (VATS) resection enables removal, the need for palpation to localize nodules during surgery raises the potential to miss small, nonpalpable lesions.[5,6]

Prior studies have highlighted the role of fiducial markers (FM) and microcoil (MC) implantation prior to VATS in facilitating the localization and safe and efficient removal of pulmonary lesions with reported success rates of over 98%.[7,8] However, these methods are not without complications which include pneumothorax, hemorrhage, and migration.[7,9] In this study, we assessed success rates for resection, pathology outcomes, and complication patterns for patients undergoing image-guided FM or MC placement in

preparation for VATS resection. We also explored associations between patient/nodular characteristics and development of complications after marker insertion.

Materials and Methods

Patient Selection

Institutional review board (IRB) approval was obtained, and a waiver of informed consent was granted for this Health Insurance Portability and Accountability Act compliant retrospective study. Clinical databases were searched to identify patients who had FM or MC placement for lung nodule resection between January 1, 1995 and January 22, 2016. Subsequently, relevant imaging and treatment records of identified patients were obtained from our clinical (Cerner Corporation, Kansas City, MO) and radiology picture archives/PACS (General Electric Centricity, GE Healthcare, Waukesha, WI).

Image-Guided Fiducial Marker and Microcoil Placement

FM or MC placement was accomplished using an interventional CT, either GE Lightspeed 16-slice scanner (GE Healthcare, Waukesha, WI) or Siemens Definition 16-slice scanner (Siemens Medical Solutions, Malvern, PA). Patients were placed in a position to minimize distance from skin to the lesion of interest without traversing a pulmonary fissure. Placement was facilitated by the use of moderate conscious sedation, typically a combination of intravenous Versed and fentanyl under continuous monitoring by a dedicated procedure nurse.

Gold fiducial markers (CIVCO Medical Solutions, Coralville, IA) measured 1.2 × 3 mm in size and were delivered via a coaxial 17 G introducer needle with the marker recessed within the lumen proximal to the tip. A central stylet was used to deliver the marker after positioning of the tip of the introducer needle along the margin of nodule of interest. In a total of 17 early patients receiving FM placement, 2 discrete markers were placed to bracket the lesion. Subsequently, with more experience, only a single FM was placed along the deep margin of the lesion to be removed. In all cases, repeat CT imaging was performed after delivery to confirm final positioning as a final guide for surgical resection and to evaluate for any postplacement complications.

Microcoil placement was achieved using Tornado Embolization Microcoils (Cook Medical, Bloomington, IN). These were typically delivered under CT guidance using a 20-gauge introducer with 1 to 3 coils placed to bracket the lesion. Again, immediate repeat CT was performed after delivery as a final guide for resection and to evaluate for complications.

Data Collection

Electronic medical records (EMR) were searched for each patient who had a FM or MC placement for lung nodule resection. Patient characteristics including age, sex, and body mass index (BMI) at the time of FM or MC placement were recorded. Computed Tomography (CT) scanning images prior to and following FM/MC insertion were reviewed by a single radiologist for nodule location and characteristics as well as postprocedure findings.

A single radiologist with 26 years of experience evaluated preprocedure imaging and determined maximum dimension of nodule, anatomical location of nodule, as well as depth of nodule both from skin and pleura along the course of planned delivery. Postprocedure imaging was performed as well with measurement of the distance from each FM or MC to the center of the nodule. Any postprocedure complications were assessed including the presence of pneumothorax

and the need for chest tube evacuation and hemorrhage. Pneumothoraces were estimated with regard to size (small−less than 10%, moderate−10%-30%, large−greater than 30%) as were complicating hemorrhage (small−minimal perilesional stranding, moderate−coalescent density 1-3 cm in size, and large−coalescent density greater than 3 cm in size).

Surgical pathology results were obtained for each lesion, and the final diagnosis for each nodule was determined.

Statistical Analysis

Statistical analysis included calculation of mean and standard deviation (SD) for patient's age, weight, height, and BMI. Similarly, mean and SD was computed for nodule size, depth of lesion from skin, and depth of lesion from pleura. Values used for a given patient represented the mean if more than one marker was placed. Prevalence of complications following FM/MC insertion was recorded as a percentage of the total patient population. Mean values were used to dichotomize age, weight, BMI, size, and depth of nodules into categorical variables. Bivariate chi-squared analysis was computed at a level of significance <0.05 to explore associations between patient/nodule characteristics and the development of complications.

Results

A total of 148 nodules in 136 patients were identified. Twelve patients had 2 lesions of interest while others had 1 each. Preoperatively, 142 fiducial markers (FM) and 33 microcoils (MC)−175 in total, were inserted to aid video-assisted thoracoscopic wedge resection in 121 and 15 patients, respectively.

The mean patient age was 61.7 years (S.D = 12.2), with slightly more males than females (73 M: 63 F). Mean weight, height, BMI, and other patient characteristics are summarized in Table 1.

In 45% [61/136] of patients, the lesion(s) of interest were located in the left lung (lower lobe = 38, upper lobe = 23) and 55% [75/136] in the right lung (upper lobe = 48, middle lobe = 6, and lower lobe = 21). The mean lesion size was 10.3 mm (SD = 4.6). The mean depth of the lesion from pleura and skin were 3.4 cm (SD = 2.2) and 8.3 cm (SD = 2.6), respectively. Table 2 summarizes the data with respect to numbers of lesions within different categories of size and information to numbers of lesions within different depth ranges.

The mean distance from the final deployed position of the FM to the center of the lesion was 7.6 mm (SD, 4.66) while the corresponding mean distance from the MC to the lesion center was 6.7 mm (SD, 5.45).

Further, 68% of the total group of patients [93/136] had complications of various types including hemorrhage [44/136, 32%],

TABLE 1
Patient demographic characteristics

Age, mean (SD), years	61.7 (12.2)
Sex, n (%)	
Male	73 (54)
Female	63 (46)
Height, mean (SD), m	1.71 (0.12)
Weight, mean (SD), kg	85.3 (24.4)
BMI, mean (SD), kg/m^2	28.9 (7.07)
Type of marker, n	
Fiducial markers	142
Microcoils	33

	Size (mm)	Nos of nodules	Depth from skin (cm)	Nos. of nodules	Depth from pleura (cm)	Nos. of nodules
	0-4.99	12	0-4.99	14	0-2.49	55
	5-9.99	68	5-9.99	98	2.5-4.99	64
	10-14.99	45	10-14.99	34	5-7.49	21
	>15	23	>15	2	>7.5	8
Total		148		148		148

FIG 2. Final image of a 9 mm lesion in the right lower lobe of a 65-year-old woman patient labeled using three microcoils, 2 anterior and 1 posterior to the nodule indicated by an arrow.

pneumothorax [35/136, 26%], a combination of both hemorrhage and pneumothorax [10/136, 7%], or migration/embolization [4/136, 3%]. Hemorrhage was graded as 37 small, 11 moderate, and 6 large, respectively. The size of pneumothorax was graded as 29 small, 5 moderate, and 11 large, respectively. Overall, 12 patients had a pneumothorax of sufficient size to warrant placement of a chest tube at the time of marker placement.

There were 2 cases of fiducial marker migration. In 1 case, the fiducial marker migrated within the lung, lodging within the subjacent pleural space. Fortunately, the tract of migration was visible at the time of surgery and proved useful to guide wedge resection. In the second, the fiducial shifted location due to pneumothorax requiring placement of a second FM in closer proximity to the lesion. There were 2 cases of intravascular fiducial embolization. In 1 case described previously,[7] the fiducial marker migrated via inadvertent intravascular deployment and embolized to the ventral aspect of the heart near the cardiac apex. Fluoroscopic evaluation demonstrated the marker to have embolized to a very distal portion of the left anterior descending artery; the position was such that retrieval was not warranted. The patient was admitted, monitored, and had a full recovery without incident. The patient later underwent successful wedge resection using guidance from a second fiducial marker that had been inserted at the time of the initial encounter. In a second case of inadvertent vascular deployment, the FC embolized into the contralateral lung; again a second fiducial placed at the time of the initial encounter successfully facilitated same-day wedge resection.

Fig 1 demonstrates a final image following labeling of a 12-mm lesion in the right upper lobe of a 74-year-old man using a single FM along the deep margin of the lesion. A corresponding image following marking of a 9-mm lesion in the right lower lobe of a 65-year-old woman patient using 3 microcoils is provided in Fig. 2 and 3 demonstrates an intraoperative specimen showing a central lesion with an immediate adjacent MC.

Nearly all patients [133/136] went to surgery for successful wedge resection on the same day the lesions were marked. Two patients had delayed surgery—one had delayed surgery due to patient preference after pneumothorax and chest tube placement, the other was delayed due to intravascular fiducial migration to the coronary artery
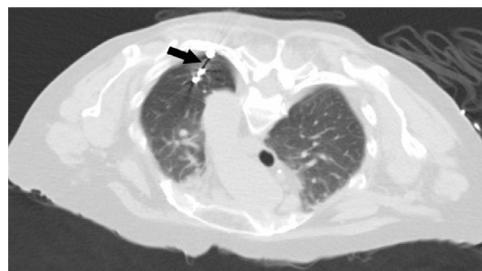
described above. A third patient ultimately had a failed attempt at wedge resection attempted the same day as FM placement. Despite successful removal of the fiducial, due to central nodule location and proximity to the pulmonary artery, wedge resection was deemed ill-advised and the patient ultimately underwent a later successful uncomplicated thoracoscopic lobectomy.

On bivariate analysis, only depth of lesion from skin (P = 0.011) and depth of lesion from pleura (P = 0.027) were significantly associated with developing any complication during lesion marking. No other nodular or patient characteristics were significantly associated with developing a complication. There was some degree of difference in complication rate between patients whose lesions were labeled with fiducial markers vs microcoils. Those receiving fiducials had a rate of hemorrhage of 34% as compared to 20% for patients receiving microcoils; the rate of pneumothorax in fiducial patients was 25% vs 13% in microcoil patients; the rate of combined pneumothorax/hemorrhage was 9% in patients with fiducial labeling vs 13% receiving microcoils. In general, there were fewer complications with microcoil use, though statistical significance was not reached—perhaps due to the smaller pool of microcoil patients.

Resected pulmonary nodules were malignant in 80% [118/148] of cases. Primary lung adenocarcinoma was most common [53/148, 36%], followed by metastatic colon cancer [23/148, 15.5%] and metastatic renal cancer [8/148, 5.4%]. Inflammation/scar tissue was the most common benign finding in 15.5% [23/148] of cases. Table 3 provides a full summary of resected nodules and pathology outcomes.

Discussion

Pulmonary nodules are becoming increasingly encountered in clinical practice for a variety of reasons including population demographics, a more widespread use of high-resolution computed

FIG 1. Final image following labeling of a 12-mm lesion indicated by an arrow in the right upper lobe of a 74-year-old male using a single FM along the deep margin of the lesion.


FIG 3. Image demonstrating an intraoperative specimen showing a central lesion with an immediate adjacent MC.

TABLE 3
Pathologic description of pulmonary nodules

Pathology	Number of nodules
Adenocarcinoma, lung primary	53
Metastatic colon cancer	23
Inflammation/scar/lymph node	23
Metastatic renal cell carcinoma	8
Squamous cell carcinoma	7
Carcinoid	4
Metastatic melanoma	6
Metastatic squamous cell carcinoma	4
Metastatic hepatocellular carcinoma	4
Bronchoalveolar carcinoma	3
Metastatic breast carcinoma	3
Metastatic pancreatic carcinoma	2
Metastatic papillary thyroid carcinoma	2
Metastatic adenoid cystic carcinoma	1
Large B-cell lymphoma	1
Metastatic angiosarcoma	1
Pulmonary hamartoma	2
Sinus histiocytosis	1

tomography in evaluating patients with known oncologic diagnosis and increasing utilization of lung cancer screening programs. Depending on imaging appearance as well as clinical and imaging history, a suspicious nodule requires consideration of prompt removal for diagnosis and an improved chance of early-stage cure. Although standard thoracoscopy methods for nodule removal have been utilized efficiently in the past, the reliance on finger palpation to identify nodules during surgery predisposes to missing small, deep, or lightly textured nodules. Studies show failure rates as high as 46% and need to convert to thoracotomy when nodules cannot be seen or palpated during surgery.[11]

Using preoperative localizing devices such as fiducials and microcoils is a safe and efficient way to solve this challenge with success rates as high as 98% in nodule removal.[7,8] Past studies have identified specific indications for employing localizations. These include when nodules are more than 5 mm from visceral surface or less than 10 mm in size or both.[11] Another study[12] suggested that localization techniques should be used if any 2 of the following criteria are met, (1) nodule diameter 5 mm or less, (2) ratio of maximum diameter of nodule to minimum distance between pleural surface and deep border of nodule is 0.5 or less, and (3) low density of nodule on CT.

Although using localization techniques are very effective, inserting fiducial markers or microcoils are not without complications including pneumothorax, hemorrhage, and migration. In our study, despite a relatively large number of overall complications, the vast majority may be categorized using Society of Interventional Radiology (SIR) guidelines as class A requiring no treatment (all hemorrhage, all nontreated pneumothoraces) or at most class B (patients for whom short-term preoperative chest tubes were placed as well as the single patient with FM embolization for whom additional evaluation was required).[10]

From the perspective of risk factors for developing complications, depth of lesion from the skin ($P = 0.011$) and pleura ($P = 0.027$) were the only specific patient factors showing statistically significant increase in risk. No other patient factor including sex, age, weight, BMI, size of lesion, and location of lesion was significantly associated with developing a complication of any type. Pneumothorax is a common complication of percutaneous insertion of localizing devices into the lung. In this study, pneumothorax occurred in 32% of patients which is similar to 33%[13] and 45%[14] described in past literature. However, rates as high as 67% have been also reported.[15] Although developing a pneumothorax is a common consequence of percutaneous lung procedures, some factors have been shown to be positively associated with higher rates of pneumothorax occurrence. These include

preexisting COPD,[16] large needle size,[14,15,17] smaller lesions,[16] deeper lesions, and increased age of patient. In our study, no factors were significantly associated with developing a pneumothorax.

Hemorrhage was a relatively common complication in our study. Further, 42% of patients had hemorrhage due to the procedure, though the majority were small as defined by our criteria and caused no restriction in successful wedge resection. No patient or lesion factor was found to be predictive of hemorrhage.

Regardless of complications, lesion marking with FM or MC was highly successful in allowing successful guidance for wedge resection. In our cohort of 136 patients, all but 3 went to successful surgery as planned on the same day as FM/MC placement. Our surgeons benefit from the utility of post-FM/MC CT imaging in providing spatial orientation of marker to lesion, facilitating ultimate surgical wedge resection with fluoroscopic intraoperative guidance. Two patients for whom operative resection plans were changed were due to complications including a combination of pneumothorax/hemorrhage requiring chest tube placement in 1 patient and intravascular FM migration in another. In both cases, though delayed, surgery was ultimately successful with wedge resection achieved. Only 1 patient ultimately had a required change in operative technique due to central location of lesion in what was ultimately deemed an unsafe proximity location to the pulmonary artery with surgery converted to lobectomy at a later date. As such, timely successful same-day surgery was achieved in 133/136 (98%) patients and ultimately successful wedge resection surgery in 135/136 (99%) patients. Importantly, 118 of 148 (80%) lesions were malignant with a range of primary and metastatic etiologies. Such a significant majority of malignant lesion etiologies demonstrate the benefit of successful lesion marking using both devices with resection achieved at an early stage of lesion growth. In the setting of primary pulmonary malignant lesions, early resection has an obvious potential benefit of a higher likelihood of cure. In metastatic disease, though, resection is not necessarily curative, proof of disease spread provides guidance for treatment planning.

Though other techniques for lesion marking exist, such as methylene blue tagging and wire localization, and other guidance mechanisms exist including endobronchial marker delivery, our current technique works well in assistance for minimally invasive lesion resection. The combination of CT guidance during radio-opaque marker placement with final imaging disclosing the ultimate relationship in three-dimensions to the lesion for resection allows tailoring by the surgeon of the wedge resection to the individual patient's anatomy—other techniques using non−radio-opaque marking (methylene blue) or non−three dimensional delivery mechanisms (bronchoscopy) lose these advantages.

Our study has several limitations. It is composed of a retrospective review of experience at a single institution—though from several hospitals—with inherent patient selection bias. Furthermore, our workflow is somewhat complicated, involving the coordination of several caregivers from both radiology and surgery in 2 different interventional environments. Our patient population is overall quite small, particularly the subset of patients who had lesions marked using microcoils. As such, we were not able to evaluate the effect of individual lesion characteristics (solid or ground glass) or impact of surrounding lung disease (emphysema or pleural effusion) on the efficacy or complication profile of lesion marking in preparation for resection.

In conclusion, we present single institution data describing results of a successful collaboration between interventional radiology and thoracic surgery in providing CT-guided presurgical lesion marking followed by successful fluoroscopic-guided wedge resection. A high percentage of patients (98%) had successful same-day surgery as planned. A significant majority of lesions proved malignant at postresection pathology supporting the benefit in resection. Though complications were not infrequent, the majority were benign in degree

and easily treated with only 2 patients suffering a complication-mediated change in timely surgical completion. The possibility of intravascular FM embolization is of concern and is particularly noteworthy in considering placement planning when lesions are in proximity to vascular structures. Though not statistically significant, patients receiving microcoils had overall less complications than those with microcoils (including no cases of embolization/migration in the latter category)—further study is warranted to evaluate the overall safety profile of microcoils in a larger population.

References

1. Yankelevitz DF, Henschke CI. Small solitary pulmonary nodules. Radiol Clin North Am 2000;38(3):471–8.
2. Jemal A, Bray F, Center MM, et al. Global cancer statistics. CA Cancer J Clin 2011;61 (2):69–90.
3. Ost D, Fein AM, Feinsilver SH. Clinical practice. The solitary pulmonary nodule. N Engl J Med 2003;348(25):2535–42.
4. Gould MK, Fletcher J, Iannettoni MD, et al. Evaluation of patients with pulmonary nodules: when is it lung cancer?: ACCP evidence-based clinical practice guidelines (2nd edition). Chest 2007;132(3 Suppl):108S–30S.
5. Powell TI, Jangra D, Clifton JC, et al. Peripheral lung nodules: fluoroscopically guided video-assisted thoracoscopic resection after computed tomography-guided localization using platinum microcoils. Ann Surg 2004;240(3):481–8. [discussion 488–489].
6. Piolanti M, Coppola F, Papa S, et al. Ultrasonographic localization of occult pulmonary nodules during video-assisted thoracic surgery. Eur Radiol 2003;13 (10):2358–64.
7. Sancheti MS, Lee R, Ahmed SU, et al. Percutaneous fiducial localization for thoracoscopic wedge resection of small pulmonary nodules. Ann Thorac Surg 2014;97 (6):1914–8. [discussion 1919].
8. Su T-H, Fan Y-F, Jin L, et al. CT-guided localization of small pulmonary nodules using adjacent microcoil implantation prior to video-assisted thoracoscopic surgical resection. Eur Radiol 2015;25(9):2627–33.
9. Gill RR, Zheng Y, Barlow JS, et al. Image-guided video assisted thoracoscopic surgery (iVATS)—phase I-II clinical trial. J Surg Oncol 2015;112(1):18–25.
10. Suzuki K, Nagai K, Yoshida J, et al. Video-assisted thoracoscopic surgery for small indeterminate pulmonary nodules*: Indications for preoperative marking. Chest 1999;115(2):563–8.
11. Nakashima S, Watanabe A, Obama T. Need for preoperative computed tomography-guided localization in video-assisted thoracoscopic surgery pulmonary resections of metastatic pulmonary nodules. Ann Thorac Surg 2010;89 (1):212–8.
12. Yousefi S, Collins BT, Reichner CA, et al. Complications of thoracic computed tomography—guided fiducial placement for the purpose of stereotactic body radiation therapy. Clin Lung Cancer 2007;8(4):252–6.
13. Kothary N, Heit JJ, Louie JD, et al. Safety and efficacy of percutaneous fiducial marker implantation for image-guided radiation therapy. J Vasc Interv Radiol 2009;20(2):235–9.
14. Bhagat N, Fidelman N, Durack JC, et al. Complications associated with the percutaneous insertion of fiducial markers in the thorax. Cardiovasc Intervent Radiol 2010;33(6):1186–91.
15. Cox JE, Chiles C, McManus CM, et al. Transthoracic needle aspiration biopsy: variables that affect risk of pneumothorax. Radiology 1999;212(1):165–8.
16. Geraghty PR, Kee ST, McFarlane G, et al. CT-guided transthoracic needle aspiration biopsy of pulmonary nodules: needle size and pneumothorax rate. Radiology 2003;229(2):475–81.
17. Vatrella A, Galderisi A, Nicoletta C, et al. Age as a risk factor in the occurrence of pneumothorax after transthoracic fine needle biopsy: our experience. Int J Surg Lond Engl 2014;12(Suppl 2):S29–32.