Percutaneous Fiducial Localization for Thoracoscopic Wedge Resection of Small Pulmonary Nodules

Manu S. Sancheti, MD, Richard Lee, MD, Shair U. Ahmed, MD, Allan Pickens, MD, Felix G. Fernandez, MD, William C. Small, MD, PhD, Sherif G. Nour, MD, and Seth D. Force, MD

Department of Surgery, Divisions of Cardiothoracic Surgery and General Surgery, and Department of Radiology, Emory University, Emory University Hospital, Atlanta, Georgia

Background. The advent of high-resolution computed tomography scanning and increase in use of chest imaging for high-risk patients has led to an increase in the identification of small pulmonary nodules. The ability to locate and remove these nodules through a thorascopic approach is difficult. The purpose of this study is to report our experience with fiducial localization and percutaneous thoracoscopic wedge resection of small pulmonary nodules.

Methods. This is a retrospective analysis of our patients who underwent computed tomography–guided fiducial localization of pulmonary nodules. Nodules were identified with intraoperative fluoroscopy and removed by thoracoscopic wedge resection.

Results. Sixty-five nodules were removed in 58 patients. Removal was successful in 98% of patients (57 of 58); 79% of the nodules (53 of 65) were cancers; 20% of these were primary lung cancers of which 9 were pure ground-glass opacities. Mean size of the nodules was 9.9 ± 4.6 mm (range, 3 to 24 mm). Mean depth from visceral pleural surface was 18.7 ± 12 mm (range, 2 to 35 mm). Mean procedure time was 58.7 ± 20.1 minutes (range, 30 to 120), and mean length of stay was 2 days (range, 1 to 6). Complications occurred in 3 patients and included fiducial embolization, fiducial migration, and parenchymal hematoma.

Conclusions. Fiducial localization facilitates identification and removal of small pulmonary nodules and alleviates the need for direct nodule palpation. As shown by our series, thoracoscopic wedge resection with fiducial localization is an accurate and efficient technique. This method provides a standardized means by which to resect small and deep pulmonary nodules or ground-glass opacities.


The increasing use of computed tomography (CT) and the advent of high-resolution spiral CT has led to an increase in the detection of subcentimeter pulmonary nodules [1]. In addition, as lung cancer screening programs develop, one can anticipate that the number of nodules found will grow exponentially [2]. The need to diagnose and treat these nodules cannot be understated. Lung cancer remains the most common cause of cancer death, with a dismal overall 5-year survival of 15%. However, the 5-year survival can improve to 60% to 80% with the diagnosis and treatment of early stage cancers [3]. In addition to identifying potential small early lung cancers, subcentimeter nodules requiring diagnosis may also be seen in patients with a history of other solid organ malignancies and in patients undergoing transplant evaluations.

Dr Pickens discloses a financial relationship with Ethicon Endosurgery.
A variety of localization methods have been developed to attempt to solve this dilemma, ranging from thoracoscopic ultrasonography [7–9], percutaneous hook wires [5], percutaneous coils [10], contrast/dyes [11, 12], radio-tracers [13], and bronchoscopically placed localizers [14, 15]. All of these techniques include various limitations and complications.

Another technique for lung nodule localization involves the placement of a 3-mm gold fiducial marker in or near the nodule or nodules of interest. These markers are placed preoperatively, adjacent to the culprit lesions, by utilizing CT guidance. Intraoperative fluoroscopy can then be used to identify the fiducial marker, which is then used as a surrogate for the nodule and facilitates the wedge resection of the lesion of interest. This study was designed to analyze the reliability, safety, and feasibility of this technique at our institution.

Patients and Methods

This study was performed as a retrospective review of our thoracic surgical database and was approved by our Institutional Review Board. Owing to the retrospective nature of this study and lack of patient-specific identifiers, individual patient consent was waived. From April 2011 to May 2013, 58 patients (22 female) underwent thoracoscopic resection of 65 pulmonary nodules with fiducial localization at Emory University Hospital.

Image-Guided Fiducial Placement Technique

Preoperatively, the fiducial marker was placed in the interventional radiology department with local anesthesia. With the assistance of CT guidance, a 1.2 × 3 mm gold fiducial marker, depicted in Figure 1 (CIVCO Medical Solutions, Coralville, IA), was placed in appropriate position to mark the lesion of interest. The marker was placed through a coaxial 17G needle with the marker recessed within the lumen proximal to the tip. An internal stylet was used to push the marker beyond the introducer tip to accomplish delivery immediately adjacent to the culprit lesion. After positioning was achieved and the marker delivered, repeat imaging documented final fiducial positioning with respect to the lesion as a final guide for surgical removal. The localization procedure was performed on the same day of the thoracoscopic surgery except in 2 cases.

Operative Technique

The CT images after fiducial placement were reviewed by the surgeon before resection to determine the location of the fiducial marker relative to the nodule. A representative CT image after fiducial placement is shown in Figure 2. Standard thoracoscopy positioning, monitoring, and anesthesia were employed in 35 cases, and in 23 cases, isolated lung ventilation was not utilized. We have previously described this technique [16]. Thoracoscopy was performed utilizing two 5-mm trocars and one 12-mm trocar. Intraoperative fluoroscopy was used to locate the fiducial marker, and the adjacent lung was grasped and elevated. A representative fluoroscopy image with fiducial marker in place is shown in Figure 3. Wedge resection of the lung parenchyma containing the fiducial marker was performed with an endoscopic stapler in standard fashion. Excision of the fiducial marker was confirmed with fluoroscopy and frozen section.

Data Collection and Analysis

The medical records of the patients were reviewed. The demographics and body mass index were collected. Fluoroscopy time and total operating room time were recorded. From pathology, the size, depth, and histology of the nodules were tabulated. Complications and length of stay were also identified. Data are reported as mean value with standard error.

Results

Sixty-five nodules were removed in 58 patients, 22 of whom were female (44%). The mean patient age was 55 years (range, 24 to 80), and the average body mass index was 29.6 ± 6.9 kg/m² (range, 20 to 50 kg/m²). Forty-six (79%) of the patients presented with a history of cancer.

Three pneumothoraces (5%) were found immediately after the fiducial placement and treated with a pleural drain without complications. Fiducial marker and adjacent
nodule removal was successful in 57 patients (98%). In 1 patient, the nodule was determined to be too deep for wedge resection, and the patient ultimately underwent lobectomy for removal of the lesion. Six procedures (10.3%) were ipsilateral reoperations after previous lung resections. No operations were converted to thoracotomy. The characteristics of the nodules are shown in Table 1.

The mean size of the nodules was 9.9 ± 4.6 mm (range, 3 to 24 mm), and the mean distance from the pleural surface to the nodule was 18.7 ± 12 mm (range, 2 to 35 mm). Pathologic diagnosis of the nodules is shown in Table 2. Fifty-three nodules (79%) were found to be malignant, with 13 (20%) representing primary lung cancers. Eleven nodules (17%) were pure ground-glass opacities (GGO), and 9 of these GGO lesions were found to be primary lung cancers.

The average operative time was 58.7 ± 20.1 minutes (range, 30 to 120), including a mean fluoroscopy time of 10 ± 21.8 minutes. The length of stay for this group of patients ranged from 1 day to 6 days, with an average of 1.8 ± 1.2 days.

Three complications (5%) were noted in our patient population. These complications included fiducial embolization, fiducial migration, and parenchymal hematoma. In all 3 patients, the respective nodule was successfully removed despite the complications.

<table>
<thead>
<tr>
<th>Table 1. Characteristics of Lung Nodules</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size (9.9 ± 4.6 mm)</td>
</tr>
<tr>
<td>---------------------</td>
</tr>
<tr>
<td>0–5 mm</td>
</tr>
<tr>
<td>5–10 mm</td>
</tr>
<tr>
<td>10–15 mm</td>
</tr>
<tr>
<td>&gt;15 mm</td>
</tr>
</tbody>
</table>

Comment

Increased utilization of high-resolution computed tomography and the implementation of lung cancer screening programs have led to a significant rise in the prevalence of indeterminate lung nodules [1, 2]. Thoracoscopy has been progressively defined as an efficient means to provide pathologic diagnosis of these nodules, with possible concurrent definitive resection. Unfortunately, these nodules can often be subcentimeter in size, deep in the pulmonary parenchyma, and varied in texture, thus precluding the ability to isolate them by standard thoracoscopic techniques of finger palpation [5]. Preoperative localization techniques provide a clear benefit as an aid to sublobar pulmonary resection in this population as well as in patients requiring metastatectomies. Several studies have documented specific indications in which localization techniques should be employed. As previously stated, Suzuki and colleagues [6] recommend that localization techniques be used when the nodules are less than 10 mm in size or more than 5 mm from the visceral pleural surface or both [6]. Nakashima [17] developed three criteria: (1) nodule diameter of 5 mm or less; (2) ratio of maximum diameter of nodule to minimum distance between pleural surface and inferior border of nodule is less than or equal to 0.5; and (3) nodule is of low density on computer tomography. The authors [16] recommended that localization techniques be used if two or more of these criteria are met. Saito and coworkers [18] determined that a linear function (depth = 0.836 × size – 2.811) could differentiate between nodules requiring localization and those that do not.

Several localization techniques have been developed to provide a means to isolate pulmonary nodules during thoracoscopy. Each one includes its own advantages and limitations. The percutaneous image-guided placement of...
hook wires or microcoils involve a morbidity rate as high as 15% including the risk of pneumothorax, pulmonary hemorrhage, and significant pleural pain [5, 19]. Also, the hook wire technique carries the increased risk of systemic air embolism [5]. Additionally, surgeons have found that in the case of a pneumothorax the hook wire can pull out of the lung parenchyma, nulling the benefit its placement. Intraoperative imaging, such as thorascopic ultrasonography, has been shown to require complete lung collapse for accurate imaging, which may prove quite difficult with emphysematous lungs or those with pleural adhesions [7, 8]. Various endoscopically or percutaneously placed injectable markers have been used, such as barium, methylene blue, colored collagen, and lipiodol [11, 12, 14, 15]. Dyes have a risk of parenchymal diffusion after placement and thus are difficult to visualize upon thoracoscopy, especially in anthracotic lungs [20]. Barium and lipiodol are water insoluble and carry the risk of embolism [11]. The risk of anaphylaxis to any injectable substance is also present [21]. Finally, few groups have studied the use of radiotracers as markers similar to those used in breast surgery. This technique is limited by fast diffusion of the contrast medium and the inability of the probe to detect deeper and posterior nodules [9, 13].

This study retrospectively reviews the Emory University data regarding our localization technique of utilizing CT-guided placement of 3-mm gold fiducial markers adjacent to the nodules. This method of tumor marking is also used by interventional radiologists and radiation oncologists in pretreatment marking and tumor tracking before radiotherapy and has been found to be safe and effective [22]. Because the marker is placed with CT guidance, the CT imaging is used to help determine the position of the nodule in relation to the marker. That presents a distinct advantage over bronchoscopically placed markers where it can be difficult to identify whether the nodule is deep to, above, or below the marker. Additionally, in 3 of our patients, the procedure was canceled when the CT imaging used for fiducial placement showed resolution of the nodule in question. The fiducial marker is located with standard intraoperative fluoroscopy and resected with the adjacent nodule thorascopically, and therefore, after resection, the specimen itself can be visualized under fluoroscopy to ensure inclusion of the fiducial marker.

This technique was used in 58 patients with an excellent success rate of 98%. Failure rates among previously published localization techniques range from 0% to 47% [8, 10]. Very small and deep nodules were able to be removed, and the procedure could be employed in large patients, who present a particular challenge when trying to identify lung nodules. The mean nodule size of 9.9 ± 4.6 mm and mean depth of 18.7 ± 12 mm were well within the proposed indications for utilization of localization techniques previously mentioned. In the isolated unsuccessful case, the nodule was too central and close to the pulmonary artery for safe wedge resection. In this case, the fiducial was removed, but the nodule was left behind, and the patient later underwent an uncomplicated thorascopic lobectomy for resection of the nodule.

Inherent advantages of this method include the ability to perform the resections with routine thorascopic instruments and standard operative fluoroscopy. No special instrumentation is needed. In our institution, two 5-mm trocars and one 12-mm trocar were utilized. Using standard thorascopic practices, we were able to perform cases that may have been limited by specialized equipment, instruments, or markers. For example, 10.3% of our cases were ipsilateral reoperations with significant pleural adhesions. The operative duration and postoperative length of stay are comparable to standard controls for thoracoscopy, and the use of fluoroscopy was kept to a minimum (mean 10.1 minutes) to lessen patient and staff exposure.

The fiducial marker is only 3 mm, and its associated delivery system is equally small. That minimizes the level of trauma to the pulmonary parenchyma, as evidenced by a low pneumothorax rate of 5%. Of note, all pneumothoraces were recognized immediately after fiducial marker placement on postprocedure CT scan. A chest tube was placed, and the patient was transferred to the operating room for subsequent thoracoscopy. The fiducial marker is constructed of gold, an inert element so the risk of allergic reaction is negligible, and it can remain in the pulmonary parenchyma without risk of reaction. Therefore, the timing between placement and resection can be variable. In our series, owing to patient scheduling convenience, all except two resections were performed immediately after fiducial marker placement. The two exceptions were performed the day after marker placement. In addition, because of its inert properties, the fiducial marker has very little effect on the surrounding tissue and subsequent histopathologic analysis [23].

Our technique proved be an efficient method to remove and diagnose a variety of pathologies. Seventy-nine percent of the nodules were found to malignant on pathology. Thirteen (20%) of these malignant lesions proved to be a primary lung cancer. Of note, our series showed the ability to resect pure GGO lesions, a radiographic finding that is difficult to isolate and resect thorascopically. Nine of these pure GGO lesions were discovered to be primary lung cancer. A definitive resection was performed during the same operation on patients found to have a primary lung malignancy. All margins were oncologically adequate for patients undergoing metastatectomies. By detecting and resecting these small malignant nodules early, the goal is to provide the patients the highest chance of cure [24].

Three complications (5%) were noted in our patient population. These complications included fiducial embolization, fiducial migration, and parenchymal hematoma. In 1 case, early in our experience, a marker was inadvertently deployed in an inferior pulmonary vein and found to have migrated over the ventral aspect of the heart near the apex during localization. An urgent echocardiogram was performed that demonstrated the marker to have embolized into the left anterior descending artery. The patient was admitted for observation but was asymptomatic with normal cardiac enzymes. No further intervention was indicated, and the patient recovered.
without incident. She subsequently returned later for thoracoscopic resection of her nodule using fluoroscopic guidance by means of an additional fiducial marker placed at the initial localization procedure. Long-term follow-up with her cardiologist yielded no adverse sequelae, and she is maintained on antplatelet therapy. In another patient, the marker was found to have migrated from the parenchyma into the pleural space. Fortunately, the track formed from the fiducial marker placement isolated the area of interest for resection, and the nodule was successfully removed. Finally, a superficial parenchymal hematoma was noted to have developed in 1 patient after placement of the marker. The finding was clinically insignificant, and the hematoma was removed along with the nodule at time of surgery.

A limitation of this series and technique is that it was a retrospective review of patients undergoing a specific procedure in one institution, with the bias inherent in all retrospective studies. This model also leads to an element of selection bias. Next, the methodology requires the coordination of the patient, the thoracic surgeon, the interventional radiologist, and the fluoroscopy technician. The utilization of multiple specialties does add to the expense and complexity of the procedure. However, surgeons at some institutions do perform their own interventional procedures, which could make the flow of steps much smoother. Ideal future studies would involve a prospective and randomized model that analyzes the various techniques of localization.

With modern imaging modalities, the discovery of small, deep, and nonpalpable pulmonary nodules is inevitable. The indication for the application of localization techniques in thoracoscopy has become clearer, and several methods of localization have been developed. Our technique demonstrated an excellent success rate with a low morbidity rate in the resection of lesions that meet the current indications for size and depth. A wide array of pathology was present in the specimens, including a large proportion of malignancies, especially consisting of the elusive pure GGO. Overall, our technique of using CT-guided placement of fiducial markers and subsequent resection with intraoperative fluoroscopy can safely and reliably contribute to the thoracic surgeon’s armamentarium in managing small, deep, and nonpalpable nodules.

References
DISCUSSION

DR TRAVES CRABTREE (St. Louis, MO): We saw a paper earlier today where the benign resection rate was around 12%, our benign resection rate at Wash U is about 12%, I think we just saw a talk in the last session where it was around 25%, and yours is around 21%. Do you think the ability to do this makes it the right thing to do?

DR SANCHETI: Thank you for your question. The appropriate clinical scenario dictates the usefulness of this approach. Many of the patients that were recommended to undergo resection in our series were preoperative solid organ transplant patients and those with a history of nonpulmonary malignancies that were found to have small pulmonary nodule. Although many lesions were benign, I do think if we are able to isolate/resect/diagnose small lesions in patients of these clinical scenarios, we can drastically alter their treatment plan. Therefore, I do think it is a useful approach in the right situation.

DR ROBERT J. CERFOLIO (Birmingham, AL): Congratulations. Good technique. How much radiation is the patient getting and how much radiation are your hands getting and do you wear gloves while you are doing it? Lead gloves? Your hands are being exposed to radiation.

DR SANCHETI: Thank you, Dr Cerfolio. We do not wear specialized gloves, but do take standard precautionary measures with fluoroscopy. Specifically, Dr Cerfolio, in terms of the fluoroscopy time, we had a few extremes, but if you take out the extremes, our times calculates to about 3.1 minutes.

DR DARRYL S. WEIMAN (Memphis, TN): My question is, you find one of these little cancers and it’s consistent with a lung primary. Now what do you do?

DR SANCHETI: That’s a good question. Thank you. If we do find a primary lung cancer in these lesions, we perform a lymph node dissection at that time. The definitive, anatomic resection depends on the clinical situation of the patient. Like previously discussed, a few of these patients had other nonpulmonary malignancies, and some were pretransplant workups. If clinically appropriate and if the patient could tolerate a lobectomy or a segmentectomy, then we would go ahead and do that either at that time or later on.

DR JOSHUA ROBERT SONETT (New York, NY): Excellent technique and I think it’s complementary to the one we saw earlier. There is no reason that when you are putting the blue dye in you could also put a fiducial in so the blue dye would mark the surface and a fiducial would mark the depth. So I think they’re complementary and you may be able to do it all in one setting without the percutaneous needle biopsy. And, too, again, I would just encourage everybody to, for nonmetastatic patients or transplants, use the NCCN guidelines or the AATS or the Chest guidelines for when we should approach and seriously consider resecting nodules, because we shouldn’t be taking out all of these just because we can.

DR MITCHELL MAGEE (Dallas, TX): One quick comment. I just wanted to say that I have used a similar technique with a fiducial marker that is radiopaque but not used intraoperative fluoroscopy as liberally as you have but to just take an X-ray film of it when you get it out, because sometimes you may not be able to see it quite as easily, and if you have got your specimen out and X-ray film it and your fiducial is in there, then you know you have gotten a lesion.

DR SANCHETI: I appreciate that comment and approach.

DR WILLIAM BOLTON (Greenville, SC): Just a comment on the podium’s last statement. So, yes, putting a fiducial marker in there with this navigational bronchoscopy would be quite easy. It would take you very little time, about less than a minute, to add that to your original procedure. So it certainly could be done.

DR M. BLAIR MARSHALL (Washington, DC): Can you provide the cost of the fiducial?

DR SANCHETI: I unfortunately do not know the cost of the fiducial.

DR DOUGLAS MINNICH (Birmingham, AL): The gold seeds are approximately $50. I was going to talk about some of this in the next presentation, but some of the other fiducials are in the $150 to $175 range.