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The Use of Robotic Bronchoscopy for Visceral Pleural Marking Prior to Surgical Resection of Pulmonary Nodules

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Abstract

Introduction: Pulmonary nodules suspicious for malignancy may require surgical biopsy. Options include wedge resection using video-assisted thoracoscopic surgery (VATS) or open thoracotomy. Nodules may be identified by visual inspection or digital palpation. Recent localization technical advancements have included preoperative hook wire placement, percutaneous dye injection and electromagnetic navigational bronchoscopy. Intraoperative conversion of VATS to open thoracotomy may stem from unsuccessful nodule localization. We hereby describe a novel approach to preoperative marking of the visceral pleura in order to assist with intraprocedural nodule localization. We present a series of patients who underwent visceral pleural marking by robotic bronchoscopy.

Materials and Methods: This study was performed at a single institution by two interventional pulmonologists and one cardiothoracic surgeon. Seventeen patients who required wedge resection of pulmonary nodules and underwent preoperative visceral pleural marking were studied. An electromagnetic navigational robotic bronchoscopy platform was utilized for dye marking, with fluoroscopy to facilitate needle placement. The primary objective was to advance the bronchoscope within close proximity of the suspicious nodule and mark the visceral pleura. A Wang needle was used to inject indocyanine green and methylene blue dyes. The robotic scope was then retracted to allow for surgical intervention. Wedge resection via robot-assisted VATS was subsequently performed.

Results: Seventeen patients underwent wedge resection for known or suspected malignancy: 13/17 were positive for malignancy, most commonly from extra thoracic metastasis; 6/17 proceeded to completion lobectomy following confirmation of non-small cell lung carcinoma (NSCLC) from intraoperative frozen section examination. There were no reported complications, including pneumothorax, bleeding or dye-related side effects.

Conclusion: Robotic bronchoscopy can be a safe and effective technique for visceral pleural marking prior to VATS resection of pulmonary nodules. Theoretically, this approach may reduce the conversion of VATS to open thoracotomy in selected cases. Further studies are needed to determine statistical differences in outcomes among different techniques for nodule localization, e.g. percutaneous vs robotic bronchoscopy. Limitations of the study include sample size, operator dependence and limited length of follow up.

Keywords: Pleural dye marking • Robotic bronchoscopy • Lung cancer • Pulmonary nodule • Interventional pulmonology

Introduction

Lung cancer is the most frequently diagnosed malignancy and has the highest neoplasm-related mortality among men and women. This is largely secondary to delay in timely diagnosis [1]. With increasing use of low-dose CT screening following results of the National Lung Screening Trial [2], pulmonary nodules have been detected with more frequency. Additionally, the use of thoracoscopic surgery for diagnostic and therapeutic management of pulmonary nodules has increased [3]. Intraoperative identification of subpleural pulmonary nodules by tactile palpation is technically challenging during video-assisted thoracoscopic surgery (VATS) and not possible during robot-assisted VATS. This can limit success of wedge resections. Proper operative localization is paramount to prevent unnecessary resections [4].

Several methods have been utilized for preoperative nodule localization, including CT-guided radiotracer injection, CT-guided wire localization, CT-guided fiducial marker placement and fluoroscopic localization, ultrasonographic and percutaneous inking with dyes [3,5,6]. Electromagnetic navigational bronchoscopy (ENB), which allows greater access to peripheral lesions by providing a three-dimensional map with real-time positional feedback, has also been successfully utilized more recently for fiducial marker placement and dye marking of nodules [4].

We report a single center experience on a novel, preoperative robotic bronchoscopic marking technique to assist in diagnostic robotic surgical resections.

Materials and Methods

This retrospective study was performed at a single academic institution. Patient data was gathered from review of electronic medical records. A literature review was performed using PubMed database. A search for

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existing articles on robotic bronchoscopy approaches for preoperative marking of lung nodules yielded no results.

Two interventional pulmonologists used a robotic bronchoscopy platform (Monarch, Auris, Redwood City, CA) to mark visceral pleura nearby suspicious nodules (Figure 1). This was performed in the operating room directly prior to robot-assisted VATS. Indocyanine green (ICG) and methylene blue (MB) were used for dye marking. The robotic bronchoscope was retracted following dye injection and surgical resection was performed, initially with wedge resection, using a robotic surgical platform (DaVinci, Intuitive, Sunnyvale, CA). Decision to proceed with a completion lobectomy was made intraoperatively by the thoracic surgeon after results of the frozen section were obtained.

Figure 1. Auris Monarch robotic bronchoscopy platform.

Description of technique

Two interventional pulmonologists and one thoracic surgeon operated on 17 patients at a single quaternary center. Patients with pulmonary nodules requiring resection were brought to the operating theater. While under general anesthesia, flexible bronchoscopy was performed to fully inspect the airway and rule out endobronchial disease. Then, electromagnetic navigation equipped robotic bronchoscopy was performed to navigate to the nodule. A 19G Wang needle was utilized to instill the dye adjacent to the nodule under fluoroscopic guidance. For marking purposes, 0.75 mL each of ICG and MB dyes were instilled under fluoroscopic guidance. MB was instilled within 3 mm of the pleura in an agitation back-forth pattern, whereas ICG was instilled as a single application within 5 mm of the pleura.Fluoroscopy was utilized for accuracy. The needle and the robotic bronchoscope were withdrawn. Patients then underwent robot-assisted surgical wedge resection. Frozen section analysis of the specimen was subsequently performed to assess the need for lobectomy with mediastinal lymph node dissection.

Results

Seventeen patients underwent preoperative dye marking of pulmonary nodules in the operating room prior to diagnostic thoracic surgery procedure. Patient ages ranged from 30 to 78, with an average patient age of 61 years. The majority (65%) were either current or former smokers, with 54% also diagnosed with chronic obstructive pulmonary disease. 59% of the patients were female. The indications for wedge resection of pulmonary nodules included suspected primary malignancy (2/17), suspected metastasis without prior biopsy (8/17), biopsy-proven metastasis (3/17), biopsy proven primary malignancy (3/17), suspected malignancy with negative biopsy (1/17). Target nodule location was variable among all five lobes. The mean duration of time required for dye marking was 23.2 minutes, with a range of 11-43 minutes. The intended specimen was contained within the resected wedge in 100% of cases following dye marking. There were no reported complications, including no episodes of bleeding, pneumothorax or reactions to dye injection (Tables 1 and 2).

Table 1. Demographics.

Variables	Percentage
Age (years)	60.94 (30 - 78)
Female/Male	59% (10/17)/41% (7/17)
Tobacco history (current or former)	65% (11/17)
Current	47% (8/17)
Former	18% (3/17)
Average pack years amongst smokers	45.7% (503 /11)
COPD	53% (9/17)
Asthma	29% (5/17)
FEV1 (% of predicted), avg	80.4% (33-114)
DLCO (% of predicted), avg	73.7% (58-101)
Personal history of cancer	65% (11/17)

Table 2. Lesion and procedure characteristics for target nodule location.

Variables	Percentage
Nodule size (mm), average	6.5 (0-20mm)
Largest dimension (diameter), average	16.5mm
Nodule location	
Right upper lobe	14.2% (3/21)
Right middle lobe	19% (4/21)
Right lower lobe	4.8% (1/21)
Left upper lobe	42.9% (9/21)
Left lower lobe	19% (4/21)
Lobectomy	35.3% (6/17)
Biopsy-proven malignancy	76.5% (13/17)
Biopsy diagnostic	100% (17/17)
Specimen within wedge	100% (17/17)

Resected nodules were positive for malignancy in 76.5% (13/17) of cases. This was most commonly due to extra thoracic metastasis (47%), followed by lung adenocarcinoma (29.4%), as detailed in (Table 3). Two nodules were related to granulomatous disease: Histoplasma capsulatum and Langerhans cell histiocytosis, respectively. A subset of patients (35.3% or 6/17) required progression from wedge resection to full lobectomy (Figures 2-5).

Table 3. Lesion and procedure characteristics for biopsied nodules.

Variables	Percentage
Malignant	82.4% (14/17)

Primary Lung Cancer	35.3% (6/17)
Adenocarcinoma	83.3% (5/6)
NSCLC	16.7% (1/6)
Extrathoracic metastasis	47% (8/17)
Benign	17.7% (3/17)
Granuloma	66.7% (2/3)
Lung parenchyma	33.3% (1/3)

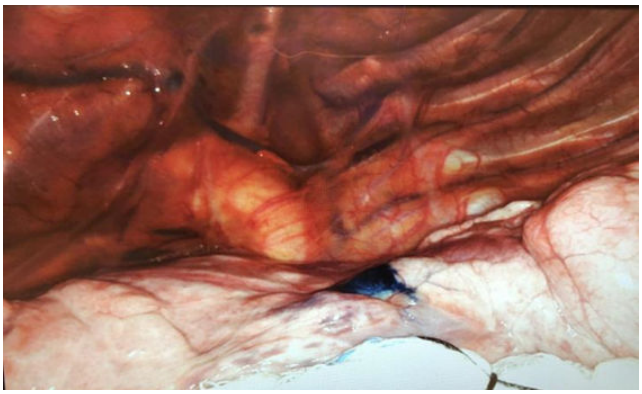

Figure 2. Visceral pleura is marked using both methylene blue and indocyanine green, This allows for intra-operative localization of target pleural nodule prior to resection.

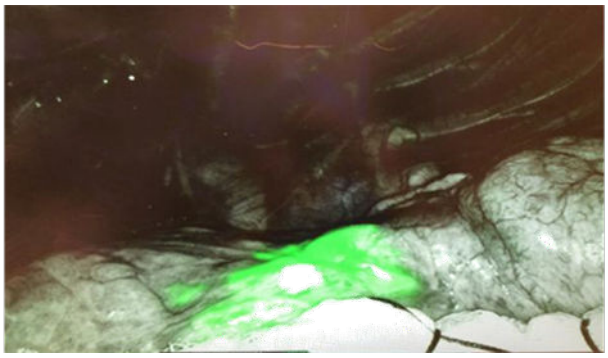

Figure 3. Pleural nodules are injected with dye, such as indocyanine green pictured above, under fluoroscopic guidance.

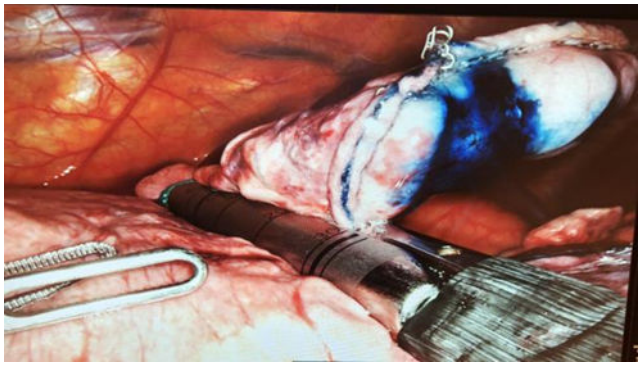

Figure 4. The decision for wedge resection versus lobectomy is made by the surgeon intra-operatively.

Figure 5. Pleural marking improves the success rate of wedge resection, reducing conversion to full lobectomy.

Discussion

As lung cancer screening with CT becomes increasingly implemented, the incidence of pulmonary nodules or ground glass opacities will continue to increase. Diagnostic and therapeutic resection via minimally invasive thoracic surgery techniques, i.e. VATS and robot-assisted VATS, remains the gold standard. Our experiences suggest that robotic bronchoscopy-guided dye marking can successfully and safely aid in the localization of these lesions intraoperatively, preventing unnecessary lobectomies. The procedure is safe and can be performed in the operating theater immediately prior to surgery, precluding transport and interdepartmental coordination. Our experience using a robotic bronchoscope rather than conventional techniques at a single institution is successful, without adverse events. Robotic bronchoscopy may improve accuracy over conventional approaches, reduce cost and prove more convenient for the patient and surgeon. Further studies will be needed to confirm these preliminary findings.

Historically, CT-guided placement of hook wires has been one of the preferred marking methods [7,8]. Chen et al. previously reported the pneumothorax rate at approximately 23%, with a wire dislodgement rate of 4.9% [9]. Additional concerns include radiation exposure, reported patient discomfort during placement of the hook wire, requiring transport after placement from an interventional radiology suite to the surgical theater and waiting for induction of anesthesia [7]. These techniques require inter-disciplinary communication and coordination of care between the radiology suite and operating room.

In a study of 258 patients across 21 centers in the US, Bowling et al. reported that fiducial marker placement using ENB was 99% accurate initially but follow-up imaging showed 15/254 (5.9%) had moved from the target site [5,6]. The rate of pneumothorax was 5.4% overall and procedure-related respiratory failure was 1.6%. Cardiac and endovascular embolization has also been reported following fiducial marker placement [10,11].

Electromagnetic navigation bronchoscopy (ENB) allows access to peripheral lung lesions beyond the reach of conventional bronchoscopy with higher accuracy [12]. It has more recently been utilized for dye-marking of nodules, with successful localization rates of 97.2 - 100% [4]. NAVIGATE, the largest prospective study of ENB, evaluated 1390 patients undergoing ENB-guided lung biopsy, fiducial marker placement, pleural dye marking and

lymph node biopsy in a multi-center review [8]. Success rates for ENB-guided biopsy (91.8%) were improved with pleural dye marking over transbronchial biopsy, the latter of which is impacted by the distance of nodule to the pleura [13]. Additionally, an airway going into the nodule on CT scan (positive bronchus sign) improves yield of transbronchial biopsy but does not limit dye marking, which sets targets at the pleura nearest to the nodule [7].

Advantages of ENB-dye marking are several. With regards to adverse outcomes, Hyun et al. reported 0/29 dye injections resulting in pneumothorax or bronchial hemorrhage. Rates are reported to be 10-fold higher for CT-guided transthoracic techniques compared to ENB-guided dye marking [7]. Awais et al. reported no complications from dye marking for 33 lesions in 29 patients using MB. The procedure is convenient and comfortable for patients, as it is conducted under general anesthesia in the operating room as opposed to waiting for induction. Patients do not require transport from a procedure suite to the operating room, improving workflow [14]. The wait time between localization and resection was reported to be significantly different by Bolton et al. with 27 minutes for and 189 minutes for CT-guided localization [15]. Awais and colleagues reported their mean EMN time for dye marking to be less than 10 minutes [3].

Robotic bronchoscopy is an emerging technology with two current platforms, Auris Monarch® (robotic bronchoscopy) and Intuitive Ion® (robotic catheter). The Monarch system has a robotically propelled outer sheath with inner telescoping endoscope that relies on electromagnetic navigation for guidance [16]. When compared to navigational modalities reliant on white light flexible instruments, the robotic bronchoscope is reported to be specifically designed to improve access to the lung periphery, where many periphery pulmonary nodules are found. This is not related to a smaller diameter but rather from improved structural support from the robotic bronchoscope outer sheath and 4-way steering of the outer and inner endoscope. An additional technical advantage of robotic bronchoscopy relies on being able to hold the endoscope in a locked curved position, allowing biopsy to be taken without having to straighten prior to sampling – minimizing migration [17]. Krimsky et al. report that the robotic bronchoscopy system is able to reach three generations further into the airways compared to the traditional thin scope [16]. This may help increase the diagnostic yield relative to conventional guided bronchoscope [18]. Conventional flexible bronchoscopy is still required to rule out lesions in the central airways.

Conclusion

Current practice for preoperative nodule localization is primarily by the means of CT-guided hook wire placement, which carries the risk of pneumothorax and requires higher levels of coordinated care. Dye marking can be achieved with minimal risk to the patient in the operating theater and under general anesthesia. Current literature supports pleural dye marking as a safe procedure with a significantly lower risk of adverse outcomes (i.e., pneumothorax) when compared with CT-guided percutaneous techniques. This initial study suggests that the robotic bronchoscope offers advantages over other existing approaches and can be executed safely. Limitations of the study include limited length of follow up, number of cases and individual operator performance with the robotic bronchoscope.

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