Original Article

Electromagnetic navigation bronchoscopy—Chungnam National University Hospital experience

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Background: To find small pulmonary nodules or ground grass nodules (GGNs) with video-assisted thoracoscopic surgery (VATS) is very difficult. There are several conventional methods to localize small nodules or GGNs, which require additional radiation exposure and may cause some complications such as pneumothorax or hemothorax. We aimed to evaluate the effectiveness and feasibility of electromagnetic navigational bronchoscopy-guided pulmonary localization in a minimally invasive thoracic surgery field.

Methods: We retrospectively reviewed the medical records from a prospectively collected database of the patients who underwent ENB procedure for biopsy and/or localization of pulmonary resection at the Chungnam National University Hospital from January 2017 to January 2018.

Results: A total of 37 ENB-guided dye-markings or biopsies for 37 lesions in 30 patients were performed. Thirty-two ENB-guided localizations using dye-marking for resection were performed in 25 patients. The median nodule size was 9 mm (IQR: 7–13 mm), and the median distance from the pleura was 6 mm (IQR: 3–10 mm). The failure of an ENB-guided localization was noted in 4 cases (12.5%). There was no major complication noted with the procedure, and just two patients showed mild intrabronchial bleeding stopped spontaneously. The most common lobar location was right lower lobe (11 cases, 34.4%), and all cases of localization failure were right lower lobe. A pathologic diagnosis was obtained from surgically resected specimen (not from ENB biopsy: 32 of 32 localizations, 100%), neoplastic lesions were 23 cases (72%). Of them, a primary lung cancer and metastatic lung cancer were noted in 11 cases, and in 11cases, respectively. All margins of the nodules were negative.

Conclusions: The ENB-guided dye localization by a well-trained thoracic surgeon enables accurate intraoperative identification of GGN or a small pulmonary nodule, with minimal complications and enables minimally invasive surgery including single port surgery.

Keywords: Electromagnetic navigation bronchoscopy; pulmonary nodule; thoracoscopy

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Introduction

Small pulmonary nodules that need to be resected for diagnostic or therapeutic purpose are increasing. The computed tomography (CT) screening of the chest for high risk patients of lung cancer allows more early detection of a lung cancer (1,2). To find small pulmonary nodules or ground grass nodules (GGNs) with video-assisted thoracoscopic

surgery (VATS) is very challenging (3-5). Previous several studies have reported that it is very difficult to localize a non-palpable small diameter and/or deeply located nodules from the visceral pleural margin during minimally invasive thoracoscopic surgery (5). Several conventional methods to localize small nodules or GGNs are used in the surgical field. Most of these procedures use the fluoroscopic-guided or CT-guided transthoracic approaches with dye marking, coil embolization, or hook-wire (6-12). These methods require additional radiation exposure, and may cause some complications such as pneumothorax or hemothorax. More importantly, the procedure-related complications lower the accuracy of localization. The endobronchial ultrasound-guided transbronchial needle aspiration is not available for peripheral lung lesions.

Nowadays, newly established method has promised to identify the small pulmonary nodules or GGNs through the electromagnetic navigation bronchoscopy (ENB)-guided transbronchial dye-marking (5,13-15). The effectiveness of the ENB procedure for a diagnostic biopsy has been reported in several studies (16-19). The ENB-guided transbronchial needle aspiration or biopsy showed a higher accuracy and lower complication rates, such as a pneumothorax or hemothorax, than the conventional percutaneous core needle biopsy. More recently, the ENB procedure is increasingly accepted as a valuable tool in thoracic surgery. A few researchers have reported that the ENB-guided localization can be of help to resect the pulmonary lesion (5,13-15). In this study, we aimed to evaluate how well the ENB-guided dye-marking is seen in the operation field, how well the marking localizes the pulmonary lesion, and whether the pulmonary lesion was resected sufficiently utilizing this procedure.

Methods

We retrospectively reviewed medical records from prospectively collected database of the patients who underwent an ENB procedure for a biopsy and/or localization of a pulmonary resection at the Chungnam National University Hospital from January 2017 to January 2018. The Institutional Review Board of the Chungnam National University Hospital approved this retrospective study.

ENB, dye marking, and surgical procedure

The patients re-checked a non-enhance chest CT according to recommended protocol of the company (Medtronic, Minneapolis, MN), to reconstruct the virtual bronchoscopy on the preoperative day. Two surgeons (M-W.K. and H.J.C) performed planning, ENB-guided dye marking, and VATS surgery. All procedures from planning to the surgery for each patient were performed by the operating surgeon in the operating room at the time of the resection. We set the target and planned the pathway to the target using the superDimension^{TM} navigation system and planning software (Medtronic, Minneapolis, MN). Initially, we tried to target directly the nodule, but later we routinely set up the several targets including direct and indirect targets for one lesion and the several pathways per target. If access to first target was not possible despite attempts through several pathways during ENB-procedure, we moved to the next target. If the dye was injected to indirect target, we considered the positional relationship between the indirect target and the actual nodule based on the chest CT to localize the nodule.

The patients underwent general anesthesia with a single-lumen intubation in operating room. Subsequently, each target was marked by indigo carmine dye using extended working catheter under locatable electromagnetic guide. After the target was located, the locatable guide was removed, and a 25-gauge needle preloaded with indigo carmine was inserted through the working catheter. We did not use fluoroscopy or CT to verify the deployment of the needle, and just inserted the needle catheter in the same length as the length of the electromagnetic guide after the location to the target. After the deployment of the bronchoscopic needle, the indigo carmine 0.5 mL was injected. Then, a needle catheter was removed and we confirmed the location of the catheter by re-insertion of the electromagnetic guide through the working catheter. After sufficient localization, the endotracheal tube was replaced with a double-lumen endotracheal tube. In the case of a single port VATS according to preoperative plan, we used a 15 mm single port for thoracoscope and instruments. If the dye was visualized on the inspection of lung and the location of stained lung was proper to anchor with the suture, a single port VATS surgery was performed (Tower crane technique) (16). If not, we changed to a conventional three-port VATS surgery. For depth of resection, we referred to the CT assessment, and the resection margin was confirmed by gross finding of cross section or frozen-section analysis of the specimen.

ENB-guided biopsy was performed using the superDimension^{TM} Triple needle brush (Medtronic, Minneapolis, MN) and/or the biopsy forceps for bronchoscope. The planning and the procedure were

Table 1 Characteristics of patients

Characteristics	Values (n=30)
Patient, no.	30
Male sex, no.	20
Median age [IQR], year	64 [58–69]
ENB-guided procedure, no. of patients	30
Localization for pulmonary resection	25
Biopsy	5
ENB-guided procedure, no. of procedures	37
Localization for pulmonary resection	32
Biopsy	5

IQR, interquartile range; ENB, electromagnetic navigational bronchoscopy.

same to ENB-guided localization, and the lesions were targeted directly. After the target was located, the locatable guide was removed, and the samples were obtained by the Triple needle brush or the biopsy forceps through the working catheter. The samples were sent to the pathology department for rapid on-site evaluation (ROSE) or frozen section. If the finding was negative for malignancy, we did re-biopsy and ended the procedure.

Results

Patient characteristics

A total of 37 ENB-guided dye-markings or biopsies for 37 lesions in 30 patients were performed. The males were 20 in number, and the median age was 64 years old. The characteristics of the patients are listed in *Table 1*. Thirty-two ENB-guided localizations using dye-marking were performed in 25 patients, and 5 ENB-guided biopsies were performed in the other patients.

Characteristics of the pulmonary lesions for localization and surgery

An ENB-guided localization was performed with dye-marking using indigo carmine, and we estimated a visualization of the dye-marking on the lung surface in the operating field. In a total of 32 ENB-guided localizations, we did not find the dye-marking or discoloration in 4 localizations (12.5%). The characteristics of the pulmonary lesions were described in *Table 2*. The median value of the nodule size was 9 mm (IQR: 7–13 mm), and the median value of the distance from the pleura was 6 mm (IQR: 3–10 mm). There are no fatal complications related to the ENB-guided dye marking, but there were two patients who had an adverse event. Mild bronchial bleeding was occurred during the ENB procedure, but the bleeding spontaneously stopped. The most common lobar location was the right lower lobe (11 cases, 34.4%), and all cases of the localization failure were at the right lower lobe. There were four cases of failed localization that was not helpful in locating the nodule because the stain was invisible or indistinguishable on lung surface (*Table 3*). In this case, an indigo carmine was injected to the chest wall in the sixth case of pulmonary localization, deep parenchyme in 8th case, and in a pleural cavity in 19th case. In the 10th case, we did not distinguish the dye-staining from anthraco pigmentation because of a severe pulmonary anthracosis. There was no operative mortality (0%). A pathologic diagnosis was obtained from surgically resected specimen (not included ENB biopsy: 32 of 32 localizations, 100%), neoplastic lesions were 23 cases (72%). In all of the cases, a primary lung cancer and a metastatic lung cancer were identified in 11 cases and 11 cases, respectively. The other cases were noted as benign lesions (*Table 4*). In these cases, all margins of the nodules were negative.

Comparisons of single port VATS and conventional three-port VATS

We routinely used conventional three-port VATS to resect the lesion, but if the location of the peripheral solid nodule was appropriate to anchor the suture and the stain was visualized on lung inspection, we tried to resect using a 15 mm single port with an anchoring suture. Eleven patients underwent single port VATS, and the remaining 21 patients conventional three-port VATS (*Table 5*). The nodule size between the two groups was not significantly different. The distance from the pleura was 4 mm in a single port VATS group and 7 mm in a conventional VATS group, but the difference between the two groups was not shown. In comparison of pathology between the two groups, the primary lung cancer was significantly lower in the single port VATS group, than in the conventional three-port VATS group. However, an additional resection due to the inappropriate resection margin was only noted as one case in the conventional VATS group.

Table 2 Clinical characteristics of pulmonary lesions for localization

Characteristics	Total	Dye (+)	Dye (–)
ENB-guided procedure for localization, no. of procedures	32	28	4
Size of nodule, no.			
≤5 mm	5	5	0
6–10 mm	14	12	2
11–15 mm	8	7	1
16–20 mm	4	3	1
>20 mm	1	1	0
Distance to pleura from nodule, no.			
≤5 mm	15	13	2
6–10 mm	10	10	0
11–15 mm	4	3	1
16–20 mm	0	0	0
>20 mm	3	2	1
Character of nodule on CT finding, no.			
Solid nodule	13	11	2
Part-solid nodule	8	8	0
Pure ground glass nodule	6	6	0
Cavitary nodule	5	3	2
Anatomical location of nodule, no.			
Right upper lobe	8	8	0
Apical segment	2	2	0
Posterior segment	3	3	0
Anterior segment	3	3	0
Right middle lobe	3	3	0
Lateral segment	2	2	0
Medial segment	1	1	0
Right lower lobe	11	7	4
Superior segment	4	4	0
Medial basal segment	0	0	0
Anterior basal segment	2	1	1
Lateral basal segment	3	0	3
Posterior basal segment	2	2	0
Left upper lobe	5	5	0
Apicoposterior segment	3	3	0
Anterior segment	1	1	0
Lingular segment	1	1	0
Left lower lobe	5	5	0
Superior segment	1	1	0
Medial basal segment	0	0	0
Anterior basal segment	0	0	0
Lateral basal segment	3	3	0
Posterior basal segment	1	1	0

ENB, electromagnetic navigational bronchoscopy.

ENB-guided biopsy

Five ENB-guided biopsies were performed in five patients. Three patients had lung or other malignancy and underwent the procedure for tissue diagnosis of metastasis or recurrence. Two patients were referred for the evaluation of solitary pulmonary nodule in location where it is difficult to perform the percutaneous core-needle biopsy. The size of the lesions was 9, 13, 30, 30, and 40 mm, respectively. Three patients were identified as the malignancy. One patient was benign lesion and the lesion was stable in 1-year followed chest CT. The other patient was also benign lesion on ENB-guided biopsy, but three months later, was confirmed as malignancy by percutaneous core-needle biopsy. There was no complication except minor bronchial bleeding.

Discussion

The incidence of small nodules that need to have identifying pathology or early stage lung cancers present as GGN are thus increasing (1,2). The lesion that is difficult to perform a percutaneous conventional method like core-needle biopsy for diagnosis which is requiring surgical resection and the demand for a sublobar resection is increasing in the early stage of lung cancer, such as a small GGN (5). An accurate localization is very important for these sublobar resection or non-anatomical resection. Several conventional methods have been performed to localize for small nodule, but these methods require additional radiation and other specialists

Table 3 Four cases of localization failure

Parameter	Case 6	Case 8	Case 10	Case 19
Sex	Male	Male	Male	Male
Age, years	72	69	69	60
Character of nodule	Solid	Cavitary	Solid	Cavitary
Location of nodule	Lateral basal segment, RLL	Lateral basal segment, RLL	Anterior basal segment, RLL	Lateral basal segment, RLL
Size, mm	8	9	18	13
Distance from pleura, mm	21	3	4	15
Cause of failure	Chest wall stain	Deep parenchyme stain	Not distinguish from anthracosis	Dye in pleural cavity
Pathology	Metastasis	Metastasis	Fibrosis	Granuloma

RLL, right lower lobe.

Table 4 Pathological results of pulmonary lesions

Pathology	Values (n=32)
Neoplastic	23
Primary lung cancer	11
Metastatic lung cancer	11
Benign tumor	1
Non-neoplastic	9
Inflammatory/granulomatous	6
Pulmonary fibrosis	3

(6-12). Also some complications such as a pneumothorax or a hemothorax reduce the accuracy of the procedure. An ENB-guided procedure has already been applied in the diagnostic field (16-19), but only recently performed in the surgical field (5,13-15). This procedure is accomplished through a transbronchial approach; therefore, it has a lower complication rate than the pre-existing transthoracic approach. In our data, just two patients showed mild intrabronchial bleeding, which stopped spontaneously. There was no hemothorax. However, we could not estimate for the occurrence of pneumothorax because we did not use a fluoroscopy or a CT during the procedure and the thoracic surgery was performed continuously after the procedure.

The nodule size 10 mm or less than 10 mm was the

Table 5 Comparisons of single port and conventional three-port video-assisted thoracoscopic surgery

Parameters	Single port VATS (n=11)	Conventional VATS (n=21)	P value
Median nodule size [IQR], mm	8 [4–11]	10 [7–15]	0.168*
Median distance from pleura [IQR], mm	4 [2–6]	7 [2–15]	0.074*
Nodule location			–
Right upper lobe	2	6	
Right middle lobe	2	1	
Right lower lobe	3	8	
Left upper lobe	1	4	
Left lower lobe	3	2	
Pathology			0.019*
Primary lung cancer	1	9	
Metastatic lung cancer	4	8	
Benign lesion	6	4	
Re-resection due to closed RM	0	1	–

*, Mann-Whitney *U* test was applied. VATS, video-assisted thoracoscopic surgery; IQR, interquartile range; RM, resection margin.

most common in this study and all nodules were resected with negative resection margin. This means that small size nodules even though less than 10 mm can be detected by an ENB-guided localization and resected with minimally invasive thoracoscopic surgery. The most common distance from the visceral pleura to lesion was less than 5 mm. In this range, two localizations were failed. Initially, we directly targeted the peripheral nodule or peripherally targeted as possible for the visualization of staining. The peripheral injecting of the dye had a risk to penetrate visceral pleura and, in case of penetration of visceral pleura, we found the dye staining of the chest wall or the dye collection in the pleural cavity. Of course, in this scenario, we had the methods available to localize the nodule. The methods included, first, to re-mark manually of the lung region to face the stained region of the chest wall after lung inflation, and second, to find the penetration point through air bubbling with saline spreading with two lung ventilation.

The failure of the ENB-guided localization was noted in 4 cases (12.5%). This failure rate was slightly higher than other conventional methods (6-8,10,11). In our study, three failure cases were occurred within the initial 3 months. After a learning period of 3 months (10 cases for two surgeons), just 1 case of 21 localizations was failed. After our initial experiences, we learned which position of the electromagnetic locatable guide tip is appropriate and how to control depth of catheter for the dye injection. We were able to reduce the localization failure due to the visceral pleura penetration by placing the electromagnetic locatable guide tip at a distance of 10 mm from the visceral pleura considering a length of dye injecting needle or by injecting dye at several depth levels. The nodules to fail for localization were all located in the right lower lobe, especially the lateral basal segment, although this segment was easy to approach the lesion by the ENB-guided procedure. However, we thought that the relation of anatomical location of the nodule and the failed localization is not meaningful because the cause of the localization failure was different in each case.

The most common pathology was primary lung cancer and metastatic lung cancer. All of the primary lung cancer was adenocarcinoma. In the sublobar resection of an early stage lung cancer, it is very important to obtain a sufficient resection margin (20,21). In our study, all patients obtained a negative resection margin, but we resected the lung under the uncertainty of a deep resection margin. In order to secure the deep resection margin, the methods to visualize the localization in three-dimensions are needed. The localization by placement of a fiducial marker through ENB-guided procedure may be helpful to ensure the deep resection margin (22-24), but additional radiation exposure is required under fluoroscopy. The use of a near-infrared fluorescence imaging, with an ENB-guided indocyanine green injection is also expected to be helpful to secure the deep resection margin without radiation exposure (25,26).

Ng *et al.* (27) reported that the single port VATS is possible for non-palpable pulmonary nodule under localization with hookwire in hybrid operating room. We don't have a hybrid operating room, so we could not use a hookwire or a fiducial marker. We tried to do the single port VATS in the super-selected case of a small peripheral solid nodule and well-stained localization. Total 11 localizations were resected by a single port VATS surgery. The median nodule size and median distance from the pleura were smaller than conventional three-port VATS surgery by our intended selection, but the differences were not significant. A benign lesion was significantly more in the single port VATS group than the conventional VATS group. There was no re-resection in the single port VATS group. This means that the single port VATS with an ENB-guided pulmonary localization can achieve a complete resection in a properly selected case.

In conclusion, this study supposes that the ENB-guided dye localization by a well-trained thoracic surgeon enables the accurate intraoperative identification of a GGN or small pulmonary nodule with minimal complications, and makes minimally invasive surgery possible even for nodules that were difficult to localize. This study need to be proven by large-scale studies and thoracic surgeons should participate for further investigation of this method.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The Institutional Review Board of the Chungnam National University Hospital approved this retrospective study.

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