Multicenter, prospective, observational study of a novel technique for preoperative pulmonary nodule localization

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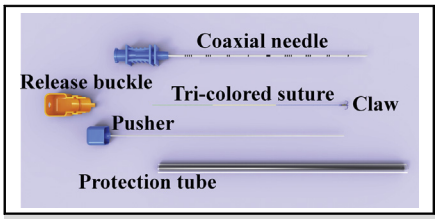
ABSTRACT

Objectives: Minimally invasive surgery provides an ideal method for pathologic diagnosis and curative intent of small pulmonary nodules (SPNs); however, the main problem with thoracoscopic resection is the difficulty in locating the nodules. The goal of this study was to determine the safety and feasibility of a new localization technique tailored for SPNs.

Methods: A computed tomography (CT)-guided technique, which has a tri-colored suture and claw with 4 fishhook-shaped hooks, was designed to localize SPN preoperatively. Then a multicenter, prospective study was conducted to evaluate the safety and feasibility of this device. The primary endpoints included safety (asymptomatic/symptomatic pneumothorax or parenchymal hemorrhage, and unanticipated adverse effects) and success rate (precise placement and device fracture, displacement, or dislodgement). The secondary endpoints included feasibility (duration of the localization procedure and device fracture or fault) and patient comfort (pain).

Results: A total of 90 SPNs were localized from 80 patients. Overall, no symptomatic complications requiring medical intervention, with the exception of asymptomatic pneumothorax (n = 7 [7.8%]) and lung hemorrhages (n = 5 [5.6%]), were observed. The device was successfully placed without dislodgment or movement in 87 of 90 lesions (96.7%). The median nodule size was 0.70 cm (range, 0.30-1.0 cm). The median duration of the procedure was 15 minutes (range, 7-36 minutes). No patient complained of notable pain during or after the procedure.

Conclusions: This new device for SPNs is safe, and has a high success rate, feasibility and good tolerance. (J Thorac Cardiovasc Surg 2020;160:532-9)



The new localization technique system tailored for preoperative lung nodule localization.

CENTRAL MESSAGE

A 4-hook anchor with scaled suture provides advantages for thoracoscopic resection of small lung nodules. Our prospective evaluation showed good success, safety, feasibility, and tolerability.

PERSPECTIVE

One critical problem with thoracoscopic resection of suspected malignant lung nodules is the difficulty in localization. A new localization device with small 4-hook anchor and scaled suture can facilitate minimally invasive surgery for patients undergoing limited resection of small lung nodules.

See Commentaries on pages 540, 541, and 542.

With the development of high-resolution, low-dose computed tomography (CT) for lung cancer screening, small pulmonary nodules (SPNs) suspected to be malignant are detected more frequently. As such, a considerable number of patients with lung cancer are detected and cured at a very early stage, which significantly extends life quality and expectancy.[1,2] For detected SPNs suspected to be malignant, minimally invasive surgical intervention provides the best approach with respect to pathologic diagnosis and curative intent[3]; however, it is challenging to identify

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Abbreviations and Acronyms
CT = computed tomography
SPN = small pulmonary nodule
VATS = video-assisted thoracoscopic surgery

Scanning this QR code will take you to the article title page to access supplementary information.

SPNs if SPNs are too small or too far away from the visceral pleura to be visible or palpable, which may result in conversion to a thoracotomy in 11.9% to 25% of patients.[4-6]

To solve this problem, many different (pre-) operative localization techniques have been developed to provide assistance for the successful resection of SPNs, such as preoperative CT-guided techniques by hookwire,[7,8] methylene blue,[9] microcoil,[6,10-12] fiducial marker,[13] lipiodol,[14] and radionuclides,[15] or intraoperative sonography.[16] Among the methods proposed, the historic and most commonly used technique in China involves the preoperative placement of a hookwire into the nodule guided by a CT scan.[17,18] Of note, hookwire is initially used for superficial breast nodules.[19] With respect to lung nodules, which have a deeper location and apparent movement with breathing, hookwires exhibit relatively high pre-, intra-, and post-operative complications, including dislodgement (0.4%-19.4%), pneumothorax (7.5%-56.2%), lung parenchyma hemorrhage (10.3%-25.8%), hemothorax (1.1%), subcutaneous emphysema (5%), vasovagal syncope (0.6%), and systemic air embolism (0.2%-0.6%).[20-24] In addition, according to the literature, a microcoil is also an effective localization device that has some similarities with our device. Indeed, a microcoil still has drawbacks, such as requiring fluoroscopy visualization, which is more costly and has increased radiation exposure, and the body is metal. In such cases, a better localization technique for patients with SPNs is needed. In this study, we designed a new CT-guided localization technique tailored for thoracoscopic resection of SPNs, then prospectively evaluated the safety and feasibility in patients with SPNs.

METHODS

New Localization Technique System

We designed and fabricated a disposable lung nodule localization device with a biotechnology company (Senscure, Ningbo, China). The device was used for the first time in humans after passing animal experiments and inspections by government agencies. The device consists of the following 5 parts: coaxial needle; pusher; anchor claw; suture; and protection tube (Figure 1). The coaxial needle (Figure 1, *A*), made of medical-grade stainless steel, has a cannula (100 mm in length and 0.9 mm in diameter) that is marked with a scale. An anchor claw, suture, and pusher (0.7 mm in diameter) are preloaded in the device (Figure 1, *B*). The anchor claw (Figure 1, *C* and *D*), which is 4 mm in length and 5 mm in diameter and made of a nickel–titanium memory alloy, has 4 blunt-ended fishhook-shaped hooks that form a cross. Importantly, at the distal end, the anchor claw is connected with a suture (86 mm in length), which is made of polyethylene terephthalate (an absorbable medical material), and tri-colored with each color representing 26 mm, 30 mm, and 30 mm in length from the anchor side (Figure 1, *C* and *D*). To avoid erroneous release of the anchor, there is a safety release buckle covering the hand of the needle and pusher (Figure 1, *E*). The detailed procedure is demonstrated in an animated video (Video 1).

Patient Enrollment

This study was in accordance with the amended Declaration of Helsinki statement (https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/). The clinical trial registration number was ChiCTR-OOC-16009360 (URL: http://www.chictr.org.cn/). Written informed consent was obtained from patients for the procedure and for the medical data to be used in this study. Four medical centers participated (Shanghai Chest Hospital [LS1617], Zhejiang Provincial People's Hospital [2016QX020], Ningbo No. 2 Hospital [PJ-NBEY-2016-010-01], and Tianjin Medical University General Hospital [IRB2016-073-02]) in this study (Table 1). The sample size was determined by single-arm objective performance criteria. The targeted success rate of localization was above 96% according to the data from the literature, the lower limit of the 95% confidence interval should be greater than 86%, the significance level (α) was 0.025, and the power of the test ($1-\beta$) was 80%. Based on these parameters, the sample size was determined as n = 72 based on the below formula.

$$n = \frac{\left[Z_{1-\frac{\alpha}{2}}\sqrt{P_0(1-P_0)} + Z_{1-\beta}\sqrt{P_T(1-P_T)}\right]^2}{(P_T - P_0)^2}$$

In this formula, n represented the sample size, P_0 is the target value, P_T is the expected effective value, α indicates type I error, and β indicates type II error. More detailed information regarding the sample size determination is shown in Appendix E1 and the study protocol (Online Data Supplement). Considering the possible shedding situation, the final sample size was planned to be 80 cases.

The main inclusion criterion was patients with suspicious-appearing malignant subcentimeter nodules (≤10 mm). The surgery indication at our center was lesion size ≥8 mm.[25] For multiple nodules, nodules <8 mm in size suspected to be malignant were synchronously resected with the main lesion. The exclusion criteria included patients with severe comorbidities, advanced disease, or patients who were not candidates for surgery. The detailed inclusion and exclusion criteria are shown in Appendix E2. From January to June 2017, 90 CT-guided localization procedures with this new system were performed prospectively in 80 patients at 4 medical centers. Figure 2 shows the design and logic of this study as well as the Consolidated Standards of Reporting Trials flow diagram.

Localization and Surgical Procedure

The localization procedure was performed in the radiology department. After a CT scan, the localizer was placed percutaneously with the distal end deep to the nodule and the suture part left in the pleural cavity. The patient was then taken to the operating room or back to the ward to undergo surgery within 24 hours. Before surgery, if the patient had additional pain at other than the puncture site, we assessed the pain with a visual analog scale and treated the patient accordingly. The nodule and localizer were removed by wedge resection (Video 2) or

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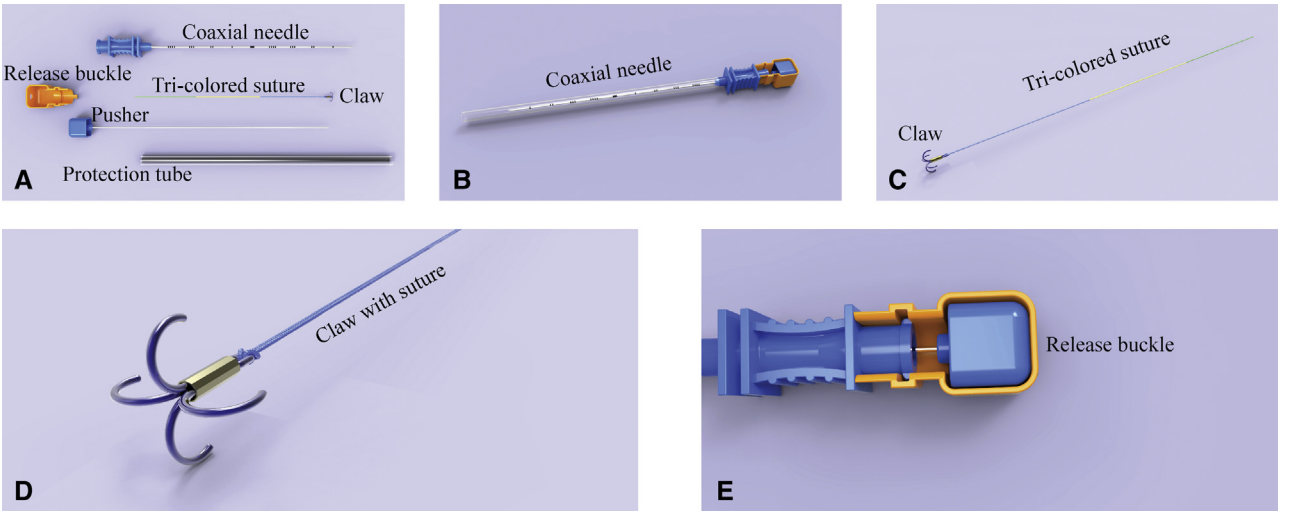
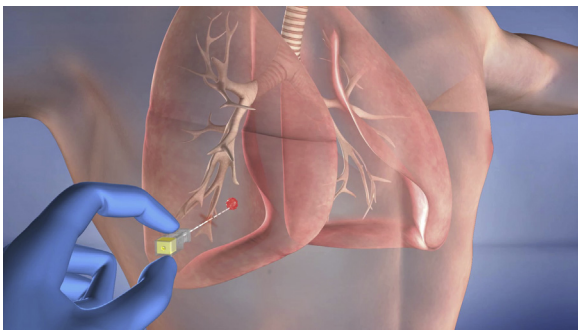


FIGURE 1. These pictures show the detailed configuration of the new localization technique. The device consists of the following 5 parts: coaxial needle; pusher; anchor claw; suture; and protection tube (A). The coaxial needle (B), made of medical stainless steel, has a cannula (100 mm in length and 0.9 mm in diameter) that is marked with a scale. An anchor claw, suture, and pusher (0.7 mm in diameter) are preloaded in the device (A). The anchor claw (C and D), which is 4 mm in length and 5 mm in diameter and made of a nickel–titanium memory alloy, has 4 blunt-ended fishhook-shaped hooks that form a cross. Importantly, at the distal end, the anchor claw is connected with a suture (86 mm in length), which is made of polyethylene terephthalate (an absorbable medical material), and tri-colored with each color representing 26 mm, 30 mm and 30 mm in length from the anchor side (C and D). To avoid erroneous release of the anchor, there is a safety release buckle covering the hand of the needle and pusher (E).

segmentectomy if adequate margins could not be guaranteed using video-assisted thoracoscopic surgery (VATS) visualization. Then, the lesions were sent for intraoperative frozen pathologic examination. A lobectomy and systemic lymph node dissection were determined by frozen pathologic examination if invasive disease and a solid:ground-glass opacity ratio >50% was determined. Figure 3 shows the major steps in the localization procedure. The detailed procedure is described in Appendix E3.

Evaluation

The primary endpoints of the study were the safety (asymptomatic/symptomatic pneumothorax or parenchymal hemorrhage, and unanticipated adverse device effects) and success rate (the distance from placement to the lesion, and device fracture, displacement, or dislodgement) of the localization procedure. Successful localization should meet all the following criteria: (1) The distance between the lesion and anchor claw should not exceed 10 mm, which was measured as the shortest linear distance from the edge of the lesion and anchor claw. (2) During the procedure, the device was placed and retrieved smoothly, and no



VIDEO 1. Animated demo for the new localization device. Video available at: https://www.jtcvs.org/article/S0022-5223(19)32767-9/fulltext.

TABLE 1. Clinical characteristics of patients with pulmonary nodules for localization (N = 80)

Variables	n (%)
Medical center	
Shanghai Chest Hospital	32 (40.0)
Zhejiang Provincial People's Hospital	23 (28.8)
Ningbo No. 2 Hospital	20 (25.0)
Tianjin Medical University General Hospital	5 (6.2)
Sex	
Male	26 (32.5)
Female	54 (67.5)
Age, y, median (range)	53 (27-72)
Smoking history	
Yes	17 (21.3)
No	63 (78.7)
Time between placement and surgery, h, median (range)	
Immediately* (n = 48)	0.5
Not Immediately (n = 32)	8 (2-24)
Patient's comfort (excluding the puncture site)	
Normal	80 (100)
Mild pain	0 (0)
Need analgesic	0 (0)

Data are expressed as n (%) unless otherwise indicated. *The time interval of patients who underwent surgery immediately after localization was assessed as 0.5 hours.

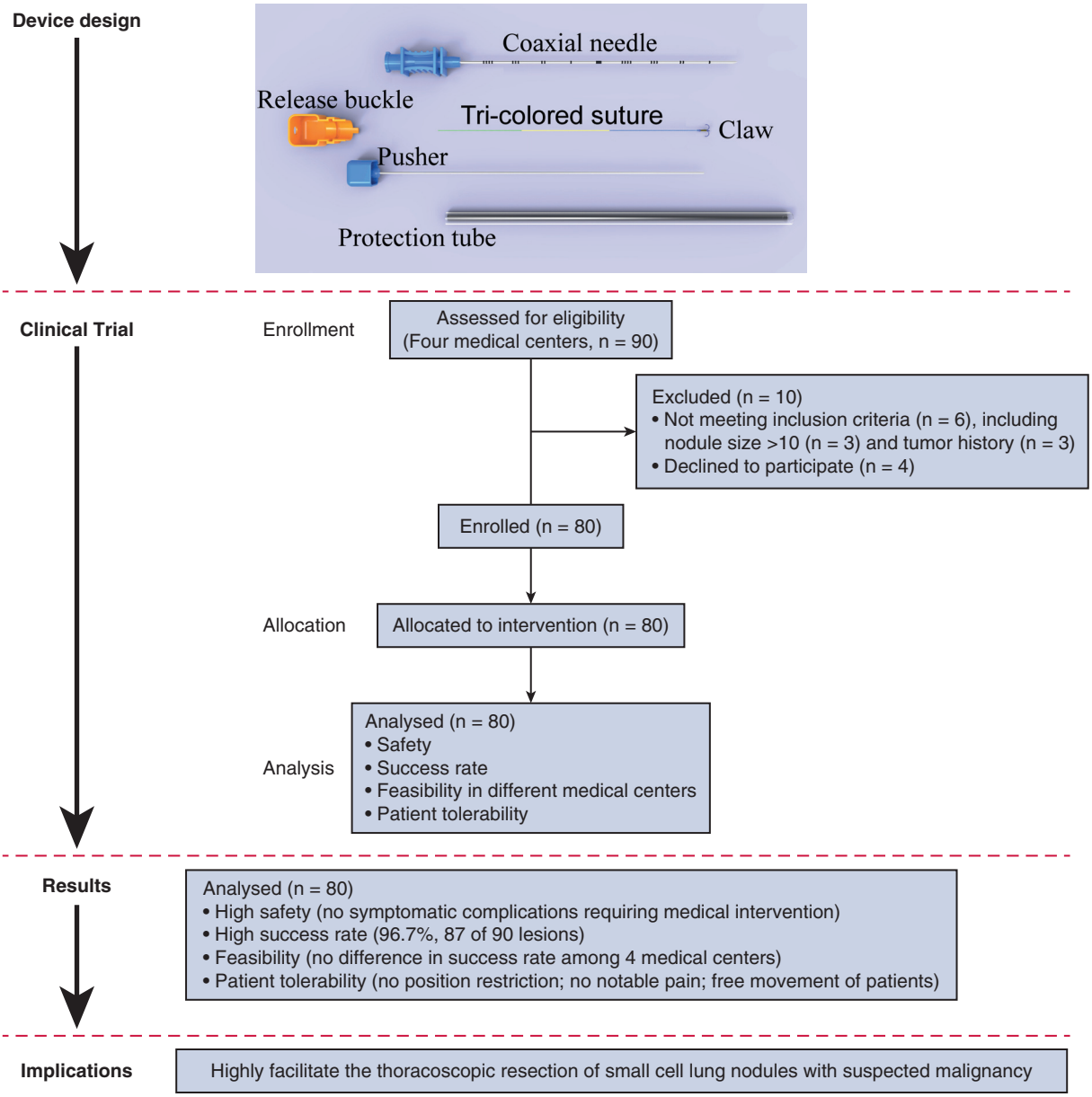


FIGURE 2. The design and logic of this study. We designed a localization device with claw and suture for pulmonary nodules and evaluated its safety and feasibility in a clinical trial with 80 cases. The Consolidated Standards of Reporting Trials flow diagram is included.

break or error occurred. (3) There was no displacement or dislodgement from the localization procedure to the first exploration of VATS. Dislodgement was defined as movement of the localizer completely out of the lung parenchyma and into the pleural cavity. Displacement was defined as movement of the localizer from the original site, but kept in the lung parenchyma (by comparing the 2 measurements of CT and suture by VATS), which can still be used as a guide to indicate the location of the nodule. (4) There was no break of the suture nor hooks while pulling the lung tissue for resection. The secondary endpoints included feasibility (the duration of the localization procedure and device fracture or fault) and patient comfort (pain). The tumor stage was determined as delineated in the Eighth Edition of the Tumor, Node, and Metastasis Classification.[26]

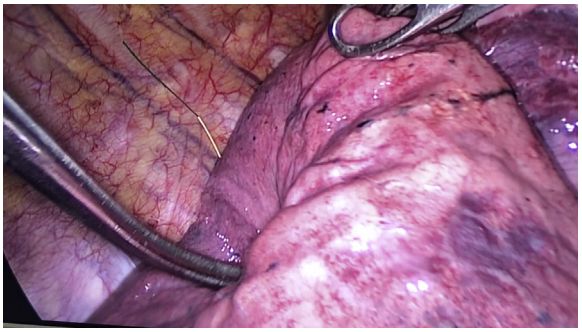
Statistical Analyses

The quantitative data are expressed as a number, median, and range. A categorical variable is described as a number and percentage. A 2-sided Student t test was used for continuous variables, and a χ^2 test or Fisher exact test was used for categorical variables. A P value $< .05$ was considered statistically significant. All statistical analyses were performed using SPSS 22 software (IBM Corp, Armonk, NY).

RESULTS

Patient and Lesion Characteristics

A total of 80 patients (26 male and 54 female; median age, 53 years; age range, 27-72 years) with 90 SPNs were



VIDEO 2. Thoracoscopic wedge resection of small lung nodules after placement of the new device. Video available at: https://www.jtcvs.org/article/S0022-5223(19)32767-9/fulltext.

eligible to enroll in the trial. Patient characteristics are shown in Table 1.

The nodules were classified as solid (2 [2.2%]) and ground-glass opacity (88 [97.8%]). The median nodule size was 0.70 cm (range, 0.30-1.0 cm). All targeted nodules were resected successfully at the first attempt, which was then rapidly found and confirmed by pathologists. Seventy-nine lesions (87.8%) were removed by wedge resection. Seven procedures were subsequently converted to lobectomies because of the invasive disease stage determined by intraoperative frozen section. The remaining 11 lesions (12.2%) were removed by segmentectomy (Table 2).

Procedure Outcomes

No deaths or major complications occurred during the entire process. Also, there were no reported symptoms related to the procedure of localization. Thirteen minor complications (14.4%), including asymptomatic pneumothorax (n = 8 [8.9%]) and parenchymal hemorrhage (n = 5 [5.6%]) occurred that did not require intervention (Table 3). No patients complained of chest pain while waiting for the VATS procedure.

Overall, the localization was successful without dislodgement or displacement in 87 of 90 lesions (96.7%). There were 9 patients who had multiple nodules and underwent simultaneous localization procedures successfully. Of these procedures, double localization succeeded in 8 patients, including 6 procedures performed in 2 different lobes and 2 performed in the same lobe. Also, device placement was successful in 1 patient with 3 lesions located in 2 lobes. All devices were visualized at the first exploration by VATS. No device fracture or fault occurred during the entire procedure. All devices were retrieved entirely from the resected specimens (Table 3).

Three cases failed in this study, which occurred in the early attempts. One failed case was further away from the target nodule. The distance between the claw and the lesion was 11 mm, which was slightly further from the target value (≤10 mm); thus, it was considered a failure. Another case failed due to displacement because the lesion was so

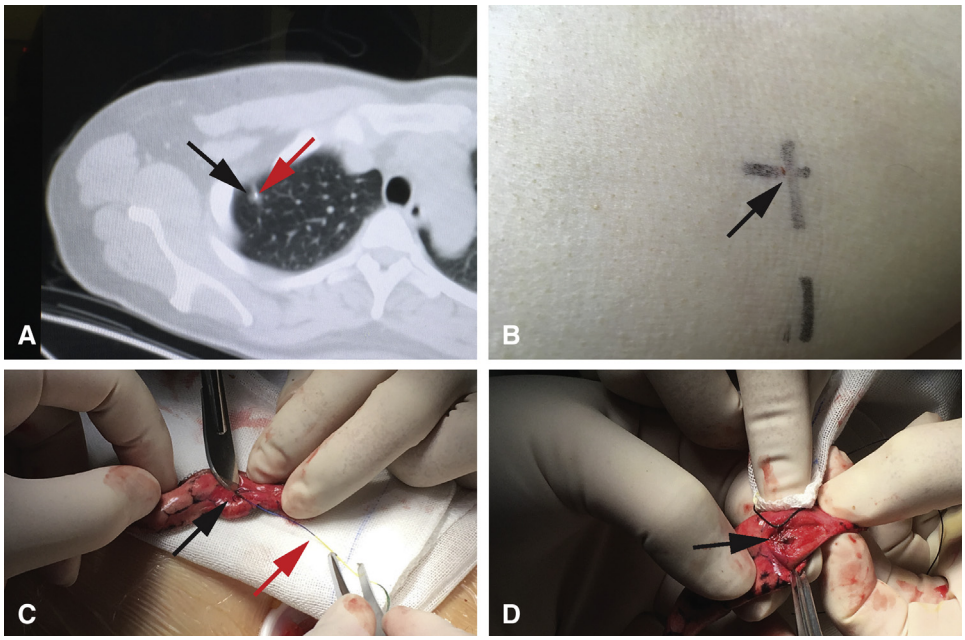


FIGURE 3. The main procedures for patients undergoing localization. A, Computed tomography shows the pulmonary nodule (*black arrow*) and placed anchor claw (*red arrow*). B, The percutaneous puncture site (*black arrow)* after localization; no part of the device remained outside the skin. C, The anchor claw (*black arrow*) and its connected tri-color suture (*red arrow*) were displayed after wedge resection of the pulmonary nodule and its surrounding lung tissue. D, The localized pulmonary nodule (*black arrow*) was found by cutting up the lung tissue under the guidance of the localization device.

TABLE 2. Clinical and pathologic characteristics of pulmonary nodules for localization (N = 90)

Characteristics	n (%)
Size, diameter, cm, median (range)	0.70 (0.3-1.0)
Nodule type	
GGO	88 (97.8)
Solid	2 (2.2)
Location	
Right upper lobe	26 (28.9)
Right middle lobe	5 (5.6)
Right lower lobe	23 (25.5)
Left upper lobe	19 (21.1)
Left lower lobe	17 (18.9)
Nodule depth, mm, median (range)	54.58 (32.00-88.70)
Resection	
Wedge resection	72 (80.0)
Segmentectomy	11 (12.2)
Lobectomy*	7 (7.8)
Pathological diagnosis	
Adenocarcinoma in situ	44 (49)
Minimally invasive adenocarcinoma	27 (30)
Invasive adenocarcinoma	5 (5.6)
Atypical adenomatous hyperplasia	4 (4.4)
Hamartoma	1 (1.1)
Granuloma	4 (4.4)
Reactive lymph node	3 (3.3)
Fibrosis scar tissue	2 (2.2)
Stage†	
Benign	14 (15.6)
0	44 (48.9)
IA1	31 (34.4)
IA2	1 (1.1)

Data are expressed as n (%) unless otherwise indicated. *GGO*, Ground-glass opacity. *Lobectomy was performed after the confirmation of invasive disease by frozen section. †Stage was determined by the Eighth Edition of the Tumor, Node, and Metastasis Classification of lung cancer.

TABLE 3. Characteristics of localization procedure (N = 90)

Characteristics	n (%)
Time of localization procedure, min, median (range)	15 (7-36)
Location of the anchor claw* (n = 88)	
In nodules	18 (20.5)
Around nodules	70 (79.5)
Distance between claw and lesion, mm, median (range)	2.5 (0-11)
Successful localization	87 (96.7)
Unsuccessful localization	3 (3.3)
Fracture or fault of device	0 (0)
Displacement	2 (2.2)
Dislodgement	1 (1.1)
Complications	13 (14.4)
Pneumothorax	
Asymptomatic	8 (8.9)
Symptomatic	0 (0)
Parenchymal hemorrhage	
Asymptomatic	5 (5.6)
Symptomatic	0 (0)
Others	0 (0)
Retrieve of device after resection	90 (100)

Data are expressed as n (%) unless otherwise indicated. *Two dislodgement cases were excluded.

shallow to the pleura that the coaxial needle did not break through the visceral pleura; however, the anchor claw still hooked on the surface of the pleura during the first thoracoscopic exploration. Thus, the lesion was successfully resected under guidance of the anchor claw. The third failed case was due to dislodgment caused by incorrect manipulation.

The median duration of the localization procedure was 15 minutes (range, 7-36 minutes). The claw was placed at a median distance of 2.5 mm (range, 0-11 mm) from the edge of the nodule (Table 3). In the current study, 48 patients (60%) underwent surgery immediately after localization. The time interval was assessed at approximately 0.5 hours, and 32 (40%) had a time interval between surgery and localization, which was 8 hours (median time; range, 2-24 hours). The delay was due to the unexpected prolonged time of other complicated operations and a high volume of patients. Of note, there were no localization failures occurred in this subset (Table 3).

DISCUSSION

Our study showed that the percutaneous placement of this new system was safe with a high success rate and feasibility for SPN localization followed by VATS resection. This device was well-tolerated by patients. This new localization technique is promising in terms of facilitating surgical procedures and the advantages are as follows.

First, the anchor claw can potentially reduce the occurrence of displacement or dislodgement. Specifically, the anchor claw, which is the most critical part of this system, has four tiny blunt-end hook-shaped hooks that form a cross (Figure 1, *C* and *D*). With this design, the anchor can grasp the adjacent lung tissue without causing much damage to the surrounding lung tissue and small blood vessels. More importantly, unlike the hookwire that keeps a piece of stainless steel outside the body after the CT-guided localization, the soft and flexible suture that is connected to the anchor claw can be pushed into the pleural cavity after finishing localization, which may avoid the tension on the anchor claw caused by the breathing movement or position change of patients, thereby reducing the rate of dislodgement. Microcoil also has this problem when the targeted lesion is very superficial. Owing to the self-tension of metal coil, the proximal part of the microcoil might drag the distal

part out of the lung parenchyma.[10] Also, the claw can withstand considerable traction, as based on our in vitro lung tissue localization experiments (data not shown), which is convenient for surgeons to pull the lung tissue to resect the nodules and preserve lung tissues to the greatest extent. Taken together, this new device could potentially increase the success rate.

Second, the scale system of this device helps in terms of effective and precise placement. The coaxial needle has a scale (Figure 1, *B*), which helps to assess the depth of the SPNs during preoperative localization (the distance between the lesions and chest wall is available by CT scan). Notably, one of the key procedures is to take out the pusher (Video 1), then withdraw the coaxial needle carefully until the end is within 0.5 to 1 cm from the inner surface of the chest wall so that the end of the coaxial needle can be exposed to the pleural cavity. The scale of the coaxial needle serves as a good reminder where the operator should stop while handling the coaxial needle. Also, there is a tri-color marking suture (Figure 1, *C*) that facilitates evaluation of the depth of the SPNs and determination of the resection area during surgery, given the more and more frequent application of segmentectomy in malignant pulmonary nodules in the early stage.[27] This scale system provided considerable traction that can facilitate the segmentectomy procedure. In addition, localization could assist segmentectomy in identifying small lesions intraoperatively, determining the intersegmental planes, and obtaining adequate resection margins.[28]

Third, there are other advantages compared with some other techniques, such as hookwire, microcoil, lipiodol, dyes, radiotracer, and near-infrared localization.[29] Specifically, short hookwire, which has some similarities with our device, has been reported to have some major adverse events (air embolism and tension pneumopericardium); thus, short hookwire should not remain inside the body for a relatively long time. It has been reported that thoracic surgeons temporarily missed the target lesions or short hookwires during VATS in 8 of 125 placements (6.4%), and 2 hookwires (1.6%) were not retrieved.[7,30] In addition, there was no need to require the patient to maintain a specific position during the waiting time for surgery, which is generally recommended for hookwire because a piece of stainless steel is retained outside the body. It traverses the entire chest wall, thus, making it vulnerable to fracture with patient movement, frequently causing chest pain, and even leading to vasovagal syncope.[22] It has been reported that microcoil could be left in the chest wall (5%-12%) as well.[10,12] Thus, patients cannot move freely during the waiting time before surgery. Furthermore, our device is able to remain inside the body relatively longer, which was supported by other researchers who replaced the metal wire with suture as well.[7] After placement with this device, the surgeons can either transfer patients immediately to the operating room or back to inward and arrange for surgery within 24 hours. In addition, the absorbable soft suture was well-tolerated by patients, because no infection, dyspnea, cough, and chest pain were observed after localization, and the patients did not complain about notable discomfort or pain. Finally, this technique is easy to operate, as shown by the high success rate. All 3 failed cases occurred in the very early attempts, and no such incidents have occurred since that time.

The limitations of our study included the limited sample size and absence of a control group. The device is not easy to place for nodules located at the apex and diaphragm. Further large-sample randomized clinical trials are warranted to demonstrate the superiority of this technique to the previously used devices, such as hookwire, in our center.

CONCLUSIONS

The new device with a claw and suture system is a safe and feasible approach for SPN localization, which can facilitate the thoracoscopic resection of small lung nodules suspected to be malignant.

Conflict of Interest Statement

Drs Yao and Zhao own the major invention rights of the localization device. Dr Yang was issued a patent for a new type of lung tumor localization needle (patent no.: ZL 2015 1 0497304.8). All other authors have nothing to disclose with regard to commercial support.

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Key Words: small pulmonary nodule, lung cancer screen, localization, video-assisted thoracoscopic surgery, complications

APPENDIX E1. SAMPLE SIZE DETERMINATION

This study was designed by single-arm objective performance criteria. Therefore, the estimation formula of sample size was as follows:

$$n = \frac{\left[Z_{1-\frac{\alpha}{2}}\sqrt{P_0(1-P_0)} + Z_{1-\beta}\sqrt{P_T(1-P_T)}\right]^2}{(P_T - P_0)^2}$$

In this formula, n represented the sample size, P_0 is the target value, P_T is the expected effective value, α indicates type I error, and β indicates type II error. The main outcome indicator of this study was the success rate of localization, which was above 96% according to the data from the literature, and the lower limit of the 95% confidence interval of it should be greater than 86%. Therefore, we set P_0 as 86%, P_T as 95%, the significance level (α) as 0.025, and the power of the test ($1 - \beta$) as 80%. Based on these parameters, the sample size was determined as n = 72. Considering the possible shedding situation, the final sample size was planned to be 80 cases.

The setting of the target value refers to the research data of hookwire for pulmonary nodule localization from literature reports, which were shown in the table seen below. If the lower limit of the $(1 - 2\alpha)$ confidence interval of the success rate of the tested product is higher than the target value, it is considered that this device meets the design requirements.

Study*	Technique	Sample size	Success rate, %
Dendo et al, 2002[E1]	Hookwire	168	97.6
Pittet et al, 2007[E2]	Hookwire	45	96
Ciriaco et al, 2004[E3]	Hookwire	53	92.5
Miyoshi et al, 2009[E4]	Hookwire	108	93.6
Chen et al, 2011[E5]	Hookwire	43	96

*In this study, we also refer to several publications that are in Chinese. Herein, only publications in English were listed.

APPENDIX E2. PATIENT SELECTION CRITERIA

Patients with solitary pulmonary nodules were recommended to undergo with thoracoscopic resection after a multidisciplinary assessment. After we obtained their informed consent, patients received localization procedure using the new device and then underwent resection for the pulmonary nodule. The performance and safety of the system were observed during the whole process.

The inclusion criteria were as follows: (1) The patient's age was between 18 and 80 years; (2) each patient had 1 or more pulmonary nodules with suspected malignancy based on the discussions from lung cancer multidisciplinary team that includes radiologists and thoracic surgeons; (3) imaging examinations showed no evidence of advanced malignancy; and (4) nodules should be smaller than 10 mm in maximum long-axis diameter and deemed to video-assisted thoracoscopic surgery resection.

The exclusive criteria included (1) patients who were judged to be unsuitable for localization before surgery, such as pleural effusion and severe lung injury; (2) patients suffering from severe comorbidity in heart, brain, lung, liver or kidney, or any infectious severe diseases within one month before surgery; (3) patients with distant metastasis; and (4) patients who participated in other clinical trials of drugs or medical devices within one month before surgery.

APPENDIX E3. DETAILED WORKFLOW PROCEDURE

1. A computed tomography (CT) scan is first performed to determine the percutaneous placement site of the needle and the distance between the nodule and chest wall.
2. Then, the localization device is taken out and the protective tube is removed.
3. After determination of the percutaneous placement site, the coaxial needle, which is preloaded with pusher, anchor claw, and suture, is placed beside the target nodules. The depth of the needle can be judged according to the measured distance on the CT and the scale on the coaxial needle.
4. Then, a CT scan is performed to check whether the device is placed in the desired location.
5. Next, take the buckle off, then push the pusher to the end to release the anchor claw.
6. The pusher is taken out, and then the coaxial needle is moved back carefully until its end is within 0.5 to 1 cm to the internal surface of the chest wall so that the end of the coaxial needle can be exposed to the pleural cavity.
7. The pusher is placed back into the coaxial needle and then pushed to the end. Thus, the entire suture can be pushed into the pleural cavity.
8. The coaxial needle, together with the pusher, is taken out of the patient's body, then a further CT scan is performed to check whether the anchor claw is still in the right place and whether there is any complication to intervene.
9. If the anchor claw dislodged, another localization procedure should proceed.
10. The patient's vital signs are checked, and the patient's puncture point is covered with some sterile gauze.
11. Then, the patient is sent to the operation room or ward according to the schedule of each center.

E-References

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