


ORIGINAL ARTICLE

A novel technique for preoperative localization of pulmonary nodules using a mixture of tissue adhesive and iohexol under computed tomography guidance: A 140 patient single-center study

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Abstract

Background: The increase in the incidence of pulmonary nodules has made computed tomography (CT) screening a requirement for diagnosis and treatment. Small pulmonary nodule detection during video-assisted thoracoscopic surgery (VATS) or thoracotomy is frequently challenging; however, accurate and efficient localization of nodules is critical for precise resection. Herein, we introduce and evaluate the feasibility and safety of a novel technique for preoperative pulmonary nodule localization.

Methods: From March 2018 to December 2019, 140 patients with 153 pulmonary nodules measuring <2 cm in diameter were enrolled in this study. Preoperative, CT-guided localization was performed on each nodule with an injected mixture of tissue adhesive and iohexol. Patient and nodule characteristics, localization data, complications, surgical data, and pathological results were analyzed.

Results: All 153 nodules in 140 patients were successfully marked preoperatively and detected during surgery ($n = 153/153$). Mean nodule size was 8.7 ± 2.6 mm, and mean distance from nodule to pleura was 7.9 ± 8.2 mm. The mean procedural time was 8.7 ± 1.0 min. Nine patients (6.4%) underwent two simultaneous nodule localizations and two patients (1.4%) underwent three simultaneous nodule localizations. Pneumothorax (17/140, 12.1%), pain (6/140, 4.3%), and pungent odor (5/140, 3.6%) were the major complications. No patient required further treatment, and no allergic reactions or embolisms were observed.

Conclusions: Preoperative CT-guided nodule localization using a mixture of tissue adhesive and iohexol is an efficient technique for localizing small and impalpable pulmonary lesions, including multiple pulmonary nodules. Our study demonstrates that this novel method is safe and straightforward to implement.

KEYWORDS

Computed tomography, localization, pulmonary nodules, tissue adhesive

INTRODUCTION

Due to the current widespread use of low-dose computed tomography in a variety of clinical settings such as screening programs for lung cancer, an ever increasing number

of indeterminate, small pulmonary nodules (SPNs) are being reported.¹ At the same time, accurate pathological diagnoses are critical for clinical decision-making. Although detailed features of pulmonary nodules may be observed from CT images, classification of lesions as benign or malignant is still difficult with this noninvasive test.² Consequently, a significant increase in the number of

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patients referred to thoracic surgeons for surgical resection has occurred.

Video-assisted thoracoscopic surgery (VATS) has been widely used for the diagnosis and treatment of pulmonary nodules. In contrast to open thoracotomy procedures, the minimally invasive nature of VATS provides numerous advantages for preventing postoperative complications, reducing pain, reducing recovery time, and improving esthetics have made VATS the procedure of choice for the management of SPNs.^{3,4} VATS provides a unique opportunity for surgeons to obtain a histological diagnosis, and also enables definitive treatment for patients with early stage lung cancer. Thus, VATS plays an essential role in managing patients with peripheral and potentially malignant SPNs. In recent years, other minimally invasive surgical methods, such as Da Vinci robotic surgery, have also been widely used for resection and biopsy of pulmonary nodules.

However, it is still challenging for surgeons to identify nodules by palpation or inspection during thoracotomy, especially when nodules are too small or lack sufficient consistency (e.g., ground-glass opacities [GGOs]). Using VATS for SPNs may also be challenging if the nodule is not easily accessible, or if it is located a certain distance from the pleural surface. Previous studies reported that lesions would not be detected during VATS in patients with nodule sizes <10–15 mm and with a nodule to pleura distance >10 mm.^{5,6} Suzuki et al. recommended preoperative localization for nodules <10 mm, when situated >5 mm from the visceral pleura.⁵ In case with those types of small nodules, extended resections or conversion to thoracotomy may occur.

Various methods have been established and applied in clinical practice for preoperative lesion marking, including hook-wire placement, microcoils, and methylene blue injection. All these techniques involve percutaneous placement of localizing material (e.g., hook-wire), or injection of a marking substance (e.g., methylene blue).⁷ Although the success rate of localizations is typically satisfactory, each method has advantages and drawbacks. The shortcomings of these procedures are generally related to migration or spillage of the material used between the radiological intervention and surgery; so ideally, the two are performed in succession as rapidly as possible. In addition, complications of percutaneous nodule marking include adverse effects similar to those reported for image-guided lung biopsies, i.e., pneumothorax, bleeding, and less frequently, air embolism.

In this study, we demonstrated a novel preoperative localization method using a tissue adhesive and iohexol mixture injected under CT-guidance which has been performed at our center since 2018. As this technique has rarely been reported, we conducted this study to evaluate its feasibility and safety.

METHODS

Patients

From March 2018 to December 2019, 140 patients with 153 nodules who underwent CT-guided tissue adhesive

and iohexol mixture localization at the Second Xiangya Hospital of Central South University were enrolled in this study. The inclusion criteria were: (i) age > 18 years; (ii) nodule size <2 cm in diameter with presumed difficulty in visual inspection, palpation, and localization during surgery; and (iii) Participants who were able to sign informed consent. The exclusion criteria were: (i) severe cardiovascular and cerebrovascular disease or liver and kidney dysfunction; and (ii) previous chest surgery that might interfere with preoperative localization. The study was approved by the Medical Ethics Committee of the Second Xiangya Hospital of Central South University, and the trial is registered with the Chinese Clinical Trials Register: ChiCTR2000035151.

Information including patient and nodule characteristics, localization results, and operative and perioperative results were prospectively collected. Statistical analyses were performed using the SPSS software (IBM SPSS statistics, version 22.0, Armonk, NY, USA). Variables are presented as percentages, proportions, mean \pm standard deviation (SD), and range (minimum and maximum values). We used the Student's *t*-test or Mann–Whitney tests to compare continuous variables.

Localization procedure

Tissue adhesive is a liquid in vitro, and polymerizes quickly when it comes into contact with tissue fluid after being injected into the body. We hypothesized that a hard artificial nodule would be formed after injection into the lung, allowing rapid detection and precise palpation or inspection during surgery. Combining the adhesive with iohexol enables clear identification of artificial nodule size and location on CT images. To prove our hypothesis and provide a basis for the feasibility of this technique, animal experiments were performed. After injection of tissue adhesive and iohexol mixture, artificial nodules were successfully formed in the lungs of two experimental pigs. Distinguishing the artificial nodules from GGOs (indicated by the black arrow in Figure 1(a, b)) was straightforward. The animals were immediately euthanized, and the heart and lungs were dissected from the thorax. The artificial nodules (marked by the white arrow in Figure 1(c, d)) were easily detected by palpation or inspection, demonstrating the feasibility of the technique.

The study patient procedures were performed by a multidisciplinary team, including thoracic surgeons and radiologists, on the morning of the day scheduled for the surgery. The position of the patient during CT scanning depended on the location and depth of the nodule. The most suitable position enabled a vertical puncture with the shortest distance from the nodule to the body surface, and without obstruction of the ribs and scapula. In general, a supine position was used for nodules located on the ventral side, a lateral position was used for nodules

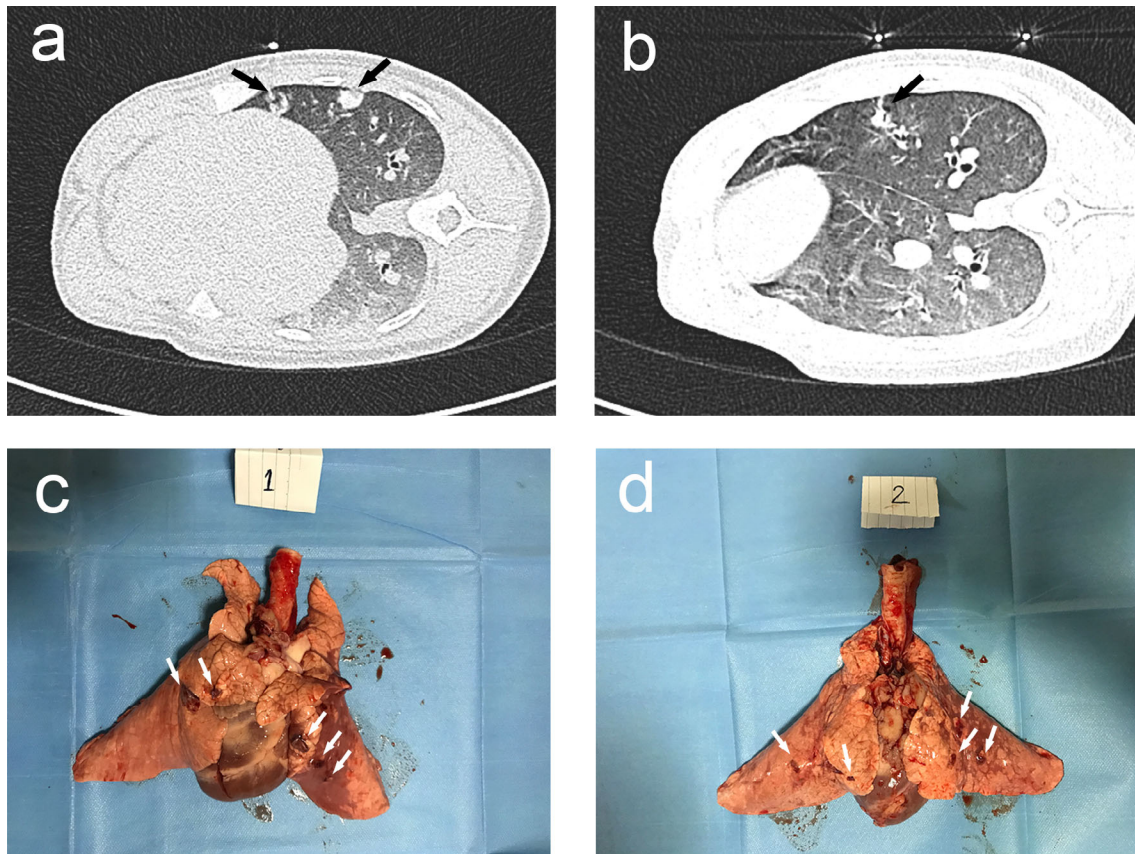


FIGURE 1 Computed tomography (CT)-guided tissue adhesive and iohexol injection in pigs. (a, b) Artificial nodules (black arrow) were formed successfully in the lungs of two animals. After CT scanning, both animals were euthanized, and the heart and lungs were dissected from the thorax. (c, d) The artificial nodules (white arrow) were detected easily through palpation or inspection

located on the lateral side, and a prone position was used for nodules located on the dorsal side (Figure 2). The patient's arm was placed beside the body or raised beside the head. After determination of the position and probable puncture region, a grid mesh constructed with seven metal wires (10 mm between each wire) was placed on the region (Figure 3(a)). CT scans were performed during a pause in normal inspiration with the Siemens Somatom Force CT scanner (Siemens Medical Solutions). Images were reconstructed using a 1-mm slice thickness and a 1-mm slice interval (Figure 4(a)). To reduce variations between the two scans caused by lung movement and define positioning more accurately, patients were asked to inhale for only 1 s and hold their breath during the CT scan. Subsequently, the radiologist and the thoracic surgeon determined the precise location for the implanted artificial nodule together as the extent of surgical resection and puncture difficulty (including ribs or scapula obstruction) should be considered. Considering that a vertical puncture was the most stable and controllable method, the projected position of the expected artificial nodule was marked on the body surface as the puncture point, and the distance to the puncture was measured (Figure 3(b)). Simultaneously, 0.1 ml of tissue adhesive (B.Braun Surgical SA) was mixed

with 0.1 ml iohexol in a 1-ml syringe. Based on the injection depth, an appropriate syringe needle was used for the puncture. Typically, 5- or 10-ml syringes were used when the injection depth was <32–35 mm, and an 80-mm long sterile needle was used when the injection depth was >35 mm. Precise adjustment of the puncture depth could be achieved by cutting the needle sheath to a proper length (Figure 3(c)). After routine disinfection and draping, patients were asked to inhale and hold a breath just as they did during the previous CT scan. Next, an assistant held a right-angle ruler with a bubble level to ensure verticality, and the surgeon performed the puncture and injection of the mixture (Figure 3(d)). Subsequently, another CT scan was conducted to evaluate the localization and observe any complications (Figure 4(b)). Patients were then moved back to the ward and prepared for surgery.

Surgical procedures

Patients received VATS or robotic-assisted surgery using the da Vinci Surgical System on the same day as localization. R0 resections were performed for all cases. During the surgery, the artificial nodules were initially detected

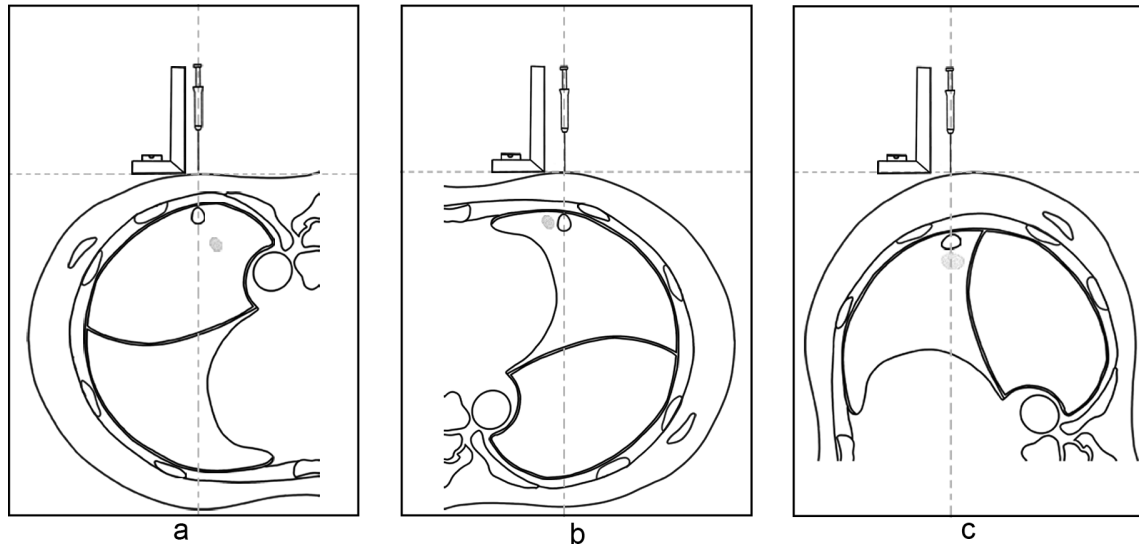


FIGURE 2 Patient positioning for CT scanning. (b) In general, the supine position was used for nodules located on the ventral side; (c) the lateral position was used for nodules located on the lateral side; and (a) the prone position was used for nodules located on the dorsal side. The open nodules represent the artificial nodules formed by injection of the mixture. The solid nodules represent the patient pulmonary nodules

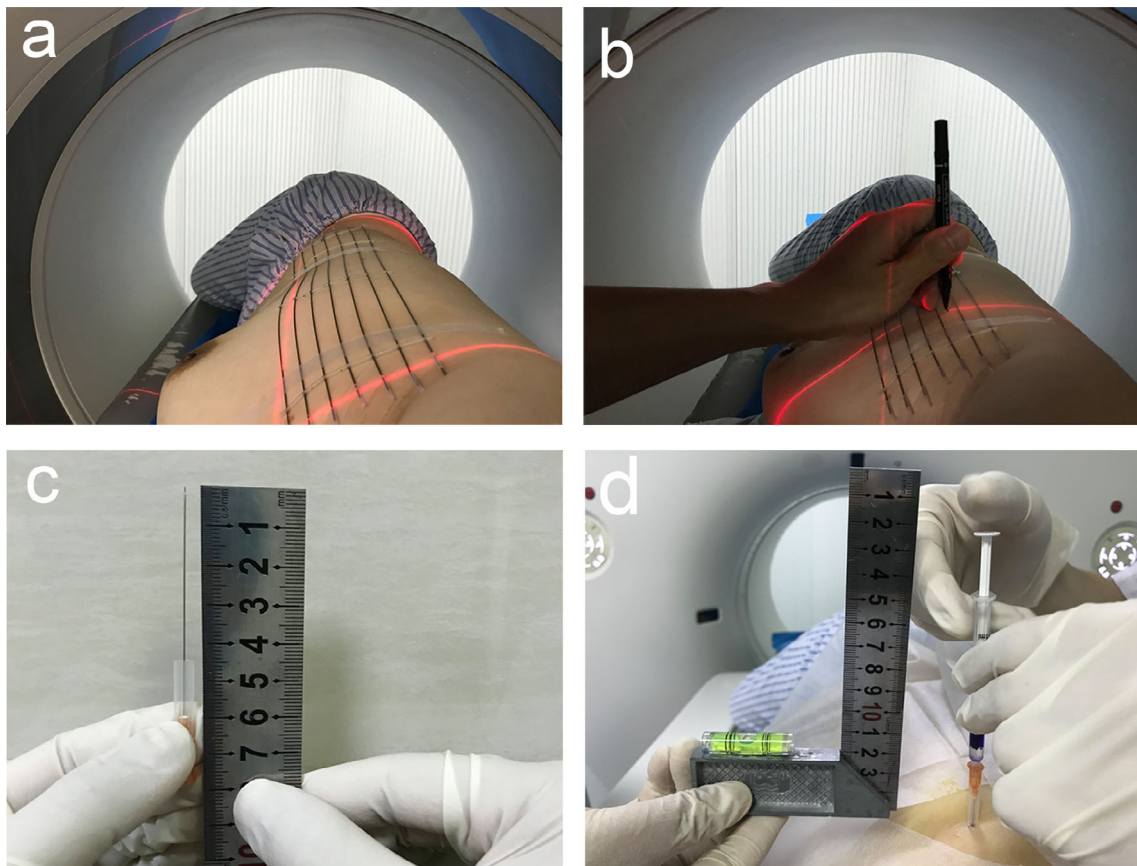


FIGURE 3 Computed tomography (CT)-guided puncture procedure. (a) A mesh was placed on the probable puncture region with proper positioning before CT scanning. (b) The radiologist marks the puncture point on the body surface under CT guidance. (c) The needle sheath is cut to the proper length to construct a cannula for the puncture. (d) The puncture and injection of tissue adhesive and iohexol mixture is performed

by palpation or inspection (Figure 5). Based on the relative position of the pulmonary nodules and the artificial nodules, the lesions and range of resection were

determined. The remainder of the procedure was dictated by the results of intraoperative frozen section analysis (Figure 5(c)).

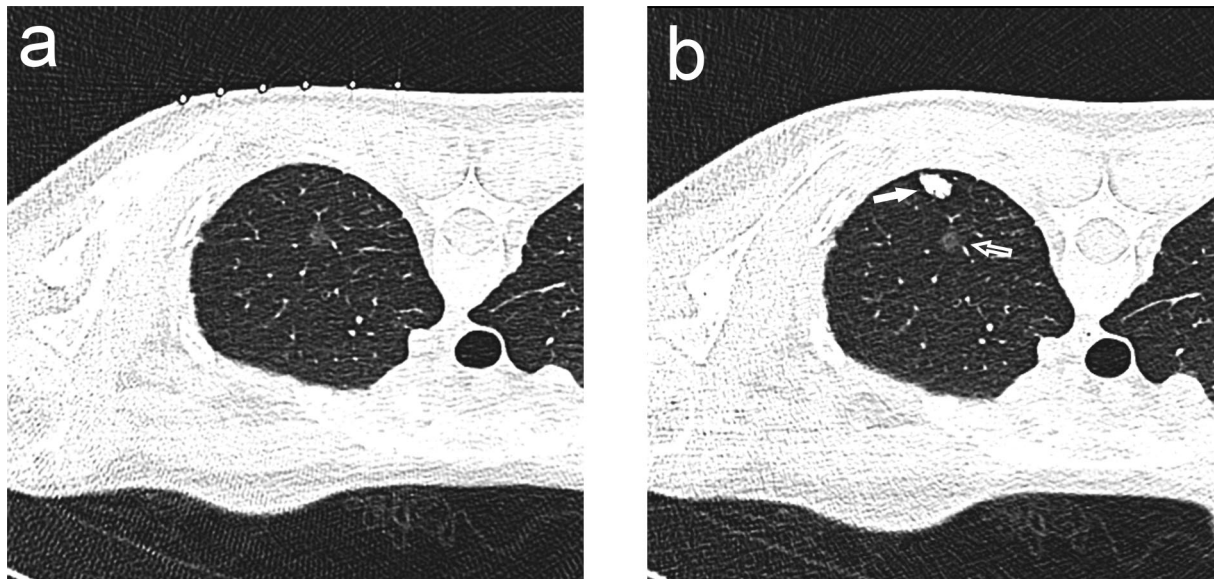


FIGURE 4 CT scan images. An initial CT scan determines the site for artificial nodules (a). After injection, a CT image shows the relative position between the pulmonary nodule (open arrow) and the artificial nodule (solid arrow) formed by injection of tissue adhesive and iohexol (b)

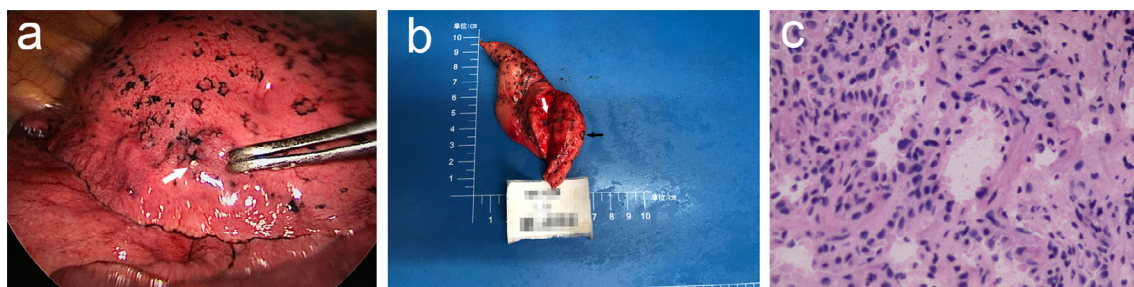


FIGURE 5 Surgical images. (a) The artificial nodule was clearly recognized during surgery by palpation or inspection. (b) Specimen from wedge resection: the white arrow represents the pulmonary nodule and the black arrow represents the artificial nodule. (c) The pathological result is determined as adenocarcinoma in situ

RESULTS

Patient and nodule characteristics

From March 2018 to September 2019, 140 patients with 153 pulmonary nodules underwent CT-guided tissue adhesive and iohexol mixture localization followed by VATS or robot-assisted surgery. The study sample included 38 men and 102 women. The mean patient age was 52.8 ± 9.6 years (range: 27–77 years). The mean size of the pulmonary nodules was 8.7 ± 2.6 mm (range: 3.4–18.4 mm), with a mean distance from the pleura to the nodules of 7.9 ± 8.2 mm (range: 0–37.7 mm). Most patients (129 patients, 92.1%) underwent a single pulmonary nodule localization, whereas nine patients underwent two localizations, and two patients underwent three localizations during the procedure. The patients and nodules characteristics are described in Table 1.

CT-guided tissue adhesive and iohexol mixture localization

Preoperative CT-guided tissue adhesive and iohexol mixture localization was successfully performed in all patients. A total of 138 of 153 localizations (90.2%) were successful at the first attempt. A total of 15 localizations failed at the first attempt, with reasons including obstructions of anatomical structures (nine cases) and tissue adhesive coagulation in the syringe before injection (six cases). All of these 15 cases were successful after the readjustment of position or reconfiguration of tissue adhesive and iohexol mixture. The mean procedural time was 8.7 ± 1.0 min (range: 6.2–16 min). The mean needle insertion depth from the body surface was 47.6 ± 13.9 mm (range: 20.8–92.3 mm). The mean size of the artificial nodules was 12.9 ± 2.9 mm (range: 3.9–27.1 mm), and was significantly different from that of the pulmonary nodules ($z = -9.520$, $p < 0.001$ by the

TABLE 1 Characteristics of patients and nodules

	N (%) or mean \pm SD (range)
Total patient numbers	140
Total number of nodules	153
Age (years)	52.8 \pm 9.6 (27–77)
Sex	
Male	38 (27.1)
Female	102 (72.9)
Number of nodules in each patient	
1	129 (92.1)
2	9 (6.4)
3	2 (1.4)
Nodule type	
Pure GGNs	90 (58.8)
Part-solid GGNs	58 (37.9)
Solid nodules	5 (3.3)
Nodule site	
Left upper lobe	35 (22.9)
Left lower lobe	26 (17.0)
Right upper lobe	59 (32.7)
Right middle lobe	9 (5.9)
Right lower lobe	33 (21.5)
Nodule size (mm)	8.7 \pm 2.6 (3.4–18.4)
Distance from pleura to the nodule (mm)	7.9 \pm 8.2 (0–37.7)

Abbreviations: GGNs, ground-glass nodules; SD, standard deviation.

Mann–Whitney test). The mean distance from the artificial nodules to the pleura was 4.71 \pm 5.8 mm (range: 0–25.9 mm), and significantly different from that of the pulmonary nodules ($z = -3.713$, $p < 0.001$ by the Mann–Whitney test). The mean distance from the pulmonary nodules to the artificial nodules was 7.1 \pm 7.1 mm (range: 0–37.0 mm). Major complications included pneumothorax (17 patients, 12.1%), pain (six patients, 4.3%) and pungent odor (five patients, 3.6%). No patients required further treatment before surgery, and no allergic reactions or embolisms were observed in any patient (Table 2).

Perioperative variables

All pulmonary nodules and artificial nodules were detected and resected using VATS (94 patients, 67.1%) and robot-assisted surgery (46 patients, 32.9%), and no patients were converted to thoracotomy. Wedge resection for 111 nodules accounted for 72.5% of surgical procedures. Other procedures included segmentectomy for 31 (20.3%) nodules and lobectomy for 11 nodules (7.2%). Lobectomies were performed in 10 patients for 11 nodules because intraoperative pathological diagnosis suggested adenocarcinoma, and we then performed lobectomies after wedge resection. Pathological results from all patients included 22 (14.4%) benign nodules, 130 (85%)

TABLE 2 CT-guided tissue adhesive and iohexol mixture localization results

	N (%) or mean \pm SD (range)
Dislodgement	0 (0)
One-time success rate	138 (90.2)
Localization procedural time (min)	8.7 \pm 1.0 (6.2–16.0)
Artificial nodule size (mm)	12.0 \pm 2.9 (3.9–27.1)
Distance from pleura to artificial nodules (mm)	4.71 \pm 5.8 (0–25.9)
Insertion depth of needle (mm)	47.6 \pm 13.9 (20.8–92.3)
Distance from pulmonary nodules to artificial nodules (mm)	7.1 \pm 7.1 (0–37.0)
Localization-related complications	
Pain	6 (4.3)
Pungent odor	5 (3.6)
Pneumothorax	17 (12.1)
Hemoptysis	0 (0)
Hemothorax	0 (0)
Allergic reaction	0 (0)
Pleural reaction	0 (0)
Embolism	0 (0)

Abbreviations: CT, computed tomography; SD, standard deviation.

precancerous and primary lung cancer lesions, and one (0.6%) metastatic cancer lesion. The shortest period between localization and follow-up visits was nine months, and the longest period was 30 months. No needle-track implantation metastasis was observed (Table 3).

DISCUSSION

Significant technical progress has been made in the field of VATS over the last 15 years. Using VATS for formal lung resection is now well accepted, and it has demonstrated survival outcomes comparable to traditional thoracotomy.⁸ However, palpation of pulmonary nodules through a standard VATS access incision may be difficult, especially when the nodule is small and deep within the lung parenchyma. These types of situations require preoperative localization. In this study, we introduced a novel preoperative localization method using an injected tissue adhesive and iohexol mixture. A total of 140 patients with 153 nodules were enrolled in this study, and all nodules were successfully marked preoperatively and detected during surgery.

Preoperative CT-guided localization has been widely used to mark pulmonary nodules. Both solid and liquid materials, such as hookwires,^{9–14} lipiodol,¹⁵ microcoils,^{12,16,17} dye^{17,18} and radiotracers¹⁹ have been developed as localization markers. We summarized the literature on preoperative localization techniques with sample numbers >100 and other similar studies published within the last five years,^{11,20–25} and compared the results with ours (Table 4). Although these methods have been applied widely in clinical practice and

TABLE 3 Operative and pathological results

	n (%)
Surgical method	
Video-assisted thoracic surgery	94 (67.1)
Da Vinci robot systems	46 (32.9)
Type of resection	
Wedge resection	111 (72.5)
Segmentectomy	31 (20.3)
Lobectomy	11 (7.2)
Pathological diagnosis	
Benign	22 (14.4)
Inflammation	6
Fibrosis	14
Lymph node	1
Granuloma	1
Precancerous lesion and primary lung cancer	130 (85.0)
Atypical adenomatous hyperplasia	14
Adenocarcinoma in situ	49
Minimally invasive adenocarcinoma	28
Invasive adenocarcinoma	39
Metastatic cancer	1 (0.6)
Colon cancer	1
Needle-track implantation metastasis	0 (0)

reported favorable results, they reveal some shortcomings. Based on a meta-analysis comparing the success and complication rates in hookwire, microcoil and lipiodol localizations conducted by Park et al., hookwire localization demonstrated the highest complication rates of pneumothorax and hemorrhage, and the lowest success rate due to dislodgement or migration.²⁶ Migration occurring in microcoil localizations has also presented problems, and dye injections, such as patent blue V or methylene blue, may cause obvious marks on the lung surface. Therefore, considering the potential for diffusion, surgery should be performed as soon as possible after dye localization to avoid resection expansion. A similar issue exists for lipiodol localizations where distribution of the lipiodol has been found in surrounding lung structures. Localization of radiotracers requires specialized equipment and radiation protection. Some new methods other than CT-guided localization have been reported in recent years including electromagnetic navigation bronchoscopy (ENB) localization,^{27,28} 3-D printing localization,²⁹⁻³¹ and virtual-assisted lung mapping (VAL-MAP).³² Although these methods have reportedly achieved satisfactory success rates, their complexity may prevent general use, and studies with larger sample sizes are needed to validate them.

In this study, we introduced a novel, preoperative CT-guided localization technique. Some differences between our method and other methods used in previously reported studies are evident. First, we used an injected mixture of tissue adhesive and iohexol as a localization marker. The tissue

adhesive consists of monomeric n-butyl-2-cyanoacrylate that polymerizes quickly when it comes into contact with tissue fluid and forms a tough artificial nodule that may be identified by palpation or inspection. Furthermore, the adhesive is nontoxic and has a favorable biosafety rating. The rapid solidification of the tissue adhesive when it comes into contact with tissue fluid also helps reduce the risk of pneumothorax and embolism. Iohexol, an iodine contrast medium, allows the artificial nodules to be displayed more clearly on CT images. It also emphasizes the spatial relationship between the artificial nodule and the pulmonary nodule, enabling surgeons to better determine the resection range during the surgery. Second, our localization procedure is quite different from other published methods. We stipulate that all punctures are performed vertically, which is the most stable and controllable direction in our opinion. The patients in our study were asked to take a normal breath and hold it for the puncture point marking and puncturing procedures during the first CT scan. Thus, since the puncture point, injection depth, and direction were predetermined, the puncture and injection could be performed in a single step. This approach allows positioning to be more accurate and saves time. Patients need only undergo two CT scans instead of three, thus reducing radiation exposure risk. Moreover, because of the low incidence of complications and favorable tolerance, our method may locate multiple nodules in the same patient. As demonstrated in our cohort, nine patients underwent two simultaneous localizations and two patients underwent three simultaneous nodule localizations. Therefore, our method is useful for the treatment of multiple pulmonary nodules. In this method, the determination of the ideal puncture pathway was a critical determinant for localization success. The puncture point and injection depth determined the difficulty of the task in localization.

There were some shortcomings in our method. First, occasionally tissue adhesive solidified in the syringe before injection, which resulted in six failed localizations at the first attempt. This kind of problem happened in the early period of our study, and has also been reported in another study.²³ Shortening the contact time between tissue adhesive and iohexol in the syringe can reduce the incidence of such events, i.e., injection as soon as possible after mixing. Second, as a CT-guided localization technique, obstructions of anatomical structures such as scapulae and ribs make it difficult to locate nodules in special localizations, such as the lung apex and scapular region. In our study, we asked nine patients to change inspiration or adjust the relative position between the scapulae and the lung by means of abduction or internal rotation of the scapulae. Third, a suitable command of inspiration is vital to our technique. We did not calculate a proper and personalized capacity for each patient in this study. Therefore, we asked patients to inhale for 1 s and hold their breath. Fourth, there is a potential risk for complications. Although the major complications in this study were pneumothorax, pain, and pungent odor, severe complications (e.g., embolism) might also occur due to the

TABLE 4 Comparison of different localization techniques

Year	Author	Techniques	Patients	Nodules	Dislodgement n (%)	Time (min) mean ± SD	Nodule size (mm) mean ± SD (range)	Distance (mm) mean ± SD (range)	Pneumothorax n (%)	Hemorrhage n (%)
Other techniques										
2015	Su et al. ¹⁶	Microcoil	92	101	2 (2.0)	N/A	8.8 ± 4.6 (2–26)	9.2 ± 8.0 (0–34)	16 (15.8)	9 (8.9)
2016	Miura et al. ¹⁵	Lipiodol	55	103	0 (0)	N/A	5.5 ± 3.4 (0.9–17)	16 ± 15 (0–91)	39 (61)	39 (35)
2016	Hanauer et al. ⁹	Hookwire	181	187	7 (3.7)	N/A	10.3 (4–29)	11.6 (0–45)	71 (38.0)	11 (5.9)
2018	Manca et al. ¹⁹	99mTc-MAA and nonionic contrast medium	395	395	4 (1.0)	N/A	13.0 (5–20)	15.0 (6–29)	12 (3)	N/A
2018	Thistlethwaite et al. ¹⁴	Needle	253	253	8 (3.2)	N/A	11.9 ± 3 (6–15)	33.7 ± 8.1 (19–49)	12 (4.7)	N/A
2019	Chen et al. ¹⁸	Patent blue V	282	282	2 (0.7)	24(3–70)	9.0 ± 5.0 (3.0–32.0)	10.0 ± 9.0 (0–32.0)	48 (17.0)	51 (18.0)
2019	Park et al. ¹⁰	Hookwire	113	113	4 (3.5)	23.7 ± 6.3	10.8 ± 6.1 (3–28)	20.2 ± 12.4 (5–55)	26 (23.0)	8 (7.1)
2019	Patella et al. ¹³	Spiral wire	93	102	3 (2.9)	N/A	11.4	23.1	5 (4.9)	19 (18.6)
2019	Wang et al. ¹¹	Hookwire	120	120	2 (1.7)	15.1 ± 5.8	9.8 ± 3.3	10.8 ± 8.0	25 (20.8)	17 (14.2)
2020	Yang et al. ¹²	Microcoil	205	218	5 (2.3)	19.3 ± 4.5	8.2 ± 3.5	11.4 ± 7.4	27 (13.2)	11(5.4)
2020	Sun et al. ¹⁷	Hookwire	102	106	5 (4.7)	14.3 ± 5.3	10.7 ± 4.3	12.9 ± 5.8	15 (14.7)	7 (6.9)
2020	Sun et al. ¹⁷	Microcoil	239	293	0 (0)	14.3 ± 5.0	8.1 ± 4.6	12.7 ± 8.7	9 (3.8)	1 (0.4)
2020		Methylene blue	103	103	0 (0)	15.0 ± 5.6	9.2 ± 4.9	8.9 ± 5.8	4 (3.9)	0 (0)
Similar techniques										
2018	Cen et al. ²⁰	Medical adhesive	188	188	0 (0)	16.3 ± 5.2	9.6 (5–29)	14 (0–52)	16 (8.5)	15 (7.9)
2018	Tao et al. ²¹	Medical adhesive	41	44	0 (0)	16 ± 8	9 ± 4 (5–18)	10 ± 7 (2–30)	3 (7)	3 (7)
2018	Huang et al. ²²	Medical adhesive	88	90	0 (0)	N/A	9.6 ± 3.4 (3–20)	22.1 ± 15.7	28 (31)	8 (9)
2019	Wang et al. ¹¹	Cyanoacrylate	149	149	0 (0)	10.9 ± 2.9	8.0 ± 3.0	9.9 ± 7.6	27 (18.1)	12 (8.1)
2019	Yao et al. ²³	Cyanoacrylate	55	69	0 (0)	13.7 ± 7.2 (7–37)	8.5 ± 3.2 (5–20)	10.9 ± 7.7 (2–36)	12 (21.8)	7 (12.7)
2020	Jiang et al. ²⁴	Glue and dye	346	383	2 (0.5)	N/A	7.7 ± 3.7 (2–30)	9.4 ± 9.3 (0–60)	16 (4.6)	7 (2.0)
2020	Wang et al. ²⁵	ZT medical glue	101	106	0 (0)	13.7 ± 7.2 (7–37)	8.5 ± 3.2 (5–20)	10.9 ± 7.7 (2–36)	18 (17.8)	1 (1.0)

Abbreviations: 99mTc-MAA, 99mTc-labeled human albumin macroaggregates; N/A, not available.

injection of the mixture. Therefore, preoperative planning of localization including positioning of the puncture point and the depth of puncture is of critical importance, and requires some practical experience. Fifth, this study was a single-center, nonrandomized analysis. Multicenter studies with larger sample sizes and control groups should be performed to confirm our results.

In conclusion, preoperative CT-guided tissue adhesive and iohexol mixture localization was proven to be a safe, straightforward and efficient technique, with a high success rate and low complication rate. This novel method is effective for localization of pulmonary nodules and its use should be encouraged.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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