World Journal of Surgical Oncology

RESEARCH

Open Access

Noninferiority comparison of electromagnetic navigation-guided versus computed tomography-guided percutaneous localization of multiple small pulmonary nodules: a prospective randomized clinical trial

Hongliang Hui[1†], Haoran Miao[1†], Fan Qiu[1†], Huaming Li[1], Yangui Lin[1*], Yiqian Zhang[1*] and Bo Jiang[1*]

Abstract

Background Accurate preoperative localization is a challenge in thoracoscopic surgery for multiple pulmonary nodules. In this study, we aimed to assess the accuracy and feasibility of electromagnetic navigation (EN)-guided percutaneous localization.

Methods We enrolled 50 patients with multiple pulmonary nodules for EN-guided (EN group) or CT-guided (CT group) localization. The primary outcome was the localization accuracy, and the primary analysis was to assess the noninferiority (noninferiority margin of 5 mm) of EN-induced localization deviation compared with that of CT-induced deviation. The secondary outcomes included the procedural duration, anxiety score, and incidence of complications.

Results Among the 50 patients randomized to the EN- and CT-guided groups, 24 patients (53 nodules) underwent EN-guided preoperative marking, and 25 patients (54 nodules) underwent CT-guided preoperative marking. The demographic, clinical, and radiological characteristics did not differ significantly between the groups ($P > 0.05$). Among these patients, the EN group was noninferior in terms of localization deviation compared with the CT group (9.0 [6.5] vs. 7.5 [6.0] mm; $P = 0.33$; absolute difference 0.9 [95% CI] 0.03–1.77]). Furthermore, the procedural duration was 16.3 (4.2) minutes for the EN group and 22.3 (8.2) minutes for the CT group ($P = 0.002$). Additionally, the EN group

†Hongliang Hui, Haoran Miao and Fan Qiu contributed equally to this work.

*Correspondence:
Yangui Lin
linyg5@mail.sysu.edu.cn
Yiqian Zhang
zhangyq235@mail.sysu.edu.cn
Bo Jiang
jiangb55@mail.sysu.edu.cn

Full list of author information is available at the end of the article

exhibited significant improvements compared with the CT group on the basis of the Amsterdam Preoperative Anxiety and Information Scale, particularly in relation to the S and C subscales' cumulative scores.

Conclusions EN was found to be noninferior to CT in terms of localization accuracy, as it significantly decreased the procedural duration and relieved psychological stress for patients who underwent simultaneous surgery for multiple pulmonary nodules.

Clinical Trial Registration Chinese Clinical Trial Registry Identifier: ChiCTR2200056734.

Keywords Electromagnetic navigation, Computed tomography, Multiple pulmonary nodules, Localization accuracy, Video-assisted thoracoscopic surgery

Background

The advent of high-resolution, low-dose computed tomography (CT) has enabled the detection of small or faint pulmonary nodules for lung cancer screening [1]. In fact, the NELSON study revealed that nearly half of the participants had multiple nodules during their CT screening for lung cancer [2]. For patients with multiple pulmonary nodules, minimally invasive surgery is an ideal approach for early diagnosis and treatment [3, 4]. However, during video-assisted thoracic surgery (VATS), particularly uniportal VATS, accurate identification of pulmonary nodules can be challenging since they are invisible and inaccessible [5]. Consequently, thoracic surgeons may need to broaden the scope of lung resection or even resort to open thoracotomy when nodules are not detected during the intraoperative phase [6]. However, this may lead to postoperative lung function impairment and a decrease in quality of life [7]. Therefore, accurate preoperative localization of multiple pulmonary nodules is essential.

Several techniques have been developed to aid pulmonary nodule localization, either through a percutaneous or transbronchial approach [8, 9]. However, no standard preoperative localization technique has been agreed upon thus far. While CT-guided percutaneous localization is widely used because of its technical maturity and high success rate [10], it is not without limitations and risks, such as localization-related pain [11], hemopneumothorax [12], high psychological stress,[7] and radiation exposure [13]. In recent years, electromagnetic navigation (EN) technology has rapidly advanced by integrating three-dimensional CT reconstruction, electromagnetic field positioning, and virtual bronchoscopy navigation. It enables precise access to any lung area through bronchoscopy, facilitating preoperative positioning via bronchial marker placement [14, 15]. Moreover, the latest generation of EN technology also permits the percutaneous localization of nodules [16]. Compared with traditional positioning methods such as CT-guided localization, EN technology has the advantages of not requiring radiation, being minimally invasive, and resulting in fewer complications. However, its measurement of accuracy and feasibility parameters requires further investigation.

Owing to the differences in localization methods, we hypothesized that the accuracy of EN-guided percutaneous localization would be noninferior to that of the CT-guided method. Therefore, we conducted a prospective randomized clinical trial to investigate the noninferiority of EN-guided percutaneous localization accuracy and feasibility over the CT-guided method.

Methods

Trial design and participants

Patients were recruited sequentially from 2022 to 2023 in the current prospective, noninferior, randomized clinical trial. Patients were randomized at a 1:1 ratio to receive preoperative localization via either EN-guided or CT-guided methods. This study followed the Consolidated Standards of Reporting Trials (CONSORT) guidelines [17]. The study was approved by the Ethics Committee of our institution and was performed in accordance with the Declaration of Helsinki guidelines. The trial was registered at the Chinese Clinical Trial Registry. The participants were informed of the potential risks associated with their participation, and written informed consent was obtained prior to participation. Participants could withdraw their consent at any time during the study without affecting their medical care.

Inclusion and exclusion criteria

Adult patients (over 18 years old) scheduled for VATS pulmonary nodule resection were assessed for eligibility by a trained research assistant. The main inclusion criteria were as follows: (i) the number of target nodules was 2 or 3; (ii) the inner margin of the target nodule was at least 20 mm from a major vessel; (iii) the maximum diameter was less than 20 mm; and (iv) the surgeon confirmed that multiple pulmonary nodules were necessary for localization (see supplementary material 1 for details). The main exclusion criteria were as follows: (i) allergy to indocyanine green (ICG); (ii) target nodule obscured by the scapula, limiting access to the puncture needle; (iii) metal implants in the body that cannot tolerate magnetic fields; (iv) abnormal coagulation; (v) abnormal liver or kidney function; (vi) vulnerable patient groups (prisoners, pregnant/breastfeeding mothers, intellectual disabilities, etc.);

and (vii) patient refusal to continue the study at any stage of the study.

Interventions and randomization

Randomization was performed using a block size of 4 to create a computerized randomization list, the results of which were placed in sealed envelopes by individuals who did not participate in this trial. After consenting to participate in the trial, the participants were assigned a randomization number on the basis of the order of their admission to the hospital. Because masking was unfeasible, the study was not blinded after randomization.

EN-guided percutaneous localization

The EN system (Langkai Medical) imports digital imaging and communications in medical data from preoperative high-resolution chest CT to reconstruct three-dimensional (3D) maps of the lungs and pulmonary nodules (Fig. 1A). Patients were administered entire intravenous anesthetic and single-lumen No. 7.5

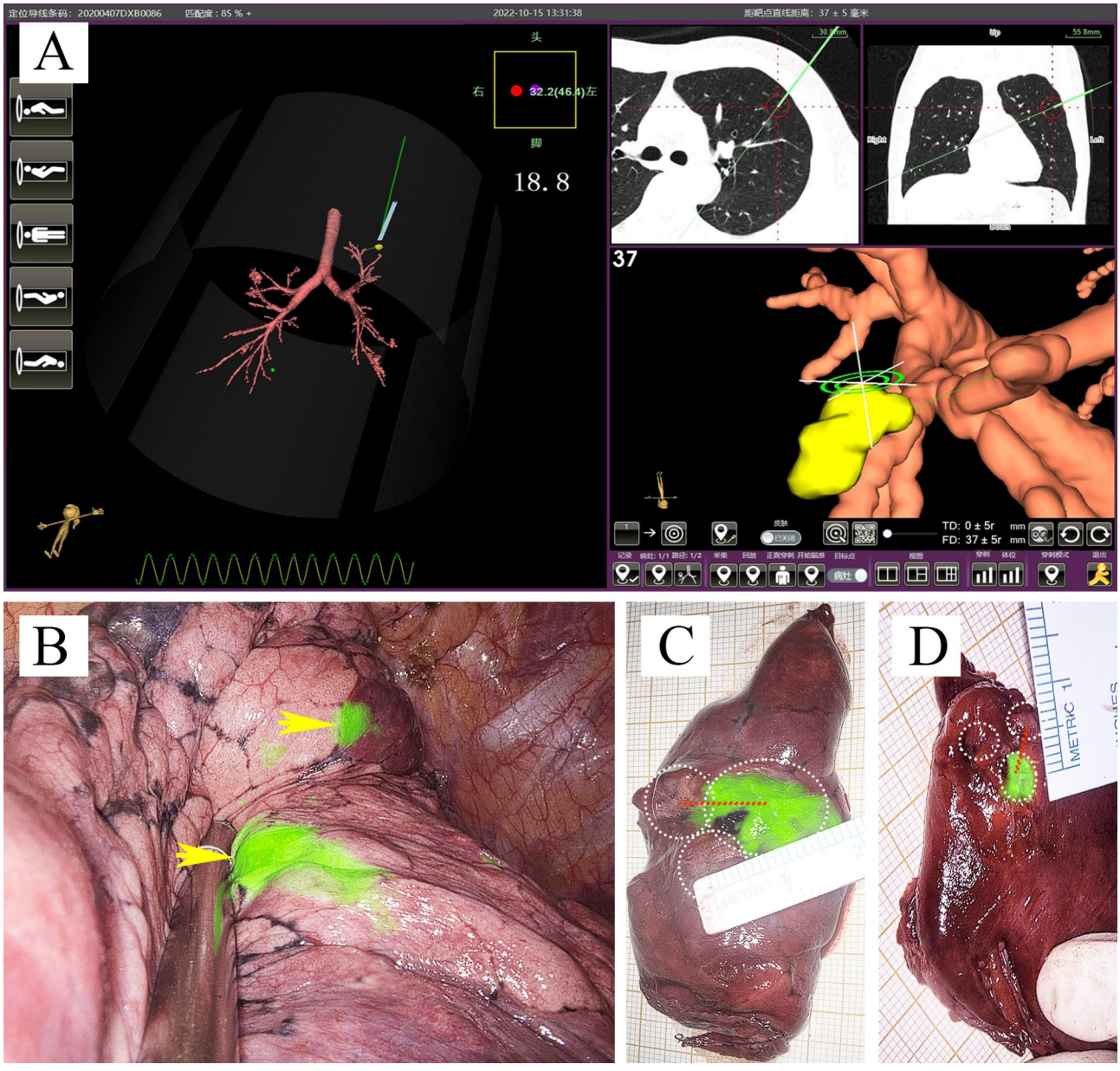

Fig. 1 Electromagnetic navigation (EN)-guided percutaneous procedure. **a** The EN system screen displays real-time imaging during EN-guided percutaneous localization. The trajectory path (green line) toward the target nodule is demonstrated in the transverse view and the coronal view. **b** Indocyanine green (ICG) fluorescence was detected via thoracoscopy in fluorescence mode, with yellow arrows indicating the localization points. **c** and **d** Pulmonary nodule profiles in ex vivo specimens; white dashed circles represent fluorescence or pulmonary nodules, and red dashed lines represent localization deviations

endotracheal intubation in a supine position on an electromagnetic bed upon entering the operating room. A 3.1 mm bronchoscope with the guidewire was inserted through the endotracheal tube to match the 3D image. The entry point of the chest wall and the navigation path to reach the target lesion are planned on the basis of 3D images. During the positioning process, electromagnetic navigation can track the puncture needle in real time by detecting the position of the electromagnetic tip tracking needle. The needle was placed at the top of the planned chest wall entry point, and under the guidance of the electromagnetic navigation system, the angle with the target lesion was selected. The needle was pushed through the chest wall toward the target lesion (Fig. 1A). Once the needle tip reached the target lung nodule, the puncture needle core was removed, and a marker solution (ICG 0.2 mL, 0.025 mg/mL) was injected through the puncture needle to complete the localization process (Video 1). After localization, VATS was performed directly in the same room.

CT-guided percutaneous localization

We conducted all the CT-guided localizations within four hours prior to surgery. The patient was placed in the appropriate position (prone, supine, or lateral) on a Siemens SOMATOM 256 spiral CT scanner (Germany). Initially, a CT scan was performed to determine the optimal puncture path (Fig. 2A). After routine aseptic preparation and local anesthesia, a 19-gauge puncture needle was inserted along the predesigned path. The needle core

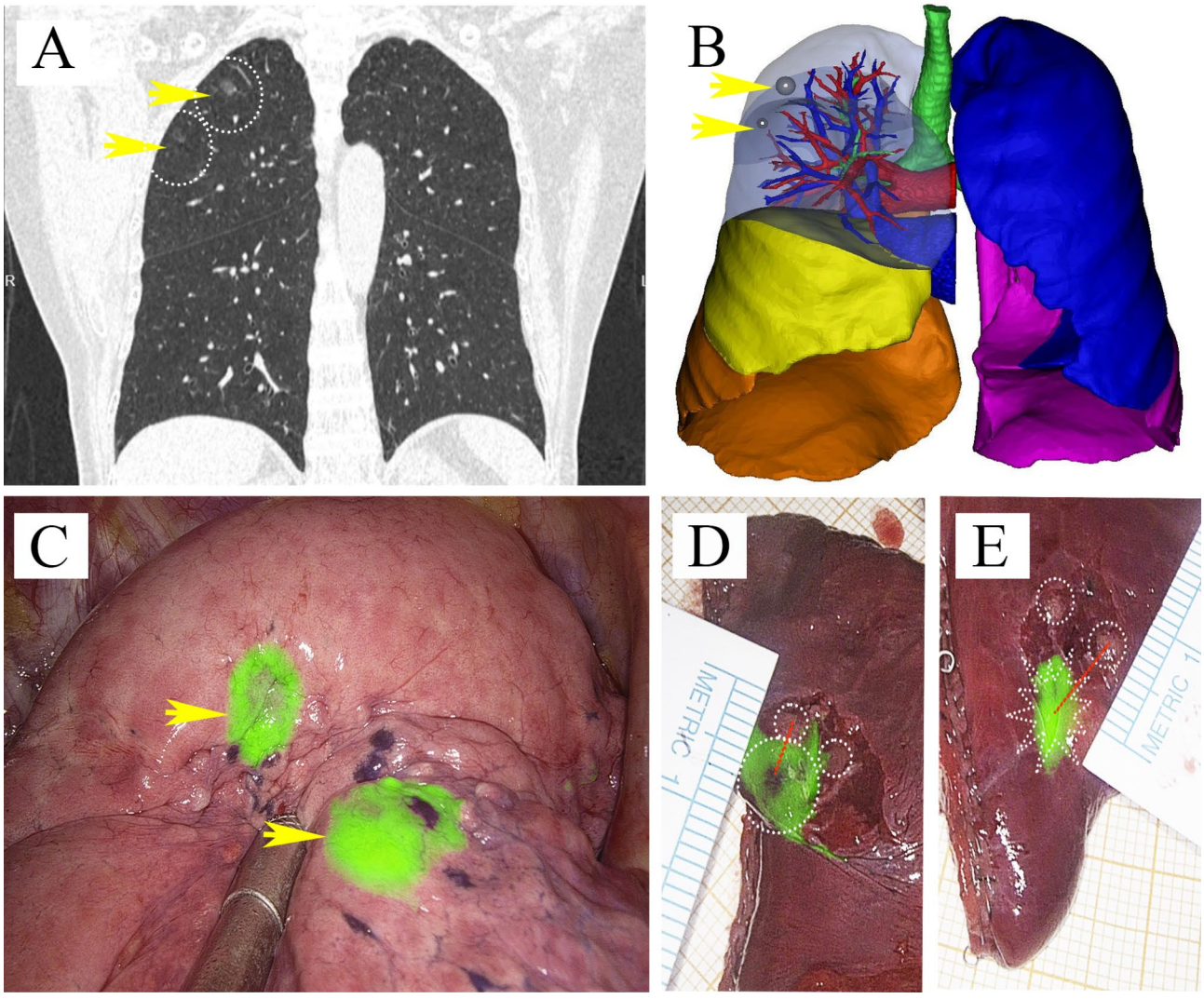

Fig. 2 Computed tomography (CT)-guided percutaneous procedure. **a** Coronal CT image with a lung window showing pulmonary nodules in the right upper lobe (yellow arrowhead). **b** Anterior view of the preoperative 3D reconstruction showing the location of the right upper lobe pulmonary nodules (yellow arrow). **c** Indocyanine green (ICG) fluorescence was detected via thoracoscopy in fluorescence mode, with yellow arrows indicating the localization points. **d** and **e** Pulmonary nodule profiles in ex vivo specimens; white dashed circles represent fluorescence or pulmonary nodules, and red dashed lines represent localization deviations

was then withdrawn, and a marker solution (ICG 0.2 mL, 0.025 mg/mL) was injected. If pneumothorax occurred and an additional lung puncture was not possible, the procedure was interrupted, and closed chest drainage was considered to control the pneumothorax if necessary. Finally, a CT scan was performed to evaluate complications such as bleeding or pneumothorax.

Uniportal VATS of the lung

CT-guided localization was followed by transport to the operating room. For EN-guided localization, a single-lumen tracheal tube with an obstruction tube was used. A 2 cm skin incision was made in the 4th or 5th intercostal space of the midaxillary line, a 5-mm, 30-degree infrared fluorescence thoracoscopy was employed to observe fluorescence staining (Figs. 1B and 2C), and the nodule and its surrounding 2 cm lung tissue were subsequently wedge shaped and resected via an endoscopic stapling device. If green fluorescence was not observed during surgery, then the pulmonary nodule was localized, and wedge resection or segmental resection was performed according to the preoperative 3D reconstruction image (Fig. 2B).

Outcomes

The primary outcome was the localization accuracy (marker deviation), which was defined as the distance between the center point of the localization mark and the target nodule in the resected specimen. Two outcome assessors completed measurements of the primary endpoints throughout the trial. After the specimen was removed, the pulmonary nodule was carefully touched, and the lung tissue was incised in a straight line between the midpoint of fluorescence on the pleural surface and the midpoint of the contacted pulmonary nodule. Then, on one side of the lung tissue section, the midpoint of the longest diameter of the fluorescent area was selected as the midpoint of the localization marker, and the distance from the fluorescent midpoint to the lung nodule midpoint was measured and recorded as the localization accuracy (Fig. 1C and D, and Fig. 2D and E). For lesions that were not successfully removed for the first time, extensive resection was needed, and the distance between them was measured after ex vivo recombination. The secondary outcomes included the following: (i) procedural duration (time from the bronchoscope entering the endotracheal intubation to the removal of the puncture needle for the EN group and time from the first CT scan to the final scan for the CT group); (ii) anxiety score (assessed at the night before the surgery via the Amsterdam Preoperative Anxiety and Information Scale (APAIS) by the research assistant); and (iii) incidence of complications, including localization-related complications, such as pneumothorax and pulmonary hemorrhage. The main outcome was noninferiority, and the secondary outcome was superiority.

Statistical analysis

In our preliminary study conducted with six patients (three in each EN and CT group and two nodules in each patient), the mean (SD) marker deviation was 9.5 (3.9) and 6.9 (3.6) mm in the EN and CT groups, respectively. Sample size calculation was performed with PASS V.11.0 (PASS, NCSS, USA). A total of 88 nodules (22 patients with at least 44 nodules in each group) were randomly assigned to obtain 90% power with a 1-sided α of 0.05 and a noninferiority margin of 5 mm. Considering the dropouts, 25 patients per group were suggested for this study.

Statistical analysis was performed with SPSS software (SPSS 21.0, Chicago, IL, USA). Continuous variables are expressed as the mean (SD) or median (interquartile range) as appropriate. Normally distributed continuous variables were analyzed via independent sample t tests, and nonnormally distributed continuous variables were analyzed via Mann–Whitney tests. The categorical variables are expressed as n (%) and were analyzed by the χ-square test or Fisher's exact test (when a cell value was lower than 5). All the statistical analyses were 2-sided, and $P<0.05$ was considered statistically significant. Through a review of relevant publications and on basis of clinical practice, 5 mm was ultimately determined to be the appropriate noninferiority margin [18]. Noninferiority was pronounced if the upper limit of the 95% confidence interval (CI) for the absolute deviation was less than 5 mm.

Results

Patient characteristics

A total of 94 patients were approached to participate in this study from May 1, 2022, to August 20, 2023; 44 patients were ineligible because they did not meet the inclusion criteria or refused to participate; and 1 patient in the EN group withdrew for refusal to receive the corresponding intervention. Finally, 49 patients completed the study protocol. The EN group comprised 24 patients, with 53 pulmonary nodules resected. The CT group comprised 25 patients, with 54 pulmonary nodules resected. A flowchart of the study participants is shown in Fig. 3. The demographic, clinical, and radiological characteristics did not differ significantly between the two groups ($P>0.05$) (Table 1).

Characteristics of pulmonary nodule localization

Each nodule was redefined as either an upper or lower nodule according to its position relative to the tracheal bulge. Despite significantly greater marker deviation in the EN-guided group than in the CT-guided group for

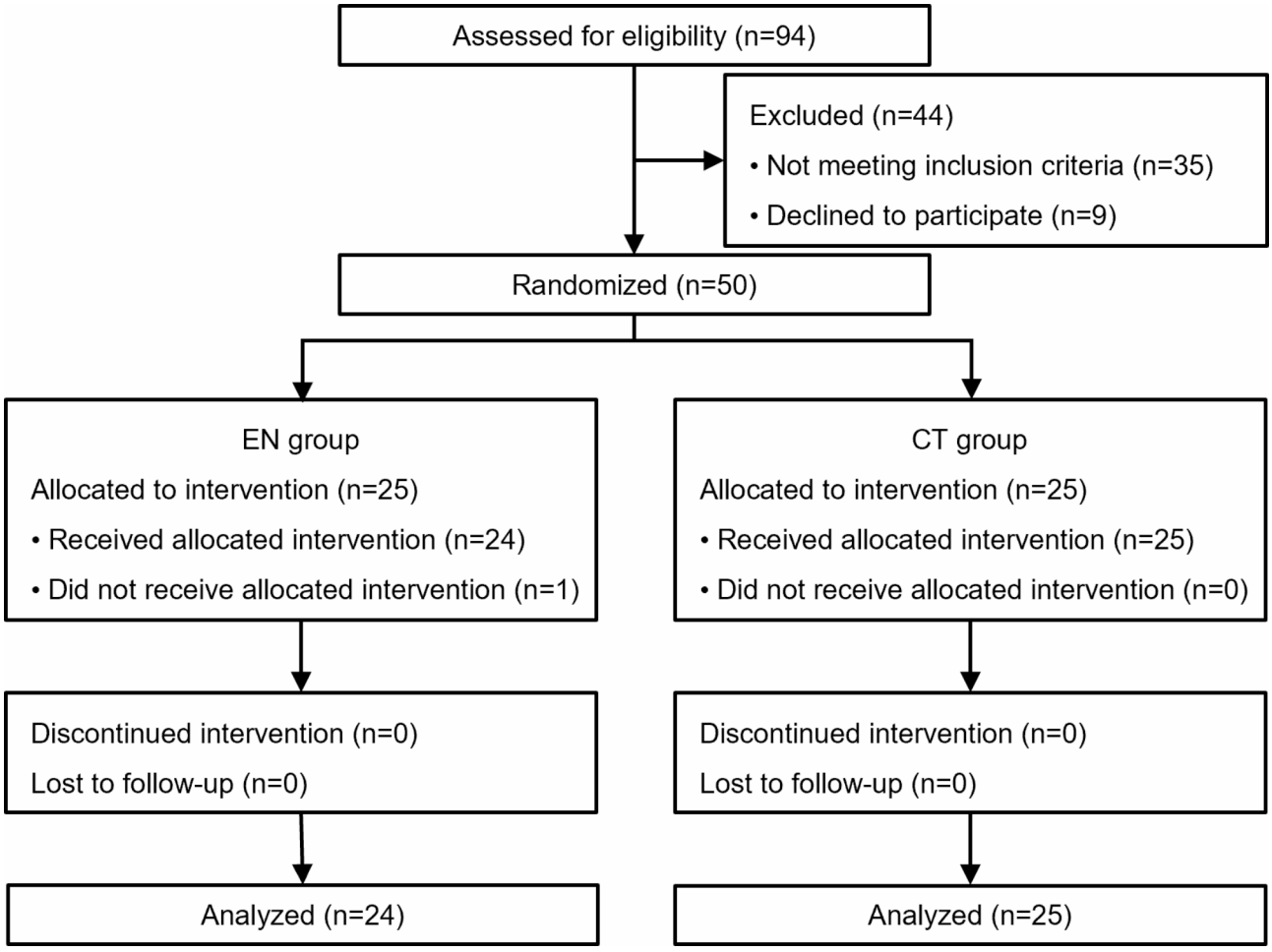

Fig. 3 Flow chart of patient selection. EN: electromagnetic navigation; CT: computed tomography

the upper nodules (median [IQR], 7.5 [7.8] versus 5.0 [7.0] mm; $P=0.049$), there was no difference in marker deviation for the lower nodules between the two groups (median [IQR], 9.0 [6.5] versus 10.0 [9.0] mm; $P=0.50$). Ultimately, no significant differences in overall marker deviation were found between the EN and CT-guided groups (median [IQR], 9.0 [6.5] versus 7.5 [6.0] mm; $P=0.33$) (Table 2; Fig. 4). The 95% CI for the difference in marker deviation between the two groups ranged from 0.03 mm to 1.77 mm, which did not reach the upper limit of the 5 mm noninferiority margin. The 95% CI for the difference in marker deviation for the upper and lower nodes ranged from 0.96 mm to 2.84 mm and from -2.06 mm to 0.66 mm, respectively, indicating noninferiority (Fig. 5).

The mean (SD) procedural duration in the EN group was significantly shorter than that in the CT group (16.3 (4.2) versus 22.3 (8.2) min; $P=0.002$). The mean (SD) procedural duration was shorter in the EN group than in the CT group when 2 pulmonary nodules needed to be localized (15.3 (4.2) versus 20.4 (7.8) min; $P=0.015$). The advantage of the mean (SD) procedural duration was more obvious when 3 pulmonary nodules needed to be localized (20.1 (4.1) versus 32.4 (9.6) min; $P=0.035$) (Table 2).

In terms of the APAIS score, the sum A, sum S, and sum C subscales yielded significantly better outcomes in the EN group than in the CT group. Although the EN group also had better outcomes than did the CT group in sum I, the differences in outcomes between the two groups were not statistically significant (Table 3).

The number of patients who experienced complications is reported in Table 2. In the CT group, 11/25 patients (44%) presented with pneumothorax or pulmonary hemorrhage, most of whom had asymptomatic small volume pneumothorax, and no patients underwent preoperative pigtail insertion. There was no incidence of complications assessed by CT scanning or other methods in patients after positioning in the EN group.

Table 1 Characteristics of patients and nodules

Characteristic	Total (*n* = 49) (nodules = 107)	EN group (*n* = 24) (nodules = 53)	CT group (*n* = 25) (nodules = 54)
Age, years	56.9 (9.6)	55.8 (9.8)	57.9 (9.6)
Sex, n (%)			
Male	24 (49.0)	11 (46)	13 (52)
Female	25 (51.0)	13 (54)	12 (48)
BMI, kg/m^2	23.1 (2.5)	23.3 (2.7)	22.9 (2.2)
FEV1, L	2.4 (0.2)	2.4 (0.2)	2.3(0.3)
Nodule number, n (%)			
2	40 (81.6)	19 (79)	21 (84)
3	9 (18.4)	5 (21)	4 (16)
Nodule location, n (%)			
Right above carinal	35 (32.7)	17 (32)	18 (33)
Right below carinal	22 (20.6)	12 (23)	10 (19)
Left above carinal	24 (22.4)	11 (21)	13 (24)
Left below carinal	26 (24.3)	13 (25)	13 (24)
Nodule size, mm	8.7 (3.2)	8.5 (3.3)	8.8 (3.1)
Distance from pleura, mm	12.4 (11.7)	13.1 (12.0)	11.7 (11.5)
Nature, n (%)			
Pure GGO	37 (34.6)	17 (32)	20 (37)
Part solid	42 (39.3)	21 (40)	21 (39)
Solid	28 (26.2)	15 (28)	13 (24)

Data are given as count (percentage) or mean (standard deviation)

EN: electromagnetic navigation; CT: computed tomography; BMI: body mass index; FEV1: forced expiratory volume in 1 s; GGO: ground glass opacity

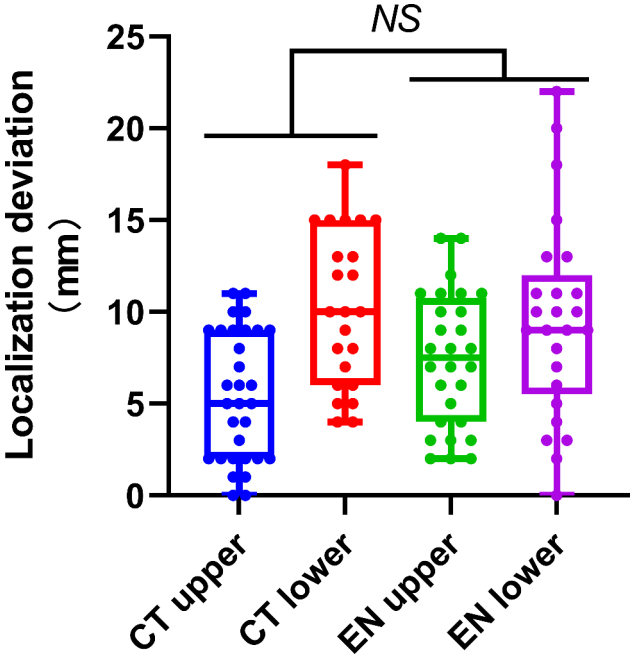

Fig. 4 Comparison of the marker deviation in each group. Nodules in each group were divided into upper and lower ones relative to the tracheal bulge. The horizontal line in each box indicates the median, while the top and bottom borders of each box indicate the 75th and 25th percentiles, respectively. EN: electromagnetic navigation; CT: computed tomography

Table 2 Characteristics of localization and surgical outcomes

Nodule Localization or Surgical Outcome	Total (*n* = 49) (nodules = 107)	EN group (*n* = 24) (nodules = 53)	CT group (*n* = 25) (nodules = 54)	*P*
Deviation, mm				
Total	8.0 (7.0)	9.0 (6.5)	7.5 (6.0)	0.33
Upper nodule	6.0 (6.0)	7.5 (7.8)	5.0 (7.0)	**0.049**
Lower nodule	10.0(7.0)	9.0 (6.5)	10.0 (9.0)	0.50
Procedural duration, min				
Total	19.4 (6.2)	16.3 (4.2)	22.3 (8.2)	**0.002**
2 nodules	20.0 (6.1)	15.3 (4.2)	20.4 (7.8)	**0.015**
3 nodules	25.6 (6.8)	20.1 (4.1)	32.4 (9.6)	**0.035**
Complications, n (%)				
Pneumothorax		-	5 (20)	
Pulmonary hemorrhage		-	6 (24)	
Primary resection success rate, % (n/n)	96.3 (103/107)	94.3 (50/53)	98.1 (53/54)	0.60
Nodule size, mm [a]	7.2 (4.2)	6.9 (4.5)	7.4 (3.9)	0.54
Margin distance, mm	18.8 (7.2)	19.5 (7.8)	18.2 (6.7)	0.36
Frozen section analysis, n (%)				0.91
Benign lesion	12 (11.2)	5 (9)	7 (13)	
Atypical adenomatous hyperplasia	11 (10.3)	6 (11)	5 (9)	
Adenocarcinoma in situ	16 (15.0)	9 (17)	7 (13)	
Minimally invasive adenocarcinoma	38 (35.5)	20 (38)	18(33)	
Invasive adenocarcinoma	29 (27.1)	13 (25)	16 (30)	
Squamous cell carcinoma	1 (0.9)	0 (0)	1 (2)	
Surgical procedure, nodule				0.98
Wedge resection	40	20	20	
Segmentectomy	48	24	24	
Lobectomy	19	9	10	

Data are given as count (percentage) or mean (standard deviation) or median (interquartile range)

EN: electromagnetic navigation; CT: computed tomography

[a] Measured on a resected sample

Surgical outcomes

The surgical outcomes are summarized in Table 2. There was no significant difference in the primary resection success rate (94.3% [50/53] versus 98.1% [53/54]; $P=0.60$) or mean (SD) margin distance (19.5 (7.8) versus 18.2 (6.7) mm; $P=0.36$) between the EN and CT groups. The results of our frozen section analysis revealed 12 (11.2%) benign lesions, 11 (10.3%) atypical adenomatous hyperplasia, 16 (15.0%) adenocarcinomas in situ, 38 (35.5%) minimally invasive adenocarcinomas, 29 (27.1%) invasive adenocarcinomas, and 1 (0.9%) squamous cell carcinoma. Following frozen section analysis, 19 nodules underwent complete lobectomy, 48 nodules underwent segmentectomy, and 40 nodules underwent wedge resection.

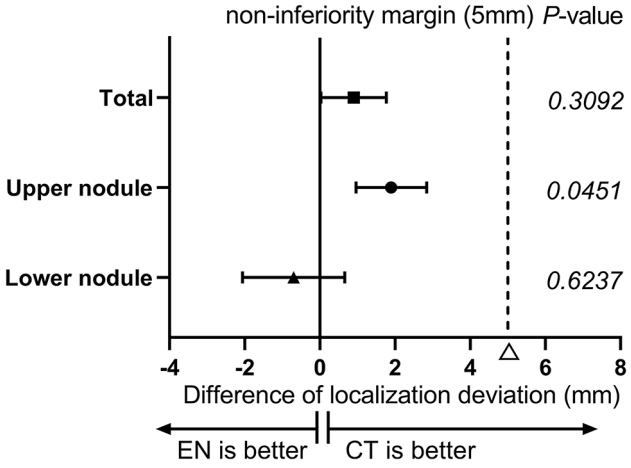

Fig. 5 Forest plot of the main analysis. Analyses were performed on the 3 datasets of lung nodule localization deviations. The results are presented as absolute differences (black dots) and 95% confidence intervals (black lines) for the primary endpoint (lung nodule localization deviation) with a noninferiority margin of 5 mm (triangles). The x-axis is the absolute difference scale. EN: electromagnetic navigation; CT: computed tomography

Table 3 APAIS scores

Subset	EN group	CT group	*P*
	(*n* = 24)	(*n* = 25)	
Sum A (items 1 + 2)	3.4 (0.5)	3.0 (0.9)	0.062
Sum S (items 4 + 5)	4.4 (1.1)	5.8 (1.5)	**0.001**
Sum I (items 3 + 6)	3.4 (0.9)	3.6 (1.1)	0.49
Sum C (sum A + sum S)	7.8 (1.0)	9.8 (1.9)	**< 0.001**

The data are presented as the mean (standard deviation)

APAIS: Amsterdam Preoperative Anxiety and Information Scale; EN: electromagnetic navigation; CT: computed tomography

Discussion

There have been rapid developments in preoperative localization techniques for pulmonary nodules in recent years [19–21], with CT-guided percutaneous localization techniques being widely used clinically [22, 23]. However, repeated CT scans increase radiation exposure, and multiple local needle insertion attempts can cause patient pain and perioperative psychological stress [24]. In this study, we compared EN-guided and CT-guided percutaneous localization of multiple pulmonary nodules and reported that the accuracy of EN-guided localization was not inferior to that of CT-guided localization. Additionally, it significantly shortens the localization duration, avoids radiation exposure, and reduces patients' perioperative psychological stress.

Owing to the explicit requirement of a nodal distance greater than 2 cm from the resection margin in the removal of early-stage malignant lung tumors [25], the accuracy of pulmonary nodule localization is of utmost importance. Therefore, in contrast to other similar studies that use the localization success rate as the primary observation indicator [26], we choose to utilize the localization deviation as the primary observation indicator. Wedge resection of the lung tissue was conducted, and the shortest distance from the lung nodule to the localization marker point in the atrophic state was measured. However, owing to the normal expansion of lung tissue during nodule localization, the value of localization deviation recorded in the atrophic state may be small. However, with the same offset trend, the effect of the difference in localization deviation between the two groups is negligible. Therefore, the upper limit of the 95% CI for the difference in localization deviation between the two groups is much smaller than the noninferiority margin of 5 mm, which is a reliable conclusion. In addition, although the localization deviation of the EN group was smaller than that of the CT group in the lower nodule subgroup, our data do not prove its superiority.

In the field of preoperative CT-guided pulmonary nodule localization markers, metal localization markers (localization needles and coils), indocyanine green (ICG) and medical adhesives are frequently used. Each of these markers has advantages and disadvantages. For example, localization pins and coils carry the risk of intraoperative loss, displacement and postlocalization discomfort; medical adhesives carry the potential risk of thrombosis; and ICG has the disadvantages of diffusion and difficulty in locating deep nodules. On the other hand, due to certain limitations, ICG is usually used as a localization marker for electromagnetic navigation positioning. In the CT control group, we chose ICG as a marker to maintain the consistency of the localization markers (controlling for a single variable). This approach helps to avoid localization differences that may arise from the use of different markers.

Previous studies have reported comparable success rates for EN-guided bronchoscopic localization and percutaneous CT-guided localization, which is in line with the outcomes of our study [27]. However, EN bronchoscopy requires skilled personnel to assist with the operation of the bronchoscope and increases the risks of intraoperative bleeding and hypoxia. On the other hand, percutaneous localization could avoid these risks and operational difficulties. Therefore, percutaneous localization via electromagnetic navigation is considered more convenient and safer. Our findings suggest that the following factors may have contributed to the superior performance of EN-guided percutaneous localization for multiple pulmonary nodules. First, EN-guided localization was conducted on patients who were intubated under general anesthesia, enabling a controlled breathing state that could fulfill localization needs and avoid position changes that may improve localization accuracy. Second, the EN system can dynamically track the position of the pulmonary nodule and guide the positioning path in real time via the system software.

Despite the real-time dynamic tracking of virtual nodules in the 3D model via the EN system [27, 28], there may be discrepancies in the actual locations of the target nodules due to differences in respiratory phases and breathing patterns. These factors can result in biases between the realistic location of the target nodule and the virtual location in the 3D model [18]. This could lead to deviation in EN-guided localization. Additionally, the shielding effects of the ribs or scapulae can make it difficult to select the optimal localization path and may lead to undesirable localization paths, further contributing to the generation of EN-guided localization deviation.

The present study demonstrated that CT-guided localization of nodules above the carina resulted in a lower deviation than did those below the carina, suggesting that upper nodules were localized with greater accuracy, which is consistent with previous research [29]. CT-guided localization is conducted under local anesthesia, which often results in obvious changes in autonomic breathing, higher respiratory activity in lower nodules than in upper nodules, and increased difficulty in precise localization. In contrast, EN-guided localization was performed under general anesthesia with artificial respiration, and the deviation in localization did not differ between the upper and lower nodules. These findings suggest that respiration may be the main contributor to differences in the positioning of upper and lower nodules. Although the CT group exhibited better localization accuracy for upper nodules, no significant difference in the primary resection success rate was detected between the EN and CT-guided groups. This finding indicates that both groups of marker deviations could meet the requirements for guiding the clinical resection of pulmonary nodules with localization accuracy.

The EN system offers the advantage of sequential localization of multiple nodes, reducing the time interval between localizations and ultimately shortening the overall localization time. In contrast, CT-guided localization of multiple pulmonary nodes may require intraoperative adjustments and rescanning, potentially necessitating multiple operators to accurately record and adjust the needle approach depth and direction for each scan. Similarly, while some patients may have multiple nodes localized simultaneously in the same position, this could still require more coordination efforts between operators. Our findings are consistent with prior research [27], indicating that the EN-guided localization duration was significantly shorter than the CT localization duration.

In previous studies, EN-guided localization has been defined as a "single-stage" workflow [15]. This involves performing localization and surgery under general anesthesia, which can help alleviate patient anxiety and fear. CT localization, on the other hand, can be associated with increased patient anxiety and discomfort due to incomplete local chest wall nerve blocks, continuous postural mobility restrictions, and longer waiting times after localization. Anxiety has been shown to not only create a negative medical experience but also impact patient prognosis [30]. In addition, the "single-stage" workflow also reduces the risk of complications. Studies have shown that the incidence of hemopneumothorax after CT localization is as high as 55.6% [31].

One potential risk associated with the CT workflow is the prolonged waiting time after localization, which may pose hazards to patients. Immediate surgery following EN localization may eliminate the need for puncture placement for drainage, even for patients with massive pneumothorax, thus minimizing the risk of complications such as hemopneumothorax. Furthermore, EN localization is performed within a safe magnetic field, which completely avoids radiation exposure.

Limitations

There are a number of possible limitations to our study. First, this was a small-scale study carried out at a single center. To verify our findings, larger multicenter studies with greater numbers of participants are needed. Second, our study focused solely on multiple unilateral pulmonary nodules, since the number of patients who underwent simultaneous resection of bilateral pulmonary nodules was limited. Third, for pulmonary nodules that failed primary resection, we performed extended resections and measurements of localization deviation after ex vivo reconstitution, which led to increased localization deviation errors. Fourth, the use of ICG as a localization marker has the disadvantages of diffusion and imprecise localization center points, which may be overcome by using localization needles or localization coils as markers. Nevertheless, our study provides valuable real-world experience with EN-guided localization, which could serve as a useful guide for further research in this area.

Conclusions

In this randomized clinical trial, we demonstrated that the EN-guided approach for localizing multiple pulmonary nodules simultaneously was noninferior to CT-guided localization in terms of diagnostic accuracy. Moreover, the EN-guided percutaneous approach has proven to be a rapid and effective method for nodule localization, alleviating perioperative psychological stress for patients.

Abbreviations

CT	Computed tomography
EN	Electromagnetic navigation
VATS	Video-assisted thoracic surgery
3D	Three-dimensional
ICG	Indocyanine green
APAIS	Amsterdam Preoperative Anxiety and Information Scale

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12957-024-03606-z.

Supplementary Material 1

Supplementary Material 2: **Video 1** The entire workflow electromagnetic navigation-guided percutaneous localization of pulmonary nodules within the operating room prior to video-assisted thoracoscopic surgery

Acknowledgements
Not applicable.

Author contributions
Hongliang Hui: Data curation; Formal analysis; Investigation; Writing-Original draft. Haoran Miao: Data curation; Investigation; Methodology; Writing-Original draft. Fan Qiu: Data curation; Formal analysis; Methodology. Huaming Li: Software; Supervision. Yangui Lin: Project administration; Resources; Visualization. Yiqian Zhang: Conceptualization; Resources; Writing-Review & Editing. Bo Jiang: Conceptualization; Funding acquisition; Project administration; Writing-review & editing.

Funding
This work is funded by the Futian Healthcare Research Project (No. FTWS2021012), Futian Healthcare Research Project (No. FTWS2023002) and the Research Fund of the Eighth Hospital of Sun Yat-sen University (GCCRCYJ026).

Data availability
The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
This trial was approved by the Ethics Committee of the Eighth Affiliated Hospital of Sun Yat-sen University (No. 2022-024-01) and was conducted in accordance with the ethical standards of the Helsinki Declaration by the World Medical Association.

Consent for publication
The written informed consent was obtained for publication before surgery.

Competing interests
The authors declare no competing interests.

Author details
[1]Department of Thoracic Cardiovascular Surgery, The Eighth Affiliated Hospital of Sun Yat-sen University, Shenzhen, Guangdong, China

Received: 21 August 2024 / Accepted: 24 November 2024
Published online: 30 November 2024

References

1. Adams SJ, Stone E, Baldwin DR, Vliegenthart R, Lee P, Fintelmann FJ. Lung cancer screening. Lancet. 2023;401:390–408.
2. Heuvelmans MA, Walter JE, Peters RB, Bock GH, Yousaf-Khan U, Aalst CMV, Groen HJM, Nackaerts K, Ooijen PMV, Koning HJ, et al. Relationship between nodule count and lung cancer probability in baseline CT lung cancer screening: the NELSON study. Lung Cancer. 2017;113:45–50.
3. Ujiie H, Gregor A, Yasufuku K. Minimally invasive surgical approaches for lung cancer. Expert Rev Respir Med. 2019;13:571–8.
4. Sarsam M, Baste JM, Thiberville L, Salaun M, Lachkar S. How bronchoscopic dye marking can help minimally invasive lung surgery. J Clin Med 2022, 11.
5. Refai M, Andolfi M, Barbisan F, Roncon A, Guiducci GM, Xiumè F, Salati M, Tiberi M, Giovagnoni A, Paci E. Computed tomography-guided microcoil placement for localizing small pulmonary nodules before uniportal video-assisted thoracoscopic resection. Radiol Med. 2020;125:24–30.
6. Thistlethwaite PA, Gower JR, Hernandez M, Zhang Y, Picel AC, Roberts AC. Needle localization of small pulmonary nodules: lessons learned. J Thorac Cardiovasc Surg. 2018;155:2140–7.
7. Hopkins KG, Ferson PF, Shende MR, Christie NA, Schuchert MJ, Pennathur A. Prospective study of quality of life after lung cancer resection. Ann Transl Med. 2017;5:204.
8. Park CH, Han K, Hur J, Lee SM, Lee JW, Hwang SH, Seo JS, Lee KH, Kwon W, Kim TH, Choi BW. Comparative effectiveness and safety of preoperative lung localization for pulmonary nodules: a systematic review and Meta-analysis. Chest. 2017;151:316–28.
9. Wang K, Huang W, Chen X, Li G, Li N, Huang X, Liao X, Song J, Yang Q, He K, et al. Efficacy of Near-Infrared fluorescence video-assisted thoracoscopic surgery for small pulmonary nodule resection with Indocyanine Green Inhalation: a Randomized Clinical Trial. Ann Surg Oncol. 2023;30:5912–22.
10. Wang L, Sun D, Gao M, Li C. Computed tomography-guided localization of pulmonary nodules prior to thoracoscopic surgery. Thorac Cancer. 2023;14:119–26.
11. Zhang H, Li Y, Chen X, He Z. Comparison of hook-wire and medical glue for CT-guided preoperative localization of pulmonary nodules. Front Oncol. 2022;12:922573.
12. Yang F, Min J. Hemorrhagic shock caused by preoperative computed tomography-guided microcoil localization of lung nodules: a case report. BMC Surg. 2022;22:247.
13. Green M, Marom EM, Konen E, Kiryati N, Mayer A. Patient-specific image denoising for ultra-low-dose CT-guided lung biopsies. Int J Comput Assist Radiol Surg. 2017;12:2145–55.
14. Mehta AC, Hood KL, Schwarz Y, Solomon SB. The Evolutional history of electromagnetic Navigation Bronchoscopy: state of the art. Chest. 2018;154:935–47.
15. Hsu PK, Wu YC. Electromagnetic Navigation-guided one-stage dual localization of small pulmonary nodules. Chest. 2018;154:1462–3.
16. Hsu PK, Wu YC. The feasibility of electromagnetic navigation-guided percutaneous microcoil localization for thoracoscopic resection of small pulmonary nodules. J Thorac Cardiovasc Surg. 2019;157:e211–4.
17. Piaggio G, Elbourne DR, Altman DG, Pocock SJ, Evans SJ. Reporting of non-inferiority and equivalence randomized trials: an extension of the CONSORT statement. JAMA. 2006;295:1152–60.
18. Zhang L, Wang L, Kadeer X, Zeyao L, Sun X, Sun W, She Y, Xie D, Li M, Zou L, et al. Accuracy of a 3-Dimensionally printed navigational template for localizing small pulmonary nodules: a Noninferiority Randomized Clinical Trial. JAMA Surg. 2019;154:295–303.
19. Nardini M, Dunning J. Pulmonary nodules precision localization techniques. Future Oncol. 2020;16:15–9.
20. Manca G, Davini F, Tardelli E, De Liperi A, Falaschi F, Melfi F, Colletti PM, Rubello D, Volterrani D, Boni G. Clinical impact of Radioguided localization in the treatment of Solitary Pulmonary Nodule: a 20-Year retrospective analysis. Clin Nucl Med. 2018;43:317–22.
21. Fan L, Yang H, Yu L, Wang Z, Ye J, Zhao Y, Cai D, Zhao H, Yao F. Multicenter, prospective, observational study of a novel technique for preoperative pulmonary nodule localization. J Thorac Cardiovasc Surg. 2020;160:532–e539532.
22. Su TH, Fan YF, Jin L, He W, Hu LB. CT-guided localization of small pulmonary nodules using adjacent microcoil implantation prior to video-assisted thoracoscopic surgical resection. Eur Radiol. 2015;25:2627–33.
23. Rodrigues JCL, Pierre AF, Hanneman K, Cabanero M, Kavanagh J, Waddell TK, Chung TB, Pakkal M, Keshavjee S, Cypel M, et al. CT-guided Microcoil Pulmonary Nodule localization prior to video-assisted thoracoscopic surgery: diagnostic utility and recurrence-free survival. Radiology. 2019;291:214–22.
24. Zhao ZR, Lau RWH, Yu PSY, Ng CSH. Devising the guidelines: the techniques of pulmonary nodule localization in uniportal video-assisted thoracic surgery-hybrid operating room in the future. J Thorac Dis. 2019;11:S2073–8.
25. Saji H, Okada M, Tsuboi M, Nakajima R, Suzuki K, Aokage K, Aoki T, Okami J, Yoshino I, Ito H, et al. Segmentectomy versus lobectomy in small-sized peripheral non-small-cell lung cancer (JCOG0802/WJOG4607L): a multicentre, open-label, phase 3, randomised, controlled, non-inferiority trial. Lancet. 2022;399:1607–17.
26. Zhang L, Li M, Li Z, Kedeer X, Wang L, Fan Z, Chen C. Three-dimensional printing of navigational template in localization of pulmonary nodule: a pilot study. J Thorac Cardiovasc Surg. 2017;154:2113–e21192117.
27. Hung CT, Chen CK, Chang YY, Hsu PK, Hung JJ, Huang CS, Wu YC, Hsu HS. Electromagnetic navigation-guided versus computed tomography-guided

percutaneous localization of small lung nodules before uniportal video-assisted thoracoscopic surgery: a propensity score-matched analysis. Eur J Cardiothorac Surg. 2020;58:i85–91.
28. Anayama T, Qiu J, Chan H, Nakajima T, Weersink R, Daly M, McConnell J, Waddell T, Keshavjee S, Jaffray D, et al. Localization of pulmonary nodules using navigation bronchoscope and a near-infrared fluorescence thoracoscope. Ann Thorac Surg. 2015;99:224–30.
29. Patrucco F, Daverio M, Airoldi C, Falaschi Z, Longo V, Gavelli F, Boldorini RL, Balbo PE. 4D electromagnetic Navigation Bronchoscopy for the Sampling of Pulmonary lesions: first European real-life experience. Lung. 2021;199:493–500.
30. Park S, Kang CH, Hwang Y, Seong YW, Lee HJ, Park IK, Kim YT. Risk factors for postoperative anxiety and depression after surgical treatment for lung cancer†. Eur J Cardiothorac Surg. 2016;49:e16–21.
31. Hu L, Gao J, Hong N, Liu H, Chen C, Zhi X, Sui X. Simultaneous preoperative computed tomography-guided microcoil localizations of multiple pulmonary nodules. Eur Radiol. 2021;31:6539–46.

Publisher's note