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DYNAMIC MANUSCRIPT

Image-guided thoracoscopic lung resection using a dual-marker localization technique in a hybrid operating room

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Abstract

Background We sought to describe the feasibility and safety of a dual-marker technique—based on a combination of near-infrared (NIR) marking and microcoil localization—before image-guided video-assisted thoracoscopic surgery (iVATS) of small and/or deep pulmonary lesions in a hybrid operating room (HOR).

Methods We retrospectively reviewed the clinical records of consecutive patients who underwent iVATS resection in a HOR using the proposed dual-marker localization technique. Patients were initially imaged with cone-beam CT, and the needle trajectory was subsequently planned with the Syngo iGuide Needle Guidance software. Using a coaxial needle technique, a microcoil was initially deployed either in the immediate proximity or within the lesion of interest followed by injection of diluted indocyanine green (ICG; quantity: 0.3–0.5 mL; dye concentration: 0.125 mg/mL) at the pleural surface. A NIR thoracoscopic camera and a C-arm portable fluoroscopic system were used to guide the subsequent resection.

Results A total of 11 patients were examined. The median lesion size was 6 mm, with a median distance from the pleural surface of 4 mm. Three nodules were solid, whereas the remaining eight were GGOs. All lesions were identifiable on intra-operative cone-beam CT images. The median time required for localization was 19 min. No conversion to thoracotomy or a multi-port approach was required, and there were no clinically significant adverse events after ICG injection or microcoil placement.

Conclusions Our study indicates that iVATS with a dual-marking approach (NIR marking and microcoil localization) is safe and useful to localize difficult-to-identify pulmonary nodules.

Keywords Near-infrared marking · Small pulmonary nodules · Indocyanine green · Image-guided video-assisted thoracoscopic surgery · Hybrid operating room · ARTIS zeego · Microcoil localization

Low-dose computed tomography (CT) has increasingly been applied to screening for lung cancer, with small pulmonary nodules being frequently detected [1]. The nature of these lesions should be considered malignant unless proven otherwise by biopsy or direct surgical excision. However, treating patients with pulmonary nodules with video-assisted thoracoscopic surgery (VATS) can be challenging because these lesions need a thorough preoperative localization to be correctly identified intraoperatively [2]. Dye marking is currently the most commonly used technique to localize superficial lesions (distance to the pleural surface < 10 mm) [3]. As far as deeper lesions as concerned, hookwire localization remains the best standard (albeit being limited by the risk of wire dislodgement) [4–6]. In an effort to overcome the limitations of the Hookwire technique, microcoil positioning has been recently proposed to mark both the lung and pleural surfaces. Unfortunately, this approach remains technically demanding [7, 8].

Removal of small pulmonary nodules is generally accomplished through a two-step procedure, according to which the lesion is initially localized in a CT suite and subsequently removed in an operating room [4]. However, recent technical advances are fueling a paradigm shift in the surgical approach to lung nodules. In this regard, hybrid operating rooms (HORs) integrate state-of-the-art imaging

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devices within the surgical theater—allowing single-stage identification and excision of nodules [i.e., image-guided video-assisted thoracoscopic surgery (iVATS)] [9].

In the current case series, we describe the feasibility and safety of a dual-marker technique—based on a combination of NIR marking and microcoil localization—before iVATS of small and/or deep pulmonary lesions in a HOR.

Materials and Methods

Ethical approval

The Institutional Review Board of the Chang Gung Memorial Hospital approved the study protocol (CGMH-IRB 201600671A3), and written informed consent was obtained from all participants.

Indications for surgery and preoperative localization

Our policy is that patients with indeterminate lung tumors should undergo surgery in the presence of the following criteria: (1) suspected pulmonary metastases, (2) enlargement of a pulmonary nodule at follow-up, (3) presence of a ground-glass opacity (GGO) harboring a solid component > 5 mm in size, and 4) persistence of a pure GGO > 8 mm in size on follow-up CT images. When these criteria were not met, tumor resection was performed at the patient's request (because of anxiety). It is also our policy to perform lesion localization in all patients presenting with GGOs or subpleural cavitary lesions. Solid nodules were subjected to localization when (1) they were < 10 mm in size and showed a subpleural localization or (2) they were located deeply in the lung parenchyma (distance from the visceral pleural surface > 10 mm).

Dual-marking technique and iVATS protocol

Video 1 shows the iVATS workflow implemented in our HOR—which was equipped with a cone-beam CT apparatus (ARTIS zeego; Siemens Healthcare GmbH, Erlangen, Germany) and a Magnus surgical table (Maquet Medical Systems, Wayne, NJ, USA). Patients under general anesthesia were placed in the lateral decubitus position. The cone-beam CT C-arm and the patient's chest were subsequently protected with sterile wraps. The study participants underwent an initial scan for surgical planning during end inspiration breath-hold using a standard 6-s DynaCT Body protocol (Fig. 1A). Under the syngo Needle Guidance provided by the syngo X-Workplace (Siemens Healthcare GmbH), we laid out the access path in the isotropic data set. The needle path was outlined by marking the needle entry and target

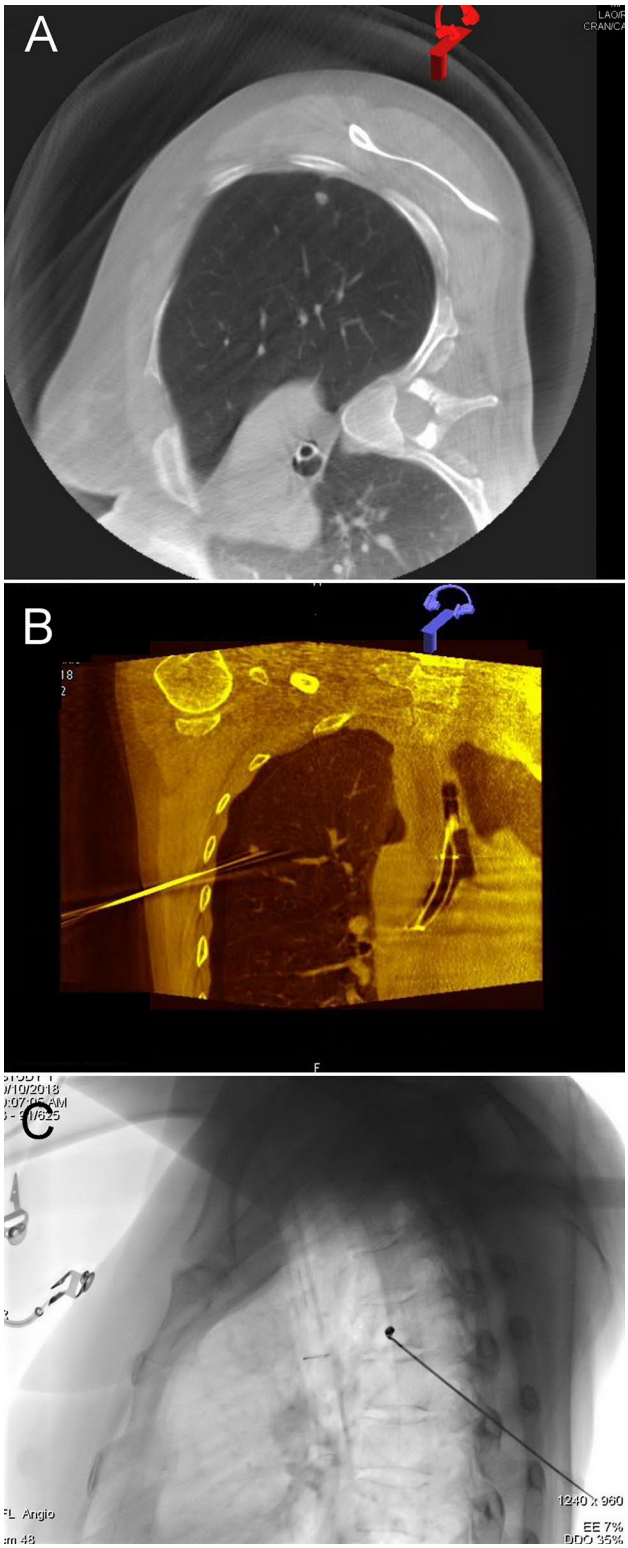

Fig. 1 **A** Cone-beam CT image of a lung nodule obtained with the patient placed in the lateral decubitus position. **B** Cone-beam CT image obtained after needle puncture. **C** Placement of the microcoil under fluoroscopy using the coaxial needle technique

points and subsequently projected with a laser beam onto the patient's skin. Using a three-dimensional, laser-supported, fluoroscopy-guided procedure, we introduced an 18-gauge Chiba coaxial needle into the patient's thorax during end inspiration breath-hold (Fig. 1B). The needle entry site and angulation were visualized by projecting a laser-targeting cross onto the patient's surface. Needle orientation and positioning were adjusted after pointing the planned, virtual needle path onto a live fluoroscopic image. A fluoroscopic "bull eye" approach was used to introduce the needle until its tip reached the internal portion of the projected target. A post-procedural cone-beam CT scan was obtained to confirm an appropriate needle location. Using a coaxial technique, one microcoil (MWCE-35-8-5-tornado coils; Cook Medical Inc., Bloomington, IN, USA) was placed at the deep lesion margin (Fig. 1C) followed by the injection of diluted indocyanine green (ICG; quantity: 0.3−0.5 mL; dye concentration: 0.125 mg/mL) at the pleural surface. Proper microcoil positioning was confirmed through a cone-beam CT scan.

Upon initiation of VATS, real-time intraoperative NIR fluorescence images were obtained using a minimally invasive ICG fluorescence system (PINPOINT®; Novadaq, Mississauga, ON, Canada) which includes a 10-mm, 30-degree NIR thoracoscopic camera for the identification of the NIR tattoo. Thoracoscopic instruments were initially used to clamp the lung and identify a putative staple line that would guide the intended resection. The microcoil location in relation to the instrument was investigated through X-ray fluoroscopy, and VATS wedge resection was subsequently performed using surgical staplers (Fig. 2). The surgical specimen was cut along the maximum diameter of the pulmonary lesion and examined with the NIR thoracoscope, with the surgical margins being macroscopically inspected (Fig. 3). A frozen section examination of the resected pulmonary specimen was initially performed. When the diagnosis of primary lung cancer was confirmed, a lobectomy was generally performed. Patients with peripheral lung cancer of limited size (< 2 cm) and adequate resection margins (either > 2 cm or > tumor size) underwent sublobar resections.

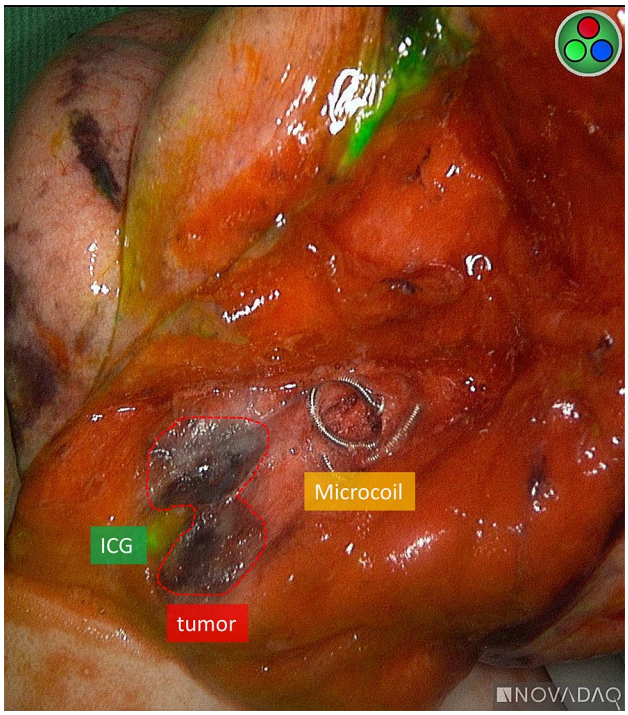

Fig. 3 Resected specimen harboring the lung nodule. ICG staining is visible on the pleural surface, with the microcoil located at the deep margin (Color figure online)

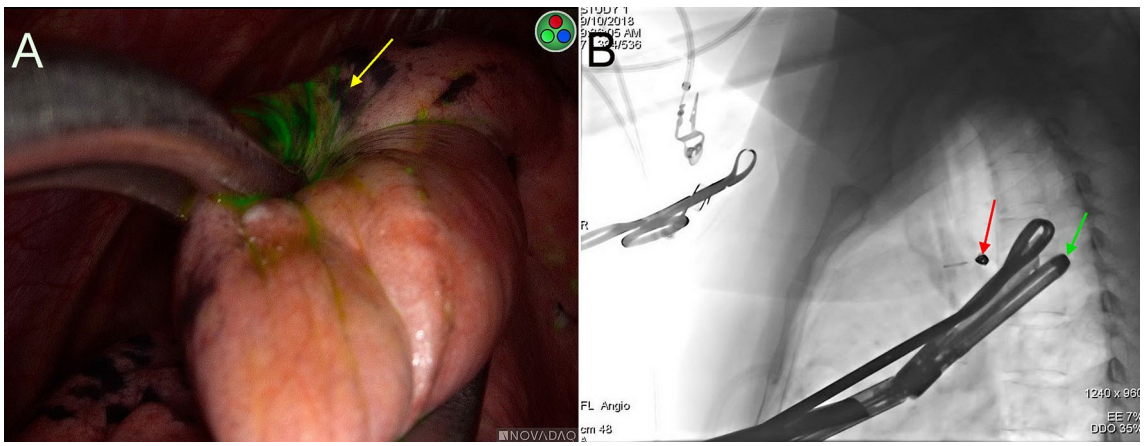

Fig. 2 **A** Thoracoscopic view after the activation of the near-infrared fluorescence system: ICG staining (yellow arrow) was evident on the pleural surface. **B** Fluoroscopic confirmation of an adequate distance between the microcoil (red arrow, lesion site) and the mechanical staple (green arrow) (Color figure online)

Data collection and statistical analysis

The study variables were summarized using descriptive statistics. Continuous data are given as medians (interquartile ranges [IQRs]), whereas categorical variables are expressed as counts (percentages). Demographic data (age, sex, smoking status), lesion characteristics (size, number, and location of nodules), information on the surgical approach (wedge resection, segmentectomy, or lobectomy), length of postoperative hospital stay, and in-hospital morbidity/mortality were extracted from clinical records. The duration of localization was measured from patient positioning and C-arm docking to the end of the localization procedure. Data on radiation exposure were obtained from the "Exam Protocol" of the ARTIS zeego instrument upon extraction of the structured report on X-ray radiation dose. When nodule illumination was observed by the surgeon following activation of the camera filter, the localization procedure was deemed successful. Results of frozen sections and final pathological findings were used for confirmation. Data analysis was conducting using the Statistical Package for the Social Sciences (SPSS), version 20 (IBM, Armonk, NY, USA).

Results

Patient and lesion characteristics

A total of 11 patients (3 men and 8 women) who underwent cone-beam CT-guided dual marking of pulmonary nodules were included in this case series (Table 1). On preoperative CT images, three nodules were found to be solid, whereas the remaining eight were GGOs. The median pulmonary lesion size on preoperative CT images was 6 mm (IQR 5.4−6.8 mm), whereas their median distance from the pleural surface was 4 mm (IQR 2.5−8.5 mm). The median tumor depth-to-size (DS) ratio was 0.7 (IQR 0.4−1.2). Indications for surgery were suspected primary lung cancer in eight patients and suspected lung metastases in the remaining three.

Table 2 illustrates the procedural details of lesion localization. Intraoperative cone-beam CT was successful in identifying all of the lesions. The median total localization time was 19 min (IQR 18−21 min), whereas the median length of access path was 55.4 mm (IQR 42.8−71.5 mm). The median skin absorbed dose (a measure of radiation exposure) was 190.9 mGy (IQR 155−307.9 mGy).

Using the NIR thoracoscope, we were successful in locating the NIR "tattoo" on the pleural surface of all patients. The median time between ICG injection and lesion visualization was 17 min (IRQ 14–22.5 min). The optimal resection margins were subsequently identified using portable C-arm fluoroscopy.

Single-port thoracoscopic resection was successful in removing all lesions, and no conversion to thoracotomy or a multi-port approach was required. ICG injection did not result in clinically significant adverse events. Pathological findings were as follows: primary lung cancer (n = 6), metastatic cancer (n = 1), and benign lung tumor (n = 4). The specific pathological diagnoses in the latter group were granulomatous inflammation (n = 2), focal fibrosis (n = 1), and intrapulmonary lymph node (n = 1). All patients had

Table 1 General characteristics of the ten patients included in the case series

Patient #	Sex	Age, years	ASA	CCI	Indication for surgery	Tumor localization	Tumor size, mm	Tumor depth, mm	DS ratio	Morphology
1	F	34	2	1	P	RML	6	4	0.67	GGO
2	F	45	3	0	P	RUL	7.5	9	1.20	GGO
3	F	57	3	0	P	RUL	11	4	0.36	GGO
4	F	58	3	2	P	RLL	4.8	2	0.42	GGO
5	F	50	3	0	P	RUL	5.8	3	0.52	GGO
6	M	46	3	2	M	LUL	8.5	0	0.00	Solid
7	F	39	3	2	P	LUL	4.9	6	1.22	Solid
8	F	60	3	0	P	RLL	6	18	3.00	GGO
9	F	54	3	1	M	LUL	2.9	9.57	3.30	GGO
10	M	64	3	2	M	LLL	6	1.7	0.28	Solid
11	M	51	3	0	P	LUL	6	8	0.75	GGO
Median		51	3				6	4	0.7	
IQR		45.5−57.5	3−3				5.4−6.8	2.5−8.5	0.4−1.2	

ASA American Society of Anesthesiologists, *CCI* Charlson comorbidity index, *DS* depth-to-size, *F* female, *M* male, *LUL* left upper lobe, *RML* right middle lobe, *LLL* left lower lobe, *RLL* right lower lobe, *RUL* right upper lobe, *GGO* ground-glass opacity, *IQR* interquartile range, *P*: suspected primary lung cancer, *M*: suspected pulmonary metastasis

Table 2 Details of the localization procedures implemented in the 10 patients included in the case series

Patient #	Time required for localization, min	Time from the end of localization to NIR illumination, min	Access path, mm	Absorbed skin dose, mGy	Operative procedure	LOS, days	Histology
1	25	28	28.8	311.4	Wedge resection	3	Benign lesion
2	20	14	74.9	220.2	Wedge resection	6	Lung cancer
3	19	19	63.8	170.3	Wedge resection	3	Lung cancer
4	19	17	42.5	190.9	Wedge resection	5	Benign lesion
5	14	14	78	374.1	Wedge resection	4	Lung cancer
6	22	14	37.5	79.8	Wedge resection	4	Metastases
7	13	14	68	172.2	Wedge resection	3	Benign lesion
8	17	12	43.1	110.5	Wedge resection	3	Lung cancer
9	29	25	95.7	634.8	Wedge resection	4	Lung cancer
10	19	30	55.4	139.6	Wedge resection	3	Benign lesion
11	20	20	53.2	304.3	Wedge resection	3	Lung cancer
Median	19	17	55.4	190.9		3.5	
IQR	18–21	14–22.5	42.8–71.5	155.0–307.9		3–4	

NIR near-infrared, *LOS* length of stay, *IQR* interquartile range

clear resection margins and were successfully discharged home. The median length of hospital stay was 3.5 days (IQR 3–4 days).

Discussion

Hookwire still represents one of the most widely used marker for CT-guided pulmonary lesion localization, albeit being limited by the risk of wire dislodgement [6, 10, 11]. In order to circumvent this issue, dye staining of deep lesions under CT guidance has emerged as an alternative approach. However, the use of a dye is not devoid of limitations as well—mainly because of its potential improper diffusion to the lung parenchyma (which may result in unnecessarily large wedge resections) or even to the entire pleural surface. The use of microcoils has been proposed as a technical advance for localizing lung lesions—holding the potential to overcome the aforementioned caveats [7]. The conventional approach for CT-guided placement of percutaneous microcoils consists in advancing one end of the coil deep to the lesion margin, while the other end is coiled along the visceral pleural space. A mark on the pleural surface is used as a guide to localize the nodule of interest during thoracoscopy [7]. With fluoroscopy guidance, the position of the lesion to be removed is further confirmed before resection. Unfortunately, this standard approach is technically demanding because a strictly calibrated positioning of coil ends (between the deep lesion margin and the visceral pleural surface) is required. Accordingly, a disproportionate deployment of the microcoil at the pleural surface may lead to its complete retraction, ultimately resulting in an intraoperative failure to localize the lesion of interest. Moreover, microcoil placement along the pleural surface may sporadically require a small pneumothorax to separate the visceral and parietal pleura. In the absence of pneumothorax, the microcoil end adjacent to the nodule may be unintentionally retracted into chest wall.

In an effort to simplify the standard approach, herein we deployed the entire microcoil either in the immediate proximity or within the lesion of interest. Specifically, the injection of ICG into the pleura surface allowed us to avoid the technically challenging marking of the pleura with a microcoil. We believe that our double-marking technique with ICG injection and microcoil positioning may provide the surgeon with accurate data on lesion location, depth, and orientation relative to the pleural surface. In addition, the presence of inadequate resection margins is immediately noticeable. A further important advantage is that both ICG and microcoil are introduced through the same needle, ultimately minimizing the additional time required by dual marking. The risk of pneumothorax is not appreciably increased and is likely similar to that associated with either technique alone. Compared to standard white-light endoscopy examination with methylene blue, the specific wavelength required for ICG fluorescence is detectable even in the presence of color and/or textural modifications of the visceral pleura (which may stem from the presence of anthracosis) [3].

However, a general disadvantage inherent in the use of NIR marking is that surgery should be performed rapidly (i.e., within 3 h from marking) to avoid diffusion of ICG into surrounding lung (which consequent failure to localize the lesion of interest) [12, 13]. The traditional two-step workflow (i.e., lesion localization in the CT suite followed

by its removal in the OR) may be too restrictive to meet such requirements. In this context, HORs may provide an optimal suit for double marking of pulmonary lesions followed by their excision (median time from ICG injection to lesion localization: 15 min), ultimately increasing the consistency and efficiency of this approach [14–16].

Some caveats of the current study merit consideration. First, our findings should be considered as preliminary owing to the relatively small sample size. Second, our sample was not limited to patients with deep lesions, but included some cases with superficial nodules as well. This was mainly performed because of the innovative nature of our technique, which was initially tested in more easily accessible lesions. Larger studies specifically focusing on the localization of deep nodules will be required to confirm the clinical utility of our dual-marking approach. Notably, our research group is currently conducting a clinical trial that will investigate whether this approach is comparable to conventional CT-guided percutaneous single-marker (microcoil or hookwire) localization (NCT03395964). Finally, cost-effectiveness analyses in comparison with other techniques for localizing deep pulmonary nodules are warranted.

Conclusions

The present study describes a double-marking approach (based on the use of both NIR marking and microcoil localization) to be used for iVATS removal of difficult-to-identify pulmonary nodules. The technique was safe, feasible, and did not require conversion to open thoracotomy.

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Compliance with ethical standards

Disclosures Yin-Kai Chao, Osbert Qi Yao Leow, Chih-Tsung Wen, and Hsin-Yueh Fang have no conflicts of interest or financial ties to disclose.

References

1. Team NLSTR (2011) Reduced lung-cancer mortality with low-dose computed tomographic screening. N Engl J Med 2011:395–409
2. Finley RJ, Mayo JR, Grant K, Clifton JC, English J, Leo J, Lam S (2015) Preoperative computed tomography–guided microcoil localization of small peripheral pulmonary nodules: a prospective randomized controlled trial. J Thorac Cardiovasc Surg 149:26–32
3. Lin M-W, Tseng Y-H, Lee Y-F, Hsieh M-S, Ko W-C, Chen J-Y, Hsu H-H, Chang Y-C, Chen J-S (2016) Computed tomography-guided patent blue vital dye localization of pulmonary nodules in uniportal thoracoscopy. J Thorac Cardiovasc Surg 152:535–544
4. Chen Y-R, Yeow K-M, Lee J-Y, Su IH, Chu S-Y, Lee C-H, Cheung Y-C, Liu H-P (2007) CT-guided Hook wire localization of subpleural lung lesions for video-assisted thoracoscopic surgery (VATS). J Formos Med Assoc 106:911–918
5. Klinkenberg TJ, Dinjens L, Wolf RFE, van der Wekken AJ, van de Wauwer C, de Bock GH, Timens W, Mariani MA, Groen HJM (2017) CT-guided percutaneous hookwire localization increases the efficacy and safety of VATS for pulmonary nodules. J Surg Oncol 115:898–904
6. Ichinose J, Kohno T, Fujimori S, Harano T, Suzuki S (2013) Efficacy and complications of computed tomography-guided hook wire localization. Ann Thorac Surg 96:1203–1208
7. Mayo JR, Clifton JC, Powell TI, English JC, Evans KG, Yee J, McWilliams AM, Lam SC, Finley RJ (2009) Lung nodules: CT-guided placement of microcoils to direct video-assisted thoracoscopic surgical resection. Radiology 250:576–585
8. Hwang S, Kim TG, Song YG (2018) Comparison of hook wire versus coil localization for video-assisted thoracoscopic surgery. Thorac Cancer 9:384–389
9. Hsieh M-J, Fang H-Y, Lin C-C, Wen C-T, Chen H-W, Chao Y-K (2017) Single-stage localization and removal of small lung nodules through image-guided video-assisted thoracoscopic surgery. Eur J Cardiothorac Surg 53:353–358
10. Gruber-Rouh T, Naguib NNN, Beeres M, Kleine P, Vogl TJ, Jacobi V, Alsubhi M, Nour-Eldin NA (2017) CT-guided hookwire localisation prior to video-assisted thoracoscopic surgery of pulmonary lesions. Clin Radiol 72:898
11. Park CH, Han K, Hur J, Lee SM, Lee JW, Hwang SH, Seo JS, Lee KH, Kwon W, Kim TH, Choi BW (2017) Comparative effectiveness and safety of preoperative lung localization for pulmonary nodules: a systematic review and meta-analysis. Chest 151:316–328
12. Anayama T, Hirohashi K, Miyazaki R, Okada H, Kawamoto N, Yamamoto M, Sato T, Orihashi K (2018) Near-infrared dye marking for thoracoscopic resection of small-sized pulmonary nodules: comparison of percutaneous and bronchoscopic injection techniques. J Cardiothorac Surg 13:5
13. Nagai K, Kuriyama K, Inoue A, Yoshida Y, Takami K (2018) Computed tomography-guided preoperative localization of small lung nodules with indocyanine green. Acta Radiol 59:830–835
14. Chen PH, Hsu HH, Yang SM, Tsai TM, Tsou KC, Liao HC, Lin MW, Chen JS (2018) preoperative dye localization for thoracoscopic lung surgery: hybrid versus computed tomography room. Ann Thorac Surg 106(6):1661–1667
15. Chao YK, Pan KT, Wen CT, Fang HY, Hsieh MJ (2018) A comparison of efficacy and safety of preoperative versus intraoperative computed tomography-guided thoracoscopic lung resection. J Thorac Cardiovasc Surg 156(1974–1983):e1971
16. Wen C-T, Liu Y-Y, Fang H-Y, Hsieh M-J, Chao Y (2018) Image-guided video-assisted thoracoscopic small lung tumor resection using near-infrared marking. Surg Endosc 32:1–8