Original Article

Preoperative computed tomography-guided dye injection to localize multiple lung nodules for video-assisted thoracoscopic surgery

Yao-Hui Tseng[1,2], Yee-Fan Lee[1], Min-Shu Hsieh[3], Ning Chien[1], Wei-Chun Ko[1], Jo-Yu Chen[1], Jang-Ming Lee[4], Pei-Ming Huang[4], Mong-Wei Lin[4], Jin-Shing Chen[4], Yeun-Chung Chang[1]

[1]Department of Medical Imaging, National Taiwan University Hospital and National Taiwan University College of Medicine, Taipei, Taiwan; [2]Department of Medical Imaging, National Taiwan University Hospital Yun-Lin Branch, Taipei, Taiwan; [3]Department of Pathology, [4]Department of Surgery, National Taiwan University Hospital and National Taiwan University College of Medicine, Taipei, Taiwan

Contributions: (I) Conception and design: YH Tseng, YF Lee, N Chien, WC Ko, JY Chen, JM Lee, JS Chen, YC Chang; (II) Administrative support: JM Lee, JS Chen, YC Chang; (III) Provision of study materials or patients: MS Hsieh, JM Lee, JS Chen, PM Huang, MW Lin, YC Chang; (IV) Collection and assembly of data: All authors; (V) Data analysis and interpretation: YH Tseng, YF Lee, WC Ko, YC Chang; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Yeun-Chung Chang, MD, PhD. Department of Medical Imaging, National Taiwan University Hospital, No. 7, Chung-Shan South Road, Taipei 10002, Taiwan. Email: ycc5566@ntu.edu.tw.

Background: Preoperative computed tomography (CT)-guided localization of small lung nodules is important for accurate and efficient video-assisted thoracoscopic surgery (VATS). Resection of multiple small pulmonary nodules in one VATS procedure can aid in patient management. The aim of this study was to evaluate the usefulness of CT-guided Patent Blue V (PBV) dye localization in patients with multiple pulmonary nodules who underwent VATS.

Methods: This retrospective study was conducted from January 2013 to December 2015. One hundred consecutive patients (59.9±10.5 years of age) with 217 nodules who underwent preoperative CT-guided PBV dye localization for multiple (2 to 4) nodules before VATS were enrolled.

Results: The mean nodule size was 0.8±0.4 cm, with a mean depth from the pleura or fissure of 0.7±0.7 cm. The mean procedure duration was 50±20 minutes. The mean amount of injected PBV dye was 0.2±0.1 mL per nodule. The overall success rate was 99% by nodule. Failed localization of two nodules in two patients was due to poor dye visualization (n=1) and significant pneumothorax (n=1). Cases of hemorrhage (24%) were mild and asymptomatic, and none of the patients had hemoptysis. None of the cases of pneumothorax (40%) required chest tube placement before VATS. One (1%) patient developed anaphylaxis. The mean post-operative hospital stay was 6.4±4.4 days.

Conclusions: CT-guided PBV dye localization for multiple small pulmonary nodules before VATS is a safe, feasible, and accurate method with high success rate. This approach makes it easy to perform multiple nodule resections during one VATS operation.

Keywords: Computed tomography (CT); patent blue V (PBV); localization

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Introduction

The detection of small early lung cancer is increasing, in part due to the implementation of lung cancer screening programs using low-dose computed tomography (CT) (1). Percutaneous CT-guided core biopsy is a minimally invasive tool used to diagnose early lung cancer (2,3). However, the false negative rate of CT-guided biopsies is high, particularly if the lesions are small, necrotic, or coexist with inflammatory processes (4). A small CT-guided biopsy specimen size may underestimate the histological grade or

Table 1 Clinical information and nodular characteristics in consecutive 100 patients receiving CT-guided PBV dye localization for multiple lung nodules before VATS

Characteristics	N or mean ± SD
Patient (n=100)	
Age (years)	59.9±10.5 (±SD, range, 30–85)
M:F	26:74
History of cancer	41
History of lung surgery	14
History of smoking	13
Visible emphysema on CT	4
Number of patients with	
2 nodules	85
3 nodules	13
4 nodules	2
Nodule (n=217) (cm)	
Size	0.8±0.4 (range, 0.3–2.2)
Depth from pleura/fissure	0.7±0.7 (range, 0–3.9)
Needle length traversing the lung	1.9±1.3 (range, 0.2–6.7)
Consistency [%]	
Solid	90 [41]
Part-solid	25 [12]
Ground glass	99 [46]
Cavitary	3 [1]
Location	
Right upper lobe	61
Right middle lobe	26
Right lower lobe	47
LUL	44
LLL	39

CT, computed tomography; PBV, Patent Blue V; LUL, left upper lobe; LLL, left lower lobe; VATS, video-assisted thoracoscopic surgery.

stromal invasion in early lung cancer (5). Video-assisted thoracoscopic surgery (VATS) has been demonstrated to be both diagnostically and therapeutically beneficial for the resection of small lung nodules, and especially for subsolid lung nodules (6). For early lung cancer, VATS with sublobar resection has been reported to be equivalent to lobectomy in terms of recurrence and overall survival (7). However, it is challenging to visualize or palpate small and deep lung nodules during VATS due to a limited field of view. Some small nodules, especially nonsolid or subsolid nodules, have similar rigidity to normal lung parenchyma due to replacement growth in early lung cancer. The rate of conversion from VATS to thoracotomy to locate small lung nodules has been reported to be as high as 63% without preoperative image-guided localization (8). CT-guided preoperative localization was introduced to help surgeons accurately locate such small lung nodules (9). Various CT-guided localization methods have been developed, including Lipiodol (10), wire (11), and microcoil (12). In this study, we investigated the safety and feasibility of CT-guided Patent Blue V (PBV) dye localization in multiple pulmonary lung nodules.

Methods

From January 2013 to December 2015, a total of 704 patients received preoperative CT-guided PBV dye localization for VATS at our hospital. Among them, 100 consecutive patients underwent CT-guided PBV dye location for more than two lesions during the same procedure (26 males, 74 females, mean age ± standard deviation 60±11 years). Clinical parameters including age, gender, history of smoking, cancer, prior lung surgery, operative method, and postoperative hospitalization stay were reviewed (*Table 1*).

The CT-guided PBV dye localization procedure has previously been described in detail (13). All of the patients were required to stop taking antiplatelet agents 5 days before the procedure, had a platelet count of more than 80×10^3/μL, and normal prothrombin and activated partial thromboplastin time. Before the CT-guided localization procedure, the patients were placed in the supine, prone, or oblique position according to the planned needle path after reviewing prior CT images. The path was planned to be as short as possible while avoiding transfissural punctures or being oriented towards major vascular structures. These procedures were performed on a 16-slice CT scanner (GE LightSpeed; GE Healthcare, Milwaukee, Wisconsin, USA) using a low-dose exposure, thin slice protocol (1.25 mm thickness, 1.3 pitch, 0.7 sec/rotation, 120 kV, 50 mA). After injecting 10 mL of local anesthetic (Xylocaine, 2%, Recipharm Monts, Monts, France), a 22-gauge Chiba needle was gradually advanced under CT-guidance until it reached the target lesion. A total of 0.1–0.3 mL PBV dye (2.5%; Guerbet, Aulnay-sous-Bois, France) was then injected via the Chiba needle. The needle

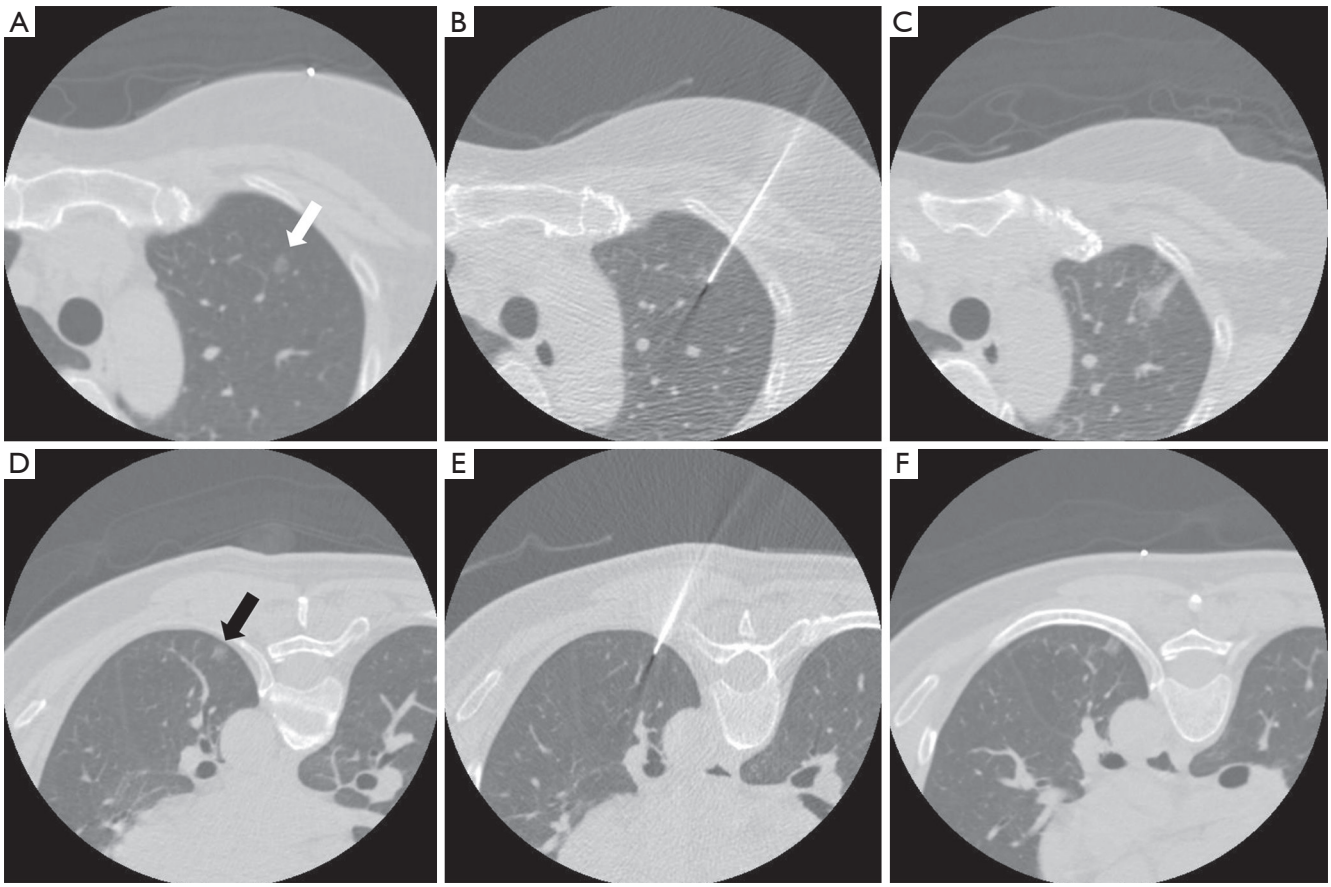

Figure 1 A 57-year-old-female with two small ground glass nodules (GGNs) that underwent resection. One 6-mm GGN was in the left upper lobe (LUL) (A). A 22G Chiba needle was inserted into the periphery of the LUL nodule (B), where 0.1 mL Patent Blue V (PBV) dye was injected. Another 0.1 mL PBV dye was injected at the subpleural lung (image not shown), leaving focal ground glass opacity along the needle tract (C). Another 7-mm GGN in the left lower lobe (LLL) (D). Similarly, 0.2 mL PBV dye was injected (E,F). Both lesions were successfully wedge resected. Final histopathology—LUL nodule: no malignancy; LLL nodule: lepidic predominant adenocarcinoma.

was then withdrawn to subpleural lung parenchyma to allow for a second injection of dye to ensure visibility during VATS if the nodule was deeply located (*Figure 1*). These two areas were both stained so that once the stained lung surface was identified by the surgeon, electrocauterization could be performed to reveal another stained deep target region, which could then be resected by endoscopic stapling. Post-localization CT scanning was performed to evaluate potential complications. The patients were then transferred back to the surgical ward to await surgery (*Figure 2*). Oxygen delivery was given via a nasal cannula and strict bed rest was required until surgery. The localization procedures were performed by one of ten radiologists (with 5–25 years of experience in thoracic imaging) in our department.

The number of nodules localized in each patient, nodule size, nodule consistency, depth from the pleura or fissure, length the needle traversed in the lung, amount of injected dye, failure rate, complications, CT localization and operative procedural time were recorded. The measurements were performed using a commercial PACS system (IMPAX 6.5; Agfa HealthCare, Mortsel, Belgium). Technical failure was defined as the surgeon being unable to visualize the stained area. The CT localization procedure time was defined as the time interval from the first to the last (post-procedure) CT scan, which was calculated from image metadata. Pneumothorax was graded as mild (<1 cm), moderate (1–2 cm), or large (>2 cm). Hemorrhage was graded as mild (less than one segment), moderate (less than one lobe), or large (more than one lobe).

This retrospective study was approved by the

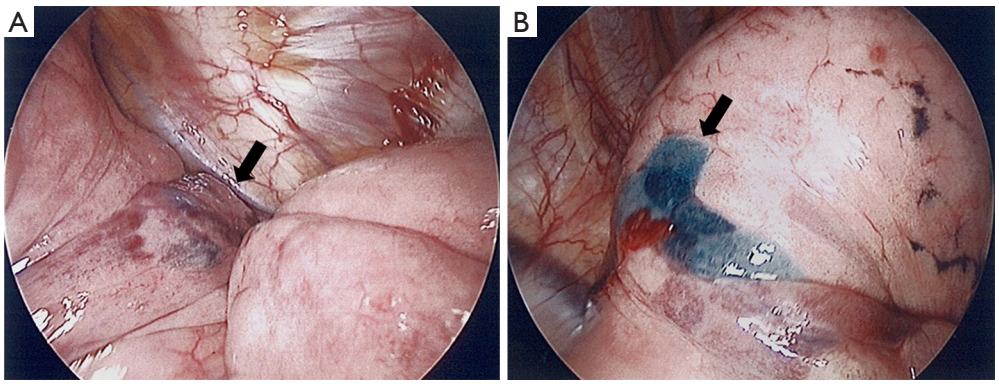

Figure 2 Images taken during video-assisted thoracoscopic surgery, showing two areas (arrows) in the right upper lobe clearly stained after computed tomography (CT)-guided Patent Blue V (PBV) dye localization.

Institutional Review Board of our hospital. The requirement of informed consent was waived.

Results

Table 1 shows the patients' information and nodule characteristics. There were a total of 217 nodules in the 100 patients. Eighty-five patients had two nodules, 13 had three nodules, and two had four nodules that underwent CT-guided localization. Most patients were nonsmokers (n=87). In the 13 patients with a smoking history, four had visible emphysema on CT images. Forty-one patients had a history of cancer. Fourteen patients had a history of prior lung surgery (three on the same side as the targeted nodules, 11 on the contralateral side).

There were 61 nodules in the right upper lobe, 26 nodules in the right middle lobe, 47 nodules in the right lower lobe, 44 nodules in the left upper lobe (LUL), and 39 nodules in the left lower lobe (LLL). The mean size of the nodules was 0.8±0.4 cm (range, 0.3–2.2 cm). Only one nodule was larger than 2 cm in diameter. Among these 217 nodules, there were 90 solid nodules (41%), 25 part-solid nodules (12%), 99 ground glass nodules (GGN) (46%), and three cavitary nodules (1%). The mean depth of the nodule from the pleura or fissure was 0.7±0.7 cm (range, 0–3.9 cm). Final histopathological diagnosis showed that 151 nodules were malignant (70%) and 66 were benign.

The procedural time of CT-guided localization, amount of dye and operative results are listed in *Table 2*. The mean procedural time for localization was 45±14 minutes for two nodules, 75±23 minutes for three nodules, and 109±9 minutes for four nodules. The overall mean procedural time was 50±20 minutes. The average volume of injected dye was 0.2±0.1 mL (range, 0.1–0.4 mL). Five nodules required transfissural punctures to reach the lesion, two of which showed only mild pneumothorax post-procedurally. Another three nodules required two needle passes because of inconsistent respiration.

Dye localization failed in two nodules (technical success rate 99%). Poor dye identification was found in one of these lesions, and progressive pneumothorax with the needle being unable to reach the target in the other. Both patients successfully underwent wedge resection after the surgeons carefully determined the location of the nodule from preoperative CT images.

Mild lung hemorrhage occurred in 24 patients, and pneumothorax occurred in 40 patients (mild 31, moderate 7, and large 2). All patients with pneumothorax remained asymptomatic, and none required further drainage before surgery. One patient who underwent localization for two nodules developed a skin rash and hypotension after being injected with 0.4 mL PBV dye. After resuscitation, the patient recovered and successfully underwent nodule resection (14).

The mean operative time was 134±73 minutes. Wedge resection was performed for 191 nodules, segmentectomy for 22 nodules, and lobectomy for four nodules. Segmentectomy or lobectomy was performed instead of wedge resection if the surgeon judged the section margin to be limited. The mean overall admission period was 6.4±4.4 days.

Discussion

Our results showed that CT-guided PBV dye localization for multiple pulmonary nodules had a high technical success rate (99%), and thus aided the thoracic surgeons to locate

Table 2 The procedure time, amount of dye, complications and final histopathological results of the 217 nodules in 100 patients receiving CT-guided PBV dye localization

Characteristics	N or mean ± SD
Procedural duration (minutes)	
Overall	50±20
2 nodules	45±14 (range, 24–90)
3 nodules	75±23 (range, 44–121)
4 nodules	109±9 (range, 102–116)
Injected dye amount (mL)	0.2±0.1 (range, 0.1–0.4)
Success rate (per nodule) (%)	99
Failed reasons	
Poor dye visualization	1
Progressive pneumothorax	1
Complications (patient number) [%]	
Mild hemorrhage	24 [24]
Pneumothorax (cm)	
Mild (<1)	31 [31]
Moderate (1–2)	7 [7]
Large (>2)	2 [2]
Anaphylaxis	1 [1]
Final histopathology	
Atypical adenomatous hyperplasia	10
Adenocarcinoma in situ	14
Adenocarcinoma	95
Squamous cell carcinoma	1
Other cancer*	41
Sclerosing hemangioma	1
Hamartoma	1
Tumorlet	2
Anthracotic nodule	13
Fibrosis	12
Granulomatous inflammation	3
Inflammation	4
Hemorrhage	1
Lymph node	15
Organizing pneumonia	1
Alveolar cell proliferation	1
No malignancy	2

*, includes 1 sarcomatoid carcinoma, 1 lymphoepithelial-like carcinoma, 2 carcinoid, and 37 metastasis. CT, computed tomography; PBV, Patent Blue V.

multiple small pulmonary nodules and perform resection. The complications were well-tolerated, except for one case with anaphylaxis after PBV dye injection (14). PBV dye has been widely used in breast sentinel lymph node biopsies, with incidence rates of an anaphylactic reaction ranging from 0.6–2.7% (15,16).

Various methods and materials have been proposed for preoperative localization including using a localization wire (11), radiotracer (17), Lipiodol (10), and a microcoil (12). The disadvantages of PBV dye localization are due to its physical property. It may be harder to visualize the injected dye in severely anthracotic and pigmented lung surfaces. PBV dye diffuses and is absorbed with time, and therefore surgery is preferred on the same day. In addition, the surgeons cannot use palpation as with wire or microcoil localization to assist in locating the nodules. The advantages of dye injection are its simplicity. Small gauge needles are used in CT-guided dye localization, which minimizes patient discomfort and the risk of complications, even if transfissural punctures are needed. In addition, no additional radiation exposure (such as from a radiotracer or intraoperative fluoroscopy) is required for either the patient or surgeon. Overall, the technical success rate enabling visualization of the injected dye and resection was high in this study (99%), which is comparable to other localization techniques.

CT-guided dye localization has limitations with deep lesions due to non-visualization of the dye on the lung surface. However, we found that by injecting the PBV dye at the lesion site and subpleural lung for visual confirmation, the surgeons could locate the direction of the small deep lung nodule and perform resection.

There are several limitations to this study. First, it is a retrospective study, and prospective studies are needed to mitigate bias and explore the efficacy and effectiveness of CT-guided dye localization. Second, different surgical techniques are used for resection (VATS, robotic-assisted thoracoscopic surgery, non-intubated VATS), and this can cause great variability in assessing surgical efficacy. However, the high technical success rate using CT-guided dye location is probably not directly relevant to different surgical methods of VATS.

Conclusions

CT-guided PBV dye localization for multiple pulmonary nodules is a feasible and safe method, with high technical success rate. It can facilitate surgeons to perform multiple sublobar resections in one surgery.

Acknowledgements

None.

Footnote

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

Ethical Statement: The study was approved by the National Taiwan University Hospital Research Ethics Committee (No. 201607035RINB) and the requirement of informed consent was waived in this retrospective study.

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