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In patients undergoing video-assisted thoracoscopic surgery excision, what is the best way to locate a subcentimetre solitary pulmonary nodule in order to achieve successful excision?

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Summary

A best evidence topic in cardiac surgery was written according to a structured protocol. The question addressed was 'In patients undergoing video-assisted thoracoscopic surgery (VATS) excision, what is the best way to locate a subcentimetre solitary pulmonary nodule (PN) in order to achieve successful excision?' Altogether, 107 papers were found using the reported search, of which 19 represented the best evidence to answer the clinical question. The authors, journal, date and country of publication, patient group studied, study type, relevant outcomes and results of these papers were tabulated. The hook-wire technique showed a varied success rate ranging from 58 to 97.6% and a relatively higher failure rate due to wire dislodgement. The most common complication of this method was pneumothorax. CT-guided spiral-wire localization displayed a success rate of 86% with the added advantage of providing more stability than the hook-wire technique and permitting manipulation. Radio-guided localization techniques and fluoroscopic-aided methods using contrast media displayed consistently high sensitivities with few complications. The radio-guided technique had the benefit of allowing a longer time-period between the staining of the nodule and the operation. Ultrasonography showed sensitivities ranging from 92.6 to 100%; however, it is highly operator-dependent. Finger palpation was shown to achieve suboptimal results and should be avoided. We concluded that radio-guided surgery is a preferable method. It showed high accuracy with minimal complications and operator dependence in detecting subcentimetre PNs when compared with other techniques such as ultrasonography, finger palpation, fluoroscopic, hook-wire, spiral-wire and microcoil localization.

Keywords: Review • Solitary pulmonary nodule • Video-assisted thoracoscopic surgery • Localization technique

INTRODUCTION

A best evidence topic was constructed according to a structured protocol. This is fully described in the ICVTS [1].

THREE-PART QUESTION

In patients undergoing [video-assisted thoracoscopic surgery (VATS) excision], what is the best way to locate a [subcentimetre solitary pulmonary nodule (SPN)] in order to achieve [successful excision]?

CLINICAL SCENARIO

You are in clinic with a 40-year old ex-smoker with a history of mild haemoptysis. He has had negative findings on sputum cytology, CXR and fiberoptic bronchoscopy. He has undergone a thorax CT scan which shows and is reported as a subcentimetre SPN on the right upper lobe of an indeterminate nature; however, there is no mediastinal lymphadenopathy and the abdomen is normal. Upon performing a PET scan, the lesion has an SUV Max of 6.9. After discussing the findings, due to a strong family history of cancer, the patient would prefer to have the nodule excised rather to be kept under CT surveillance. You discuss the operation via the VATS technique and the possibility of not being able to localize the nodule; subsequently, a mini-thoracotomy is considered. The patient is otherwise healthy with normal respiratory function. You are unsure as to what would be the best method to locate the nodule and decide to check the literature.

SEARCH STRATEGY

Medline 1990 to August 2011 using the OVID interface:

[video assisted thoracoscopic surgery/OR VATs.mp.] AND [pulmonary nodule/OR solitary pulmonary nodule.mp] AND [localisation technique/OR localization technique.mp]

Table 1: Best evidence papers

Author, date, journal and country Study type (level of evidence)	Patient group	Outcome(s)	Results	Comments/weaknesses
Powell *et al.* (2004), Ann Surg, Canada [13] Human phase I trial (level 2b)	CT-guided localization using microcoils combined with fluoroscopic visualization *n* = 12 Included: growing PNs <20 mm in maximum diameter in peripheral lung	Mean nodule size Success rate Mean time for coil insertion Number of patients with complications	11.8 ± 3.2 mm 100% 42 ± 16 min 2 (16.7%)—1 pneumothorax, 1 small haemothorax (asymptomatic)	- VAT resection of the nodules was successful in all patients - Safe, effective, fast technique - Very small sample size, single institute-based study
Mayo *et al.* (2009), Radiology, Canada [14] Prospective cohort study (level 2b)	CT-guided localization using microcoils *n* = 69 (30 males, 39 females, mean age: 60.7 ± 10.1 years) Included: PN >30 mm, located in peripheral lung tissue	Success rate Mean nodule size Complications Conversion to thoracotomy	97% 12.4 ± 4.5 mm 3 patients (4%)—2 pneumothorax requiring a chest tube, 1 haemothorax 2 patients (3%)—endostapler could not be closed around PN	- Microcoil technique more successful than non-guided approach (97 vs. 54%) - Low rates of procedural complications (coil displacement—3%) - Study limited by all resections performed at one centre by three surgeons, one experienced radiologist performed all localizations, 73 procedures but 69 patients—some had multiple lesions
Eichfeld *et al.* (2005), Ann Thorac Surg, Germany [15] Prospective cohort study (level 2b)	CT-guided spiral-wire localization *n* = 22 (14 males, 8 females, average age: 60.4 years)	Mean nodule size Success rate Average procedure time Complications Conversion to thoracotomy	8 mm (range: 2–22) 86% 24 min 14 patients had a small pneumothorax not requiring any intervention (64%) 3 patients (14%)—intubation problems, pleural adhesions and dislocated wire	- Main advantages were low complication rate, short duration, safe and stable fixation of the nodule (spiral wire is more stable than a hook wire and also allows manipulation) - Small sample size, lack of experience using the technique
Miyoshi *et al.* (2009), Eur J Cardiothorac Surg, Japan [2] Retrospective cohort study (level 2b)	CT-guided short hook-wire and suture marking system *n* = 108 (44 males, 64 females, mean age: 59.1 years) Selection for localization based on: Lesion diameter ≤10 mm, distance from pleural surface >5 mm, lesion mostly comprising ground glass appearance	Success rate Missing events (missing unresected lesion or hook wire) Number of patients with complications	93.6% 8 (6.4%) missing events—5 unresected lesions, 3 hook wires not recovered 5 (4.5%)—4 pneumothorax, 1 displacement of hook wire	- Showed reasonable clinical outcomes regardless of the lesion characteristics - Retrospective study, short hook wire provides less anchoring power for traction on lung tissue compared with long
Pittet *et al.* (2007), World J Surg, Switzerland [3]	CT-guided localization using suture hook-wire system	Nodule size	<10 mm in 68% (range: 2–20 mm)	- Hook-wire system shown to be successful, quick and low complication rate

Continued

Table 1: Continued

Author, date, journal and country Study type (level of evidence)	Patient group	Outcome(s)	Results	Comments/weaknesses
Retrospective cohort study (level 2b)	*n* = 45 (23 males, 22 females, average age: 58 years) Excluded: PN in direct contact with pleura, PN >1 and <1 cm beneath pleural surface	Success rate	96%	- Possible reduced procedure-related costs as duration of general anaesthesia reduced due to hook-wire being placed under local anaesthesia - Retrospective study, single institute-based, bilateral resection performed in 4 patients
		Average procedure time	50 min	
		Complications	3 patients (6%)—1 haemothorax, 2 pneumonia	
		Conversion to thoracotomy	2 patients (4%)—not possible to resect lesion by VATS	
Dendo *et al.* (2002), Radiology, Japan [4] Retrospective cohort study (level 2b)	Localization using short hook-wire and suture system *n* = 150 (71 males, 79 females, mean age: 61.8 years) Group A1: Patients at institution A with procedure performed in 1993–1996 Group A2: Patients at institution A with procedure performed in 1996–2000 Group B: Patients at institution B with procedure performed in 1998–2000	Mean nodule size	A1—9.4 ± 6.8 mm A2—11.0 ± 4.8 mm B—10.6 ± 6.5 mm	- Usefulness of short hook-wire and suture system affirmed by high success rate, applicability to multiple lesions and patient comfort - 168 procedures yet 150 patients—some had multiple lesions
		Success rate	97.6% (A1—92%, A2—100%, B—98%)	
		Complications	Pneumothorax—32.1% Pulmonary haemorrhage—14.8% Haemothorax—0.6%	
Ciriaco *et al.* (2004), Eur J Cardiothorac Surg, Italy [5] Retrospective cohort study (level 2b)	CT-guided hook-wire localization *n* = 53 Included: PN was not apical/diaphragmatic, size <10 mm, distance from pleural surface >15 mm	Mean nodule size	16 ± 6 mm (range: 5–28)	- Preoperative hook wire is an effective technique when the PN size is <10 mm and distance is >15 mm. Permitted a VATS resection that otherwise would not have been possible due to size or PN/distance from pleural surface - Retrospective analysis, single-institution-based study
		Success rate	58%	
		Average procedure time	40 ± 7 min	
		Complications	Pneumothorax in 4 patients (7.5%), hook-wire dislodgement in 4 patients (7.5%)	
		Conversion to thoracotomy	4 patients (7.5%) Reasons: impossibility to localize PN, pleural adhesions, local enucleation	
Chen *et al.* (2007), J Formos Med Assoc, Taiwan [6] Retrospective cohort study (level 2b)	CT-guided hook-wire localization *n* = 41 (20 males, 21 females, mean age: 52.5 ± 5.1 years)	Mean nodule size	9.7 ± 1.6 mm	- Hook-wire localization helps precise lesion identification and may serve as a traction device to lift up the lung for wedge resection - Retrospective study, included foreign body removal rather than PN in 3 patients, 2 patients had 2 nodules removed
		Success rate	95%	
		Mean localization time	30.4 ± 2.8 min	
		Complications	8 minimal pneumothoraces (18.6%), 6 minimal haemorrhages (13.9%), 1 haemothorax (2.3%), 3 hook-wire dislodgement (7%)	
Gonfiotti *et al.* (2007), Eur J Cardiothorac Surg, Italy [7]	Hook-wire vs. radio-guided surgery	Mean nodule size	Group A: 11 mm Group B: 11 mm	- No statistical significance between the two groups in locating the nodule, both far superior compared with finger palpation

Continued

Table 1: Continued

Author, date, journal and country Study type (level of evidence)	Patient group	Outcome(s)	Results	Comments/weaknesses
Prospective randomized study (level 1b)	*n* = 50 (32 males, 18 females, average age: 56.3 years) Group A (hook wire): 25 Group B (radio-guided using Tc-99): 25 Finger palpation tried in both groups Included: Nodule maximum diameter <20 mm, distance from nearest pleural surface 1.5–3 cm, consent Excluded: Multiple nodules, mediastinal lymphedenopathy, suspicion of metastases	Success rate Average procedure time Number of patients with complications	Group A: Hook wire—84% Palpation—28% Group B: Radio-guided—96% Palpation—24% Group A: 41 min (range: 24–98) Group B: 43 min (range: 20–85) Group A: 6 (24%) cases of pneumothorax Group B: 1 (4%) case of pneumothorax	- Radio-guided had fewer complications and failures. Hook-wire demonstrated complications linked primarily to external technical factors - Small sample size, single institute
Burdine *et al.* (2002), Chest, USA [11] Prospective cohort study (level 2b)	CT-guided localization using radiolabelled technetium *n* = 17	Mean nodule size Success rate Complications	9.2 ± 3.7 mm 100% 1 pneumothorax (6%)	- The use of a radiolabelled marker precluded conversion to thoracotomy - Limited information on patient characteristics, all patients had known malignancies, very small study sample
Chella *et al.* (2000), Eur J Cardiothorac Surg, Italy [12] Prospective cohort study (level 2b)	Radio-guided localization using technetium-99 *n* = 39 (27 males, 12 females, average age: 60.8 years) Included: Patients with PNs <20 mm in maximum diameter for at least 5 mm from visceral pleura	Mean nodule size Success rate Average procedure time Complications	8.3 mm (range: 4–19) 100% 130 min (range: 60–190) 6 cases of asymptomatic pneumothorax (16%)	- Radio-guided localization by gamma-probe allows the detection and excision of small nodules in an easy and safe way, with minimal complications and a high success rate - Single institute, small sample size
Watanabe *et al.* (2006), J Thorac Cardiovasc Surg, Japan [18] Prospective cohort study (level 2b)	Fluoroscopic-assisted resection using lipiodol *n* = 174 (average age: 62 ± 11 years) Included: nodules < 10 mm, ground glass opacity lesions Excluded: nodules >30 mm, nodules within inner two-thirds of lung, nodules >10 mm and within 10 mm from pleural surface	Mean nodule size Success rate Complications	10 ± 6 mm 100% Chest pain requiring analgesia—16 patients (11%), haemosputum—11 patients (6%), pneumothorax—30 patients (17%), haemopneumothorax—1 patient (0.6%)	- Lipiodol is a safe and inexpensive procedure for localizing small PNs for VATS resection - Complications associated with insertion of the needle rather than the lipiodol itself
Moon *et al.* (1999), Ann Thorac Surg, Korea [19] Retrospective cohort study (level 2b)	Fluoroscopic-aided resection using contrast media *n* = 28 (15 males, 13 females, average age: 53 years) 23 patients had solitary nodules, 5 had multiple nodules	Mean nodule size Success rate Average procedure time Complications	17 ± 7.6 mm 100% 27.5 ± 11 min 4 minor complications related to CT localization	- Water-insoluble contrast media enable better imaging of nodule as they do not diffuse - Apart from lengthy CT time and time concomitant of portable fluoroscopy personnel, method is safe and effective - Small sample size, study included patients with multiple nodules

Continued

Table 1: Continued

Author, date, journal and country Study type (level of evidence)	Patient group	Outcome(s)	Results	Comments/weaknesses
Nomori *et al.* (2002), Ann Thorac Surg, Japan [20] Retrospective cohort study (level 2b)	Fluoroscopy-assisted resection using lipiodol and coloured collagen *n* = 16 (10 males, 6 females, age range: 45–79 years)	Mean nodule size Success rate Complications	7 mm (range: 4–10) 100% 1 case of pneumothorax (6%)	- Marking procedure using both lipiodol and coloured collagen (atelocollagen and methylene blue) can localize small and deeply situated PNs safely and successfully - Small sample size, retrospective study, single institute-based results, does not specify exact inclusion/exclusion criteria
Lenglinger *et al.* (1994), Am J Roentgenol, Austria [16] Prospective cohort study (level 2b)	Methylene blue staining *n* = 15 (9 males, 6 females, average age: 60 years) Only CT was used to guide all localizations	Mean nodule size Success rate Average procedure time Complications Conversion to thoracotomy	16 mm (range: 8–33) 100% 32 min (range: 18–47) Pulmonary haemorrhage—3 patients (20%), pneumothorax—5 patients (33%), no adverse reactions to dye 4 patients (27%)—1 due to haemorrhage, 1 for lobectomy treatment, 2 problems with technical devices	- Staining of PNs before VATs is an accurate technique for localization, less costly than placement of hook wires, and obviates wire-related complications - Use of methylene blue may be limited in patients with extensive anthracotic pigmentation - Very small sample size
McConnell *et al.* (2002), J Pediatr Surg, USA [17] Retrospective cohort study (level 2b)	Methylene blue staining using autologous blood *n* = 17 (average age: 11 years)	Mean nodule size Success rate Average procedure time Complications	9 mm (range: 3–38) 100% 70 min 1 patient conversion to thoracotomy due to stapler malfunction (6%)	- Using methylene blue with autologous blood binder provides accurate localization several hours after injecting nodule - Small sample size, all sample children, more nodules resected than were localized preoperatively (study not based on solitary nodules), retrospective study
Piolanti *et al.* (2003), Eur Radiol, Italy [21] Prospective cohort study (level 2b)	Ultrasonography *n* = 35 (23 males, 12 females, age range: 18–75 years)	Mean nodule size Success rate Complications not reported	13.2 ± 5.9 mm 92.6%	- Showed good sensitivity, affordable localization technique, non-invasive, no exposure to radiation - Requires skilled ultrasound operator - Small sample size, single institute-based study
Matsumoto *et al.* (2004), Eur J Cardiothorac Surg, Japan [10] Prospective cohort study (level 2b)	Ultrasonography during VATS vs. video imaging and palpation *n* = 23 (14 males, 9 females, average size: 61.8 years) Included: patients with nodules located in the peripheral lung, <30 mm in diameter on CT, no definitive diagnosis	Overall success rate for each nodule Average time for ultrasonography during VATS Complications	Ultrasonography: 100% Palpation: 88% Video image: 60% 7 min None reported	- For nodules <10 mm on CT scan, the detection rate by ultrasonography was significantly higher than by video imaging ($P = 0.012$)

Continued

Table 1: Continued

Author, date, journal and country Study type (level of evidence)	Patient group	Outcome(s)	Results	Comments/weaknesses
Santambrogio *et al.* (1999), Ann Thorac Surg, Italy [22]	Ultrasonography	Success rate	100%	- Thoracoscopic ultrasound is a difficult technique requiring experience; however, it can quickly, safely and effectively localize solitary nodules
	n = 18 (12 males, 6 females, average age: 63 ± 11 years)	Mean nodule size	13.9 ± 4.4 mm	
		Average procedure time	10 ± 4 min	
Prospective cohort study (level 2b)	Included: Patients with deep nodules <20 mm without a definitive diagnosis	Complications	None reported	- Small sample size

SEARCH OUTCOME

One hundred and seven papers were found using the reported search. From these, 19 papers were identified that provided the best evidence to answer the question. These are presented in Table 1.

RESULTS

Several techniques for the localization of SPN were described and are well known in their positive or negative aspects: finger palpation, intraoperative ultrasound, hook-wire, spiral-wire, fluoroscopic and radio-guided detection are most commonly used.

The hook-wire technique showed a sensitivity ranging from 58 to 97.6% in various studies [2–7] and a relatively higher failure rate due to the dislodgment of the wire reaching up to 47% [7–9]. Commonly associated complications such as pneumothorax were fewest with the short hook-wire technique used by Miyoshi *et al.* [2]. In the only randomized trial comparing techniques of localization, Gonfiotti *et al.* [7] simultaneously reviewed the radio-guided surgery technique using technetium-99 against the radio-guided hook-wire technique in 50 patients. The technetium-99 group had a better success rate at 96% compared with the hook-wire technique group at 84%. However, this was not a statistically significant difference. Finger palpation was also carried out in both subgroups; however, the radio-guided and hook-wire techniques were found to be far superior (96 vs. 24% and 84 vs. 28%, respectively). In addition, finger palpation achieved suboptimal results in the study carried out by Matsumoto *et al.* [10]. Finger palpation for subcentimetre nodules during VATS resection is not advisable as small port size and operator dependence make it unreliable.

Both studies that solely utilized radioactive technetium [11, 12] to localize pulmonary nodules (PNs) achieved 100% success rates. The radionuclide has a half-life of 6 h, increasing the available time frame between PN labelling and operating. Centres must have the necessary equipment and radiation protection regulations in place to offer this method of localization.

In 2004, Powell *et al.* [13] carried out a study involving just 12 patients with undiagnosed growing PNs of ~12 mm mean size. These were marked preoperatively using percutaneously placed CT-guided platinum microcoils and then excised by a fluoroscopically guided VATS resection. A sensitivity of 100% was shown using this technique with all patients achieving a successful resection. Selection bias and small sample size may limit its clinical implications. With a similar technique, Mayo *et al.* [14] achieved a success rate of 97% and much fewer complications (4 vs. 16.7%).

Eichfeld *et al.* [15] used spiral-wire localization in 22 patients to localize PNs with a mean size of 8 mm and achieved an 86% success rate. The spiral-wire technique gives good stability and permits manipulation. An added advantage is that the marked nodule can be pulled towards the thoracic wall before resection, therefore allowing the exact placement of the linear stapler. Complications are fewer using the spiral-wire technique when compared with the hook-wire technique.

Methylene blue staining of the nodules produced high sensitivities [16, 17], although the studies were based on small sample sizes of 15 and 17, respectively. It provides an accurate method for localizing PNs, although the density of colouration of the target area may be affected by the time elapsed between methylene blue labelling and thoracoscopy. The use of methylene blue may also be limited in patients with anthracotic pigmentation as the dye may be difficult to see during VATS. Fluoroscopic-aided resection using contrast media also yielded high success rates [18–20]. Water-insoluble contrasts such as lipiodol provide good-quality imaging of PNs even several hours after localization.

Ultrasonography demonstrated sensitivities ranging from 92.6 to 100% in localizing PNs across three studies [10, 21, 22]. This method offers a quick, more affordable, less invasive way of localizing lesions with virtually no complications reported but is highly operator-dependent and is limited by the presence of air in the lungs.

CLINICAL BOTTOM LINE

Radio-guided surgical localization is preferable to pinpoint subcentimetre nodules during VATS. In comparison with the other techniques, it offers a higher sensitivity, minimal operator dependence, minimal complications and lower risk of failures.

Conflict of interest: none declared.

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