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REVIEW

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Computed tomography-guided localization of pulmonary nodules prior to thoracoscopic surgery

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Abstract

With the increasing awareness of physical examination, the detection rate of pulmonary nodules is gradually increasing. For pulmonary nodules recommended for management by video-assisted thoracic surgery (VATS), preoperative localization of the nodule is required if its location is difficult to determine intraoperatively by palpation. The computed tomography (CT)-guided preoperative localization technique is the most widely used method with low operational difficulty and high efficiency, which can include hook wire, microcoil, medical dye, medical surgical adhesive, combined application, and emerging localization techniques according to the material classification. Each method has its corresponding advantages and disadvantages, but there is still a lack of unified guidelines or standards for the selection of CT-guided preoperative localization methods in clinical practice. This review summarizes the operation precautions, advantages, and shortcomings of the above localization techniques in order to provide references for clinical application.

KEYWORDS
CT-guidance, preoperative localization, pulmonary nodules

INTRODUCTION

Video-assisted thoracic surgery (VATS) has been widely used in treating pulmonary nodules as a minimally invasive diagnostic and therapeutic method. However, some pulmonary nodules cannot be seen with the naked eye and cannot be palpated with the fingers during surgery, which brings more challenges to clinical diagnosis and treatment.[1] Preoperative localization to mark the location of nodules is recommended for patients with isolated peripheral pulmonary nodules <1 cm in diameter within the lung, imaging presentation of pure ground-glass or subsolid nodules, and difficulty in localizing the lesion by surgical evaluation. Localization by computed tomography (CT) guidance is the most widely used localization method. The more studied localization methods include hook wire, microcoil, dye, medical surgical adhesive or radionuclide, etc. However, each method's usability, security, and efficacy are still hot spots of concern. In this article, we review the current methods for the localization of various types of CT-guided pulmonary nodules based on material classification. The operational considerations and advantages and disadvantages of each method are summarized in Table 1, and the relevant details involving the literature in this review are organized in Table S1.

HOOK WIRE LOCALIZATION

CT-guided hook wire localization is the most commonly used technique for the localization of pulmonary nodules and has the advantages of simplicity and short localization time. The hook wire localization needle consists of a puncture needle and a memory alloy wire inside the needle tube. The tip of the double hook wire is positioned as close as possible to the nodule or through the nodule itself during the localization operation. After localization, the patient should avoid significant activity and be transferred to the operating room as soon as possible or directly.[2]

The rate of dislocation and danger of negative outcomes are both high for hook wire location. In a study by Hanauer

TABLE 1 Operational consideration, advantages, shortcomings, nodule characteristics, duration of localization, and major complication rates of different preoperative computed tomography (CT)-guided lung nodule localization methods for thoracoscopic surgery

Methods	Operational considerations	Find locations	Advantages	Shortcomings	Characteristics of the applicable pulmonary nodules, means, mm, (range)	Positioning duration, *n* or means, min (range)	Major complications rate, means, (range)
hook wire localization	Puncture as close to or through the node as possible; patient should avoid significant movement; patient needs to be transferred to the operating room as soon as possible	Head end of hook wire	Easy and fast	Patients have a high risk of complications (pneumothorax, pulmonary hemorrhage, displacement or decoupling)	Single nodule; depth: 22.5 (0–45.0); size: 15.6 (2.2–29.0)	17.9 (5.8–30.0)	Pneumothorax: 30.2% (22.3%–38.0%); bleeding: 5.6% (5.2%–5.9%); shedding: 3.2% (2.7%–3.7%)
Microcoil localization	The depth of insertion of the microcoil and the length of the tail should take into account the respiratory stretch of the lung to prevent positioning failure	Head end of microcoil	No restrictions on patient movement; not easily dislodged; fewer complications	Complex positioning materials; cumbersome operating methods	Single/multiple nodules; depth: 9.8 (0.7–18.8); size: 6.5 (0.2–12.7)	22.1 (9.5–34.6)	Pneumothorax: 12.8% (9.9%–15.2%); bleeding: 8.0% (5.6%–13.7%)
Medical dye location	The dye spreads easily; surgery needs to be performed as soon as possible	Stain location/infrared imaging equipment probing	Easy to obtain and handle	Color background can interfere with the surgical field; not suitable for patients with significant carbon particle deposits in the lung parenchyma; patients are prone to pleural irritation	Single/multiple nodules; depth: 7.5 (0.3–14.7); size: 5.5 (0.3–10.6)	18.3 (2.8–33.8)	Pneumothorax: 18.0% (3.4%–25.5%); bleeding: 4.0% (3.9%–4.0%)
Medical surgical adhesive location	The injection should not cross the nodule itself otherwise it might affect the extent of excision, specimen preparation and pathological analysis	Location of hard knots formed by glue	Simple operation; Easy to reach markers; safer materials; no restriction of patient movement; prevents pneumothorax and bleeding;	The odor of the material or positioning too deep can induce nausea and coughing in patients	Single/multiple nodules; depth: 17.8 (1.1–34.4); size: 10.8 (7.6–13.9)	43.6 (11.7–76.0)	Pneumothorax: 11.9%; bleeding: 13.1%

(Continues)

TABLE 1 (Continued)

Methods	Operational considerations	Find locations	Advantages	Shortcomings	Characteristics of the applicable pulmonary nodules, means, mm, (range)	Positioning duration, *n* or means, min (range)	Major complications rate, means, (range)
			flexible follow-up surgery time				
Contrast agent location	Confirm that there is no backflow of blood from the puncture site during positioning; injection dose should <0.5 ml	Intraoperative fluoroscopy again	Lower material cost; less diffusion; suitable for deep nodules; does not affect pathological judgment	Needs to be performed in a compound operating room; risk of embolism; may cause local inflammation or infection	Single/multiple nodules; depth: 15.0 (0–30.0); size: 16.0 (2–30.0)	<27.5 (<25.0–30.0)	Pneumothorax: 17.0%; bleeding: 6.0%
Radionuclide localization	The physician must adjust the concentration of the positioning mixture taking into account the surgical articulation	Intraoperative radiographic probe detection	Low cost, easily available materials; suitable for both deep and superficial nodules	Not suitable for locating nodules in the vicinity of emphysema herpetiformis; short half-life of the material; intraoperative repositioning with a radiographic probe	Single/multiple nodules; depth: 25.0 (0–50.0); size: 14.2 (0.3–28.0)	-	Pneumothorax: 29.4%; bleeding: 20.5%
Colocation technology	Take note of the positioning, operation time and the patient's physical state	-	Compensating for the shortcomings of a single technique	Complex operation and long positioning time	Single/multiple nodules; depth: 30.0 (0–60.0); size: 19.0 (2.0–36.0)	<25.0 (20- <30)	Pneumothorax: 4.6%; bleeding: 2%; total incidence rate: 3%
Emerging CT location technologies	The physician needs to be proficient in human anatomy	The head end of the hook wire/virtual reconstruction after the corresponding place	Precise positioning; individualized; low patient radiation exposure; safer/ noninvasive	High cost of supporting equipment, not yet promoted	Single/multiple nodules; depth: 42.9 (0–85.8); size: 12.7 (2.6–22.8)	13.0	Total rate: 2.3%

et al.,[3] seven of 181 patients (3.7%) who underwent hook wire positioning experienced dislocation, three patients (1.7%) had no lesions found in the surgical specimen, and 13 patients (7%) had unplanned intermediate chest openings. After hook wire localization, pneumothorax and pulmonary bleeding occurred 35.8 and 6.0% more frequently, respectively, according to the study by Zhong et al.[4] Iguchi et al.[5] reported a high complication rate of 89.5%; the longer the localization time, the greater the risk of difficulties. The emerging four-hook localization needle is a modified version of the traditional hook wire localization needle, with a metal four-hook anchoring the pulmonary nodule at the front end and the metal wire at the tail end replaced by a marker wire left in the visceral pleura, which can reduce the risk of decoupling and displacement and alleviate the irritating pain brought by the metal wire at the tail end to the patient.

MICROCOIL LOCALIZATION

There are two main types of microcoil localization. One is the complete implantation of the spring coil into the lung, which requires intraoperative fluoroscopic determination of the position, followed by complete removal of the lesion and the microcoil. The other is the "trailing approach", which enables direct intraoperative viewing of the placement position without the need for further fluoroscopic positioning by inserting the head end of the microcoil into the lung and leaving the tail end outside the pleura in the visceral layer.

Microcoil location is safer, the coil is not easily displaced or dislodged, it can remain in the patient's lung for a long period, and the patient can move freely and almost painlessly. The operative interval after applying the microcoil was 8.5 ± 6.0 h in the study by Teng et al.[6] The microcoil can block the needle tract during positioning, which also effectively reduces the occurrence of pneumothorax and bleeding. When compared to hook wire placement, the incidence of pneumothorax[7] (15.2% vs. 48.5%) and parenchymal hemorrhage[8] (7.6% vs. 24.2%) was reduced with microcoil location. In a study of dual microcoil placing by Yang et al.[9] the positioning success rate was 97.9% in 76 patients, with pneumothorax occurring in nine (11.8%) and hemoptysis in two patients (2.6%). However, the trailing method of microcoil location requires more skill and experience from the interventionalist.[10] If the front end of the microcoil placed in the lung is shallow, it is prone to retraction toward the chest wall or fixation to the pleural chest wall, or even dislodgement. If the tail end is left short, the tail of the lung will fall on the pleural surface of the visceral layer after anesthetic pumping during VATS; if the tail is left too long then displacement of the microcoil may occur.

MEDICAL DYE LOCATION

Medical dyes are also widely used in clinical applications as liquid positioning materials, mainly including methylene blue (MB), indigo carmine (IC), and indocyanine green (ICG), etc.

Methylene blue and IC are suitable for more superficial pulmonary nodules, with clear staining and easy intraoperative search for localization.[11] In a comparative study by Kleedehn et al.,[12] the application of MB localization was equivocal compared to hook wire, but MB localization had a lower overall complication rate (46% vs. 54%), a lower incidence of pneumothorax (25% vs. 38%), and a lower perilesion bleeding rate (4% vs. 12%). If too much dye is injected during localization, or in patients with significant carbon particle deposition in the lung parenchyma such as anthrax and silicosis, the spread of MB and IC is faster, which may lead to pleural irritation and difficulty in identifying the localization of MB and IC during subsequent surgery.[13,14] In addition, MB staining of resected specimens can cause some difficulties in histopathological evaluation.

Indocyanine green is a negatively charged amphiphilic tricarbocyanine dye with high tissue penetration and low autofluorescence,[15] commonly used to determine cardiac output, liver function, and ocular perfusion,[16] and is representative of a wide range of NIR spectroscopic dyes used in clinical practice and medical research. In contrast to MB, ICG is not visible to the naked eye and does not interfere with the surgical field of view without the use of NIR light imaging systems. In addition, ICG visualizes the localized area better than MB and IC in patients with pulmonary anthrax.[13,17] Gkikas et al.[18] used ICG as a CT localization marker with a high success rate (96.7%) and a false negative rate of only 2.4% (26/1089). A common cause of failure was ICG spillage during localization and subsequent spread in the chest cavity, with a complication rate of 15.2% (150/989) during hospitalization. ICG localization has corresponding limitations; the dye requires specialized near-infrared fluorescence equipment for identification during subsequent pneumonectomy, some findings suggest that ICG fluorescence diminishes at depth, and thus localization of nodules located deep in the lung parenchyma poorly.[17]

MEDICAL SURGICAL ADHESIVE LOCATION

Medical surgical adhesive, composed of 2-octyl cyanoacrylate, is an ideal material for the treatment of refractory fistulas, abdominal wall hernias, gastrointestinal disorders, and other diseases,[19,20] as well as for thoracic surgery,[21] and is nontoxic, safe, and has few allergic reactions. The hard knots created by the medical surgical adhesive in contact with the tissue can be easily identified and reached by the surgeon. The rapid solidification of the glue also effectively blocks the puncture site, reducing lung gas leakage and bleeding. The medical adhesive can be left in the lung for a long time after positioning without restricting the patient's movement, and the position of the adhesive does not change, allowing for a more relaxed surgical interface. In the study by Zhang et al.,[22] the mean time from the end of localization to the start of surgery was 16.02 ± 6.59 h in the medical adhesive group, which was significantly longer than in the hook wire localization group (2.12 ± 1.36 h). The use of surgical adhesive to localize pulmonary nodules was shown to delay surgery by 60 days in the study by Imperatori et al.[23] It is also indicated for patients with multiple nodules. However, this adhesive may induce transient irritating cough in some patients when the localization depth is too deep to reach more than 20 mm; and as a chemical substance, some patients are intolerant to its odor, which may also cause dry heaving, nausea, and cough. It should be noted that medical adhesive needs to be injected in the area around the lung nodule, and the needle for positioning must not pass through the lung nodule, otherwise, the glue will affect the production of pathological specimens and subsequent analysis. If the area of glue injection is too large, it may also enlarge the scope of wedge resection of the patient's lung.

CONTRAST AGENT LOCATION

CT-guided application of contrast agent localization, such as iodine oil and barium, requires intraoperative fluoroscopy again to confirm the location. Iodine oil is a simple and affordable localization material, does not spread readily which prevents excessive excision of normal lung tissue around the nodule, and is also suitable for the localization of deep nodules. However, iodine oil is insoluble in water and carries a risk of embolism, so before injecting iodine oil, the physician should withdraw the syringe to make sure there is no backflow of blood from the puncture site, and the amount of injection should not be excessive, within 0.5 ml.[24]

Barium sulfate suspension is mostly used in barium meal examination because it will stay in the lung for a long time, it is not commonly used in clinical bronchography, but it is suitable as localization material for lung nodules. Kobayashi et al.[25] applied CT-guided localization by bronchoscopy to mark the nodule at the patient's left lung, and the patient showed better tolerance of the procedure. The localization remained in place until the resection surgery was carried out 7 days later, and the barium had no impact on the pathological investigation. However, the surgery is difficult and time-consuming since barium localization needs both bronchoscopy and CT guidance, which restricts the application of this localization technique in the clinic.

RADIONUCLIDE LOCALIZATION

Technetium-99 m (99Tc) is a low-cost and easily available radionuclide with a half-life of about 6 h. In order to pinpoint the target nodule under CT guidance, doctors frequently mix 0.2 ml of 99Tc-labeled human serum albumin (5–10 MBq) with 0.1 ml of nonionic contrast agent. Subsequent thoracoscopic procedures require the connection of a radio detector needle to find the location again. Stiles et al.[26] applied this method to successfully localize and resect pulmonary nodules in 96% of cases. Ambrogi et al.[27] demonstrated that using this protocol correctly localized and resected nodules in 99% of patients (208/211), with a significantly lower rate of complications like pneumothorax and bleeding.

Radionuclide localization applies to any part of the lung and does not interfere with histological examination, but if there is emphysema herpetiformis in the vicinity of the target nodule, there is a risk of radionuclide diffusion in the lung parenchyma, resulting in a decrease in the accuracy of localization. Another limitation of radionuclide localization is its relatively short half-life, which requires surgery as soon as possible after localization; if surgery is delayed, the radionuclide may dissolve the day after placement and no longer be detectable. Grogan et al.[28] improved the stability of radionuclides in the lung to 18 h by elevating the concentration of the nuclide, making more flexible preoperative localization and surgical resection time and the localization effect of the modified solution was further confirmed by Galetta et al.,[29] where the stability of the radionuclide was 18–20 h in that study.

COLOCATION TECHNOLOGY

Currently, more and more surgeons are using the combined application to avoid the shortcomings of a single technique. The results of a study by Jiang et al.[30] showed that the application of MB combined with medical glue localization had a high success rate of 99.5% (381/383); in two cases of failed localization, the medical glue and dye were injected onto the surface of the visceral layer of the pleura and did not enter the lung parenchyma, only the pleural surface. The residual medical glue and dye still successfully enabled the surgeon to locate the nodule intraoperatively. In a study by Martin et al.[31] on preoperative localization of VAT resection of pediatric cancer lung metastases, a hook wire, dye-based dual localization method was applied to preoperatively localize six deep lung metastases in four pediatric patients, and all lesions were successfully marked and identified at the time of surgery. Jin et al.[32] used a mixture of lipiodol and MB (MLM) The results showed that the staining range of MLM was significantly smaller than that of MB (0.6 vs. 1.0 cm). The staining ability of MLM was higher than that of MB (2.8 vs. 2.2), and lipiodol reduced the diffusion of MB and improved the success rate of percutaneous localization. Hasegawa et al.[33] applied a mixture of IC and lipiodol (MIL) to localize pre-VATS pulmonary nodules, and the localization success rate was 100%.

EMERGING CT LOCATION TECHNOLOGIES

CT virtual 3D-assisted localization is an emerging localization technology that requires importing the patient's thin-layer CT image data into the corresponding system for processing and finally obtaining a 3D digital model, which can be roughly divided into two localization methods.

One is to determine the puncture point and depth based on the location of the patient's thorax, ribs, and nodes after 3D reconstruction, print out a positioning navigation template for that patient using a 3D printer, affix it to the patient's corresponding chest wall location during positioning, then apply a hook wire or microcoil to locate the target node, rescan the CT after placement, and send it to the operating room with successful positioning. In the study by Zhang et al.,[34] 12 pure ground-glass nodules were successfully localized using this method and resected by VATS wedge resection.

Another approach is to build a virtual 3D image model for localizations. After the patient has had a CT scan, the anatomical structure of the trachea, bronchus, target nodule, and other related surrounding parts of the patient's scanned area is reconstructed by system calculation. Additionally, the relative position relationship is determined, and the marginal range is delineated, and the marginal range is then surgically removed. This technique requires physicians to master human anatomy and use 3D reconstruction software with skill, requires high equipment configuration in medical units, has high surgical costs, is applied less frequently, and is not popular at the moment. However, this technique is a noninvasive localization technique with good potential, as demonstrated by the results of Zhang et al.,[35] which showed better safety and shorter surgical times.

DISCUSSION

We observed that the mean success rate for all techniques of positioning methods in the included relevant studies was 98.1% (94.9%–100%). After localization, most nodules (2751/2753) can be subjected to intraoperative frozen pathological sectioning. In the references where the surgical approach was documented (total:1596), 1488 nodules were ultimately removed by VATS, 93 applied thoracotomy or mini-thoracotomy, of which 20 were unplanned, and 15 nodules were operated on with da Vinci robotic surgery.

We derived that the most used metal localization technique nowadays is hook wire, which is more suitable for single-node localization, and microcoil, which is more suitable for multiple nodes and has a lower shedding rate. The medical surgical adhesive is the most often utilized liquid localization technique. The surgical adhesive is a safer substance that works for both single and multiple nodes and has a simpler localization process when compared to dyes, contrast agents, and radionuclides. The dye localization technique is more suitable for nodules in superficial areas, and medical surgical adhesives should not be used to localize nodules deeper than 20 mm. Surgery is needed as soon as possible after metal, dye, and contrast positioning, particularly hook wire. The surgery schedule is more flexible after the medical surgical adhesive location, and the study results show that the surgical adhesive positioning site is still valid in the patient's lung after 60 days. If necessary, a combined metal-fluid localization strategy can be used to increase the localization success rate and extend the interval to surgery. The localization technique that makes use of 3D technology now exhibits the highest level of accuracy, but there is still a long way to go from the clinical pilot to the method's widespread adoption due to the method's greater need for medical facilities and technology.

Furthermore, we note that in actual clinical practice, considering the depth and location of the patient's pulmonary nodules, physicians usually select the patient's CT positioning position based on the ideal positioning path of exposure, including supine, prone, and lateral positions, unilateral body pad, etc. According to the results of our review, patients who undergo localization of pulmonary nodules are generally middle-aged or elderly. For this population, it may be difficult to maintain one position for a long time in the awake state, and the patient's physical condition might be unable to tolerate position placement by the physician. However, most studies do not seem to focus on this practical problem. For example, if the patient is too weak to hold the position for an extended period, the physician should probably choose a method, such as a surgical adhesive, that is quick and does not restrict the patient's post-position after localization.

CONCLUSION

In conclusion, there are benefits and drawbacks to each CT-guided preoperative localization strategy. The imaging physician and surgeon need to select the appropriate localization method based on the patient's lung nodule characteristics (depth, size, and number), level of physical function, and family financial status as well as hospital medical equipment. Hook wire is appropriate for single nodes, whereas other localization procedures are suited for single and multiple nodes. Surgery should be scheduled in patients as soon as feasible following hook wire localization. Dye, contrast, and medical surgical adhesive are acceptable for superficial nodules, and surgical arrangements become more flexible following medical surgical adhesive localization. Although difficult, the combined localization strategy can compensate for the inadequacies of a single technique. The localizing surgeon should also improve the localization technique to reduce the number of patient exposures under CT and to avoid more localization complications. The combination of multiple localization techniques and emerging localization techniques all reflect better potential, and further clinical exploration and innovation are still needed in the future to provide patients with safer, more efficient, and personalized CT-guided preoperative localization techniques.

Due to the limited number of available studies, some of which were not comprehensive in describing the details of the localization and surgical procedures, our review summary has limitations. More studies are needed in the future to further refine the advantages, disadvantages, applicability, and considerations of each positioning method through surgical practice with more comprehensive summaries of previous studies to guide the selection and application of a wider range of clinical practice.

AUTHOR CONTRIBUTIONS

Lixin Wang designed the study and wrote this draft; Daqian Sun and Min Gao surveyed and analyzed the relevant literature; Chunhai Li revised and-re organized the manuscript. All authors approved the final manuscript.

CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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