Review Article

Image-guided video-assisted thoracoscopic surgery (iVATS): a single center experience and review

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Abstract: Lung cancer screening techniques using low-dose computed tomography (LDCT) scans have improved over the last decade. This means that there is an increased rate of detection of small, often non-palpable, nodules and ground-glass opacities. Obtaining a definitive diagnosis of these nodules using techniques such as percutaneous image-guided biopsy or intraoperative localization is challenging, and these nodules have traditionally undergone routine surveillance. Image-guided video-assisted thoracoscopic surgery (iVATS), which is performed in a hybrid operating room, has made it more feasible to biopsy and resect these nodules. The first thoracic surgery hybrid operative room was introduced at our institution at Brigham and Women's Hospital. Herein, we describe our experience implementing this technique including the methods we used to train key personnel such as radiologists, surgeons, and anesthesiologists to ensure that this technique successfully translated to a clinical setting. We review the benefits of iVATS, which includes decreased rate of fiducial dislodgement, real-time imaging which facilitates successful fiducial placement, and smaller sized resection of lung parenchyma. We will also describe the comparisons between traditional diagnostic methods and iVATS, patient selection criteria and important technical details. Some centers describe alternative techniques for several of the technical aspects, including patient positioning, which we also mention. Lastly, we describe adverse events after iVATS, which are comparable to those seen after a standard VATS.

Keywords: Image-guided video-assisted thoracoscopic surgery (iVATS); ground-glass nodules; sub-centimeter nodules

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Introduction

Lung cancer continues to have a high mortality worldwide, and in the United States, it is the largest cause of cancer-related death for individuals 50 and over (1,2). In recent years, countries including the U.S. have developed low-dose computed tomography (LDCT) screening programs that help detect lung cancer at earlier stages, reducing mortality up to 20% when compared to surveillance with chest radiography alone (3-6). These new imaging guidelines have also led to an increase in the detection of small lung nodules and ground-glass opacities (GGOs) suspicious for cancer, which typically require interval follow-up and tissue biopsy to assess for features of malignancy (7,8). Obtaining a definitive diagnosis of these nodules thus poses logistical

and technical difficulties. The accuracy of percutaneous, image-guided biopsy decreases with nodule size, and intraoperative localization of small or subsolid nodules for excisional biopsy can also be challenging. In response to these challenges, image-guided video-assisted thoracoscopic surgery (iVATS) techniques were devised to facilitate the localization and resection of small lung nodules (9).

Benefits of iVATS

Many techniques for the preoperative localization of small and subsolid lung nodules have been reported (10-13). These methods include the percutaneous, image-guided placement of fiducial markers and the injection of radiopaque dyes to localize lesions prior to surgical resection by standard minimally invasive techniques. A key feature of these techniques is the placement or injection of the marker in the computed tomography (CT) suite, after which the patient is transferred to the operating room (OR) for resection. During the transfer, there is an increased risk of dislodgement of the fiducials, which results in suboptimal lesion localization. Unlike these techniques, iVATS takes place in a hybrid OR, allowing for localization and resection to be performed as a single-stage procedure. The fiducial marker or dye is placed in the operating suite and followed immediately by surgical resection. By eliminating the need for patient transfer, iVATS allows for fiducials to be placed in the same position the patient will be in at the time of surgery, which prevents dislodgement.

Patients are at risk of adverse events in the interval between fiducial placement and skin incision, with studies reporting events such as parenchymal hemorrhage and pneumothorax to occur in up to 30% of cases (13-15).

The iVATS technique offers additional benefits beyond minimizing the risk of adverse events associated with nodule localization. By utilizing a hybrid OR, iVATS techniques allow for real-time imaging that raises the rate of successful fiducial placement (16). Furthermore, eliminating patient transfer reduces the likelihood of marker migration or dislodgement when hookwires or similar techniques are used, and the reduction in marking-to-incision time also limits the risk that radiopaque marking dyes will diffuse beyond the target region. The iVATS technique also obviates the need for manual palpation of small nodules, facilitating a more minimally invasive resection. This may reduce postoperative pain and recovery times (9). It also reduces the time during frozen section, especially for non-palpable lesions.

iVATS selection criteria

As in any surgical technique, patients must be appropriately selected to undergo iVATS procedures. Indications for iVATS include the presence of screening-detected, subsolid lung nodules <30 mm in diameter located in the outer third of the lung parenchyma (9). In our cohort, the CT ratio of the tumors was 0–0.5. For more centrally located tumors (inner two-third of the lung parenchyma) and for lesions larger than 2–3 cm, we do not incorporate iVATS and perform an anatomic resection instead. Patients should have sufficient cardiopulmonary reserve to tolerate thoracoscopic wedge resection. It is also important to select patients with imaging and clinical findings highly suggestive of malignancy. Because iVATS is often performed on lesions which are too small or lacking the density to be accurately biopsied, it may be unrealistic to expect a preprocedural, histologic diagnosis for all patients undergoing resection with this technique. As has been noted elsewhere, this illustrates a need for technologies to facilitate histologic diagnosis of small, subsolid lung lesions. iVATS is one method (17). By using iVATS in well-selected patients, this technique can allow for curative resection of early-stage lung cancer, optimizing margins while minimizing the resection of normal lung parenchyma (18).

GGOs

As mentioned previously, an important advantage of iVATS is the ability to target smaller nodules and GGOs. Debates surrounding appropriate management for GGOs are ongoing. Many patients with GGOs have historically undergone routine surveillance. However, histopathological evaluations of GGOs resected via iVATS have identified that 57–95% of these nodules are malignant. Most were primary lung cancer, but metastatic GGOs were discovered as well (9,19-24). The primary malignant nodules were mostly well-differentiated adenocarcinoma (with predominant subtype of non-lepidic) (25,26). The observed benign pathologies included granuloma, hamartoma, tuberculosis and organizing pneumonia (9,18-20,23,24). Our own experience demonstrated that of the 37 patients who had partially solid nodules on imaging, 29 of them

(78%) were found to be invasive cancers on pathology (9). Therefore, consideration for resection should also be given to GGOs and heterogenous lesions.

Technical details

Hybrid OR

The procedure takes place in a hybrid OR and is run by a multidisciplinary team consisting of radiologists, anesthesiologists, and surgeons. To successfully perform iVATS, it's important to clearly communicate plans with the entire team prior to intervention so that unanticipated events can be safely addressed (17).

The first thoracic surgery hybrid OR was introduced at our institution. It implemented an Advanced Multimodality Image Guided Operating (AMIGO) suite for patients to undergo general anesthesia and examination via bronchoscopy. The suite was 5,700 square feet with three adjoining rooms that contained CT, magnetic resonance imaging (MRI), PET, and near-infrared imaging (9,18). Thereafter, other country/region such as China and Taiwan established smaller, hybrid multidisciplinary suites at their centers. These centers included three-dimensional imaging modalities, or image-guided electromagnetic navigation bronchoscopy (ENB) (16,19,27). ENB alone has low radiation capability to localize and capture lesions and is therefore often utilized in combination with CT scans (27).

Using three-dimensional models generated by preoperative imaging scans, we determine the ideal placement for the fiducials. Fiducials are markers, typically metal, that are used to mark the target lesion. Several imaging devices have been utilized. We use the C-arm at our institution, which is the most common (9,18). The O-arm CT scan can also be used (28). Like the C-arm, the O-arm is also a mobile imaging system that can be used intraoperatively to provide high quality two- or three-dimensional images. Compared to the C-arm, O-arm CT scans have higher radiation exposure and cannot be moved around as easily (20). Other imaging techniques include a combination of a three-dimensional bronchial reconstruction using CT images along with ENB (29). This method is theoretically better for accessing apical lesions or lesions located near major blood vessels (30).

Once the patient is intubated, a cone is performed to generate a view of the field containing the nodule (9,18). The scan is taken during an end-inspiratory hold following a protocol with 248 projections of 0.36 µGy/projection at 200° over 5 seconds. Compared to scans performed over 6 seconds, this 5-second scan can decrease radiation exposure by 60% (20).

We recommend placing patients in a lateral decubitus position because this prevents any unexpected change in position and subsequent localization failure (31). Some centers have reported prone or supine positioning based on the location of the nodule. This may be helpful for obese patients (9,18,20-22,32).

During iVATS, there is a risk of equipment collision, particularly when patients are obese (17,21,30). To avoid collision, our strategy is to place the C-arms in a cephalad position. We also use extension tubing for arterial and venous lines and for the ventilator circuit to ensure adequate length during scans. Lastly, we recommend a test scan prior to prepping the patient. This helps ensure that positioning errors do not occur during the operation (31).

Navigation techniques

Our institution implemented nodule localization using T-bars through a needle guidance software called Syngo iGuide (Siemens Healthcare AG, Forchheim, Germany). This software has also been used in other centers (9,18-20,23,27,31). C-arm fluoroscopic image guidance markers and laser-target crosshairs generate optimal needle pathway directions. A combination of Syngo DynaCT and ENB can provide a clear view of the field to help lead and verify the navigating route. Once a steady navigating route is generated, the navigation system is turned off, and a 5–6-second end-inspiratory pause occurs as previously described. DynaCT allows for a more precise lesion localization, especially for GGO nodules. It is also associated with lower radiation doses compared to the conventional pre- and postoperative fluoroscopic images (18,29).

Nodule localization and capture techniques

There are three main methods used to localize nodules. These include metallic implants, dye, and radionuclear labeling. Metallic implants include hookwires, microcoils, and T-bars (16,29). We commonly use T-bars at our institution. Using fluoroscopic guidance as mentioned previously, we place the T-bars as close as possible to the target lesion. This helps minimize the size of the lung parenchyma that is resected. To place microcoils,

one end is carefully inserted into the target lesion and the other end into the visceral pleura (24). Compared to hookwires, microcoils have a lower risk of pneumothorax but have a higher probability for dislodgement particularly during patient transfer or during lung deflation at the time of anesthesia induction (24,29). Interestingly, one study reported that 47% of the patients developed a pneumothorax after hookwire placement, although additional intervention was not required since the patients were subsequently undergoing a wedge resection (19). The risks of dislodgement are lower during iVATS because patients do not need to be transferred between wire placement and resection since they are already located in a hybrid OR. The average risk of dislodgement after iVATS is 3.3% compared to 9.5–22% reported after conventional methods (31). Adverse events reported after metallic implants include air embolus, hemothorax, pneumothorax and pleuritic pain (16).

Contrast or dye injection (e.g., methylene blue) is another method to localize the pulmonary nodules. Most centers report using indocyanine green (ICG) and patent blue V (PBV). During localization, a near infrared thoracoscope is needed to detect the ICG stained lung tissue (24). Because ICG is easily diffused in the lung parenchyma, nodule localization should be performed within 3 hours of its injection (19,24). There are several advantages of ICG compared to PBV. These include the ability to detect nodules regardless of textural or color changes of the visceral pleura and minimal associated adverse effects (23). Alternatively, PBV is cheaper. Many studies have reported the use of PBV for superficial nodules (pleural distance <20 mm) or for GGOs with a 100% success rate (20,22,25), while others have favored ICG due to the aforementioned advantages (21,23).

Studies comparing dye injection to the hookwire technique have differed in their findings. Chao *et al.* found no significant difference in time to localization between the two. In contrast, Cheng *et al.* recorded a shorter localization time in the dye-injected group since those patients were already located in the hybrid OR (21,25). Dyes are cheaper than many metallic implants and are associated with lower rates of pneumothorax (25). However, failure to localize the nodule due to parenchymal dye diffusion is one of the main disadvantages of this technique. If this happens, more lung parenchyma may need to be resected to ensure that the nodule is removed. Therefore, time from injection to resection should be minimized.

Implementing dual markers (e.g., both a microcoil and ICG) has been reported to increase accuracy in localization, particularly for deeper lesions, with success rates of 90–100% (24,27). We have also found that a combination of T-bars and dye markers could be successful in identifying occult nodules (17).

Radionuclear labeling is a third localization method. A technetium-99 (99TC) radiotracer is injected into the lesions and can last up to 24 hours. Unlike dye injection, radionuclear labeling allows for a longer time interval between localization and resection. However, centers need to be equipped with gamma probes and offer appropriate protection against radiation. Additionally, this technique is not ideal for localizing deeper or posterior nodules (16).

Surgery

We make three incisions when performing iVATS. Some centers have reported the use of uniportal iVATS (9,18,25,31), although its comparability to standard iVATS is currently unknown. There are several strategies we employ to ensure safe margin resections, especially when the lesion is not palpable. First, we use ring forceps to estimate the distance. The distance across the ring from the tip to the crosspoint of the instrument is known and is a convenient intracorporeal measuring device. Also, the staplers have metric marks on the staple loads. Finally, the placement of the fiducial includes an exact measure of distance from skin to target and pleura to target. Combined, these make it straightforward to obtain proper depth for R0 resection. After the nodule is resected, an x-ray is taken to confirm the fiducial is in the sample. The tissue is then sent for frozen section. If malignancy is confirmed, a segmentectomy or lobectomy can then be performed (18,26).

Operative times and localization times vary across literature and are dependent on several factors including type of localization marker used, patient factors, and surgeon expertise. Studies that used dual makers have reported an average localization time of 18–24 minutes, and the total operative time of 120 minutes. Our localization times using T-bars have ranged from 13–35 minutes, and our total operative times have ranged from 39–129 minutes (9,18).

Several studies have compared conventional VATS with iVATS. iVATS was superior to VATS in localization accuracy, shorter operative time, higher patient satisfaction, and lower risk for adverse events such as pneumothorax, hemothorax or wire dislodgement. There was no difference

in blood loss between the two techniques (19,25,26,29).

Bilateral iVATS is uncommon and has only been described in one study that included seven patients. Methylene blue dye was used to localize the nodules. The authors reported an average operative time of 245 min with median nodule sizes of 11 mm (IQR, 6–15 mm). The distance from the nodule to the pleura was 10.5–17 mm (33). Only one patient developed hydrothorax, and none of the other six patients experienced any adverse events.

Adverse events and outcomes

The success rate for localizing a lesion using iVATS is remarkably high, with studies citing a range from 90% to 100% (19-21,31). The most common reasons for failure include dislodged T-bars, equipment malfunction and dye spillage. However, these are infrequent. Based on our published experience treating 75 patients, only three had a dislodged T-bar and none of them experienced any significant effects as a result.

In general, the rate and severity of adverse events after iVATS are low and comparable to those seen after a standard VATS. Only 6 of 75 total patients in our trials experienced adverse events, all grades II or III, which included pneumonia (two patients), ileus (1), prolonged air leak (2) and splenic bleed requiring embolization (1). Other adverse events reported in literature include Non-ST-Elevation Myocardial Infarction (NSTEMI), atrial fibrillation, pneumothorax and hemothorax (19). There was no 30- or 90-day mortality or perioperative deaths (9,18). There were two conversions to lobectomies. One demonstrated micropapillary pattern and another had an aggressive pattern on frozen pathology. There were no conversions to segmentectomies.

Based on our experience, transitioning iVATS to clinical practice at a large academic institution is safe and feasible if an organized series of steps are followed. To train staff including radiologists, surgeons, and anesthesiologists, we created a detailed manual and step-by-step procedure video. We also held several training sessions before formally enrolling patients. Over four years, we trained six thoracic surgeons, two radiologists, six anesthesiologists and six radiology technologists. Fifty patients were enrolled and safely underwent the procedure (18). The average hospital cost was approximately $89,000. Remarkably, 97% of the nodules were successfully resected, which was significantly higher compared to our initial success rate of 87% in 2015. Additionally, our R0 resection rate was 100%. The specific learning curve for iVATS is further described by Hsieh and colleagues. The authors divided 30 consecutive patients who underwent resection via iVATS for solitary pulmonary nodules into two groups of 15 patients each (early group I and late group II). Between the early group and late group, the authors discovered a reduction of approximately 50% in localization time (49 *vs.* 24 minutes) and radiation exposure (224 *vs.* 70.7 mGy). There was also an inverse association between procedural time and surgical experience (20).

There are a few key limitations of this technique, which include the need for a hybrid OR and well-trained multidisciplinary staff. However, our success surrounding transition to clinical practice demonstrates that incorporating iVATS at adequately equipped hospitals is possible.

Strengths and limitations of this review

As previously mentioned, the first thoracic surgery hybrid OR was implemented at our institution. Therefore, describing our experience with this technique and how we translated it into the clinical realm we believe is of value. In this review, we also mention a myriad of diverse studies published from centers around the world and offer our comments on the techniques described. However, this is not meant to be a systematic review of literature. There might be additional studies describing alternative techniques or other adverse events, for instance, that we did not discuss. This review is meant to provide a general understanding of key aspects of iVATS along with our experiences. If necessary, readers are encouraged to conduct their own research to supplement what is mentioned here.

Conclusions

Use of a LDCT scan for lung cancer screening has made it easier to detect smaller nodules and ground glass nodules. The rate at which these nodules are detected is increasing as the number of patients eligible for lung cancer screening increases. Traditionally, these nodules underwent routine surveillance with emotional stress for the patient and the family between scans. Alternatively, a “wide wedge” using anatomic landmarks was sometimes required to remove the nonpalpable nodule. A growing body of literature suggests that these smaller lesions and ground glass nodules may harbor malignancy and should be resected early. iVATS has

made it more feasible to intervene upon these lesions and is one of the solutions needed to address the ever-growing burden of increased detection.

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Footnote

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