A novel minimally invasive near-infrared thoracoscopic localization technique of small pulmonary nodules: A phase I feasibility trial

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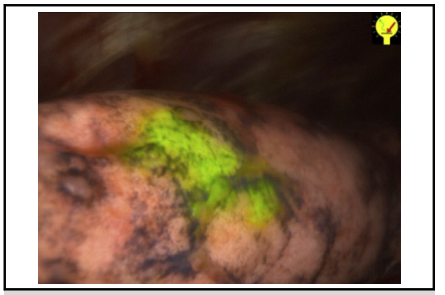
ABSTRACT

Objectives: Localization and resection of nonvisible, nonpalpable pulmonary nodules during video-assisted thoracoscopic surgery are challenging. Our study was to determine the feasibility and safety of indocyanine green fluorescence localization and resection of small nodules using a near-infrared fluorescence thoracoscope.

Methods: Twenty patients with undiagnosed peripheral nodules smaller than 3 cm scheduled for computed tomography–guided microcoil placement followed by video-assisted thoracoscopic surgery wedge resection were enrolled. After microcoil deployment, 100 to 150 μL of diluted indocyanine green was injected percutaneously near the nodule. The nodule initially was localized solely by using a near-infrared thoracoscope to visualize indocyanine green fluorescence. Thoracoscopic instruments were used to determine the staple line. Wedge resection was performed after confirmation of the location of the microcoil using fluoroscopy.

Results: Twenty patients underwent near-infrared, image-guided, video-assisted thoracoscopic surgery resection. The median computed tomography tumor size was 1.2 cm. The median depth from the pleural surface was 1.4 cm (range, 0.2-4.8 cm). The median computed tomography–guided intervention time was 35 minutes, and video-assisted thoracoscopic surgery procedural time was 54 minutes. Indocyanine green fluorescence was clearly identified in 18 of 20 patients (90%). The surgical margins were all negative on final pathology without the need for additional resection. The final diagnoses included 18 primary lung cancers, 1 metastatic lung cancer, and 1 benign lung tumor.

Conclusions: Computed tomography–guided percutaneous indocyanine green injection and intraoperative near-infrared localization of small nodules are safe and feasible. These offer surgeons the ease of localization through direct indocyanine green fluorescence imaging without the use of fluoroscopy and may be a complementary technique to preoperative microcoil placement for nonvisible, nonpalpable intrapulmonary nodules. (J Thorac Cardiovasc Surg 2017;154:702-11)



Intraoperative image of fluorescent ICG with a NIR thoracoscope.

Central Message

Intraoperative NIR thoracoscopic localization using ICG injection is a safe and feasible procedure.

Perspective

CT-guided percutaneous ICG injection and intraoperative NIR thoracoscopic localization of small pulmonary nodules are safe and feasible minimally invasive procedures. They offer surgeons the ease of localization through direct ICG fluorescence imaging without using fluoroscopy and are complementary to preoperative microcoil placement.

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Approvals: A Health Canada No Objection Letter was obtained for the off-label use of indocyanine green (#9427-D2777-21C). An Investigational Testing Authorization–Class II was obtained (#219223) for the use of the near-infrared fluorescence thoracoscope (Pinpoint System, Novadaq Technologies Inc, Mississauga, Ontario, Canada). This study was approved by the Institutional Review Board of the University Health Network (REB #12-5454).

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Abbreviations and Acronyms
CT = computed tomography
C/T = consolidation/tumor
ICG = indocyanine green
NIR = near-infrared
VATS = video-assisted thoracoscopic surgery

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Lung cancer is the leading cause of cancer death in many parts of the world.[1] With the application of computed tomography (CT) to lung cancer screening, sub-centimeter pulmonary nodules are frequently detected.[2,3] A recent clinical trial has demonstrated the efficacy of low-dose CT screening for high-risk individuals, potentially increasing the expected detection rate of early-stage lung cancer.[4] Early diagnosis of lung cancer can lead to more treatment options, less-invasive surgery, and a higher survival. In addition, minimally invasive surgery, including video-assisted thoracoscopic surgery (VATS), has been known to be ideal for resection of small nodules, because it results in minimal postoperative morbidity and mortality along with less pain and a better quality of life than with an open thoracotomy.[5,6] However, localizing the small-sized pulmonary nodules during VATS is challenging when no changes appear on visceral pleura.[7,8] Inadequate nodule localization may lead to prolonged operative time while searching for the nodule or result in conversion to an unplanned open thoracotomy.[7-9] Inadequate tumor margins increase local recurrence rates with the potential for microscopic spread of cancer cells from the surgical margin.[10,11] With the current shift toward minimally invasive surgery, intraoperative localization of small lung nodules has become a critical challenge. Preoperative localization techniques have been introduced as a method of improving the success rates of VATS and preventing unwanted thoracotomy.[7,8] Microcoil and hook wire have been used to localize the pulmonary nodules using the CT-guided percutaneous approach before surgery and are visualized by fluoroscopy and thoracoscopy during surgery.[9,12-17] The standard procedure at Toronto General Hospital for intraoperative localization of small-sized nodules is CT-guided metallic microcoil placement performed before VATS.[13-15] Preoperative CT-guided placement of a metallic object with intraoperative fluoroscopic assistance has become the prevalent method of localizing small pulmonary nodules and has been highly successful in localizing nodules, with success rates greater than 97%.[13-15] The microcoil is then visualized with fluoroscopy intraoperatively and resected together with the pulmonary nodule. However, the metal tag placement procedure requires a preoperative invasive procedure that can result in patient discomfort, and complications such as metal tag dislodgement, pneumothorax, and hemoptysis may occur. Furthermore, use of fluoroscopy makes intraoperative radiation exposure inevitable for both patients and operating room staff.

In a previous animal study, we demonstrated a novel near-infrared (NIR) thoracoscopic lung nodule localization technique using injection of fluorescent indocyanine green (ICG).[18] We have been working on the translation of the novel technique into a clinical setting. The purpose of the current study is to determine the feasibility and safety of ICG fluorescence localization for resection of small pulmonary nodules with a NIR fluorescence thoracoscope in a phase I feasibility study.

MATERIALS AND METHODS

Study Plan and Patient Groups

This prospective phase I clinical trial used ICG for ''off-label use'' as an intraparenchymal injection, and a Health Canada No Objection Letter was obtained (#9427-D2777-21C). An Investigational Testing Authorization–Class II was obtained (#219223) for the use of the near-infrared (NIR) fluorescence thoracoscope (Pinpoint System; Novadaq Technologies Inc, Mississauga, Ontario, Canada). This study was approved by the Institutional Review Board of the University Health Network, and all patients gave informed consent (REB #12-5454). The inclusion criteria for our phase I study (NCT02090660) were patients with undiagnosed peripheral

FIGURE 1. The guided therapeutic operating room equipped with image-based surgical navigation technologies, including the dual-source dual-energy CT scanner (Definition FLASH CT; Siemens, Washington, DC), robotic cone-beam CT (Artis Zeego, Siemens), endoscopy, and tracking/navigation systems.

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