Near-infrared imaging for complex thoracoscopic resections

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Introduction

Lobectomy by video-assisted thoracic surgery (VATS) is now considered as a standard in the treatment of early-stage lung cancer with equivalent oncologic outcome as open lobectomy (1). Consequently, the widespread practice of thoracoscopic procedures pushed surgeons to perform more extended and complex resections. The feasibility of pulmonary segmentectomy, pneumonectomy, sleeve or carinal resections by VATS has been demonstrated in expert centers (2-4). However, the clinical and oncologic safety of such procedures has yet to be established.

The intra-operatory use of imaging technologies may help to perform complex resections with better oncological control and to avoid technical failure. Near-infrared (NIR) imaging with indocyanine green (ICG) is widely used in surgery, including in thoracic surgery (5,6). The ICG is a water-soluble fluorescent dye that can be injected into the vein. In the blood stream ICG binds to plasma proteins. The ICG is excited by a laser light with a wavelength between 790 and 805 nm. ICG will then re-emit light with a precise wavelength of 835 nm, which can be detected by a dedicated camera. The vascularization and perfusion of any organ can thus be visualized. The half-life of the ICG in the blood stream is about 4 minutes and it is eliminated through the liver in about 15 minutes. The side effects of ICG such as anaphylactic shock, hypotension, tachycardia or dyspnea are rare (7).

In thoracic surgery, NIR imaging offers many possibilities to help the surgeon during complex resections by VATS. It allows to visualize the intersegmental plane (ISP) in segmentectomy, may identify the sentinel lymph node (SLN), assess the perfusion of bronchial and esophageal anastomoses, as well as the vascularization of muscle flaps.

We describe in this mini-review the different possibilities and the perspectives of NIR imaging in thoracoscopic surgery.

NIR imaging for thoracoscopic segmentectomy

Pulmonary segmentectomy is widely accepted as a safe and feasible technique for treatment of suspicious nodules, metastases or in early stage lung cancer ≤2 cm without nodal involvement (8,9). Segmentectomy by VATS remains technically challenging because of anatomical variations and the difficulty to identify the ISP. However, a precise anatomical resection allows to obtain a quality oncological resection. The use of NIR imaging with ICG for the identification of the ISP is well described during the last decade in experimental animal and human studies. It requires intravenous injection of ICG after the section of the arterial branch of the target segment, as described by Guigard *et al.* (10). The well-vascularized parenchyma then becomes fluorescent whereas the devascularized segment does not. Consequently, the boundaries between adjacent segments become visible and can be marked. The ISP is then divided using staplers.

The accuracy of NIR imaging to define the ISP is described by Misaki *et al.* (11). They demonstrated that the macroscopic marking of pulmonary segments with ICG is correlated with the microscopic findings. The effectiveness of the identification of the ISP by VATS with ICG varies from 85% to 95% (12-15). The collateral vascularization could explain that the identification of the ISP is not accurate in all cases. In our institutional series, NIR imaging resulted in a modification of the anatomical resection in 10% of patients (14). For example, devascularized parenchyma could be resected to avoid lung infarct or infection. Additional artery resections were performed if the angiography showed an inadequate margin or if the targeted segment was not completely devascularized. The ICG can be injected again if necessary to a maximum dose of 5 mg/kg. In conclusion, NIR imaging in VATS segmentectomy improves the quality of the anatomical resection.

Appropriate lymph node dissection (LND) is crucial to accurate lung cancer staging and for good oncological outcome. A preoperative positron emission tomography-computed tomography (PET-CT) alone is insufficient to determine the nodal staging. According to a Cochrane review, the sensitivity of the PET-CT was of 77.4% (95% CI: 65.3% to 86.1%) and the specificity was of 90.1% (95% CI: 85.3% to 93.5%) (16). Therefore, the finding of postoperative unexpected nodal involvement is reported in up to 25% of patients undergoing lobectomy. Nodal upstaging even became a quality marker of a well-performed LND. Nodal staging is also critical during segmentectomy. In fact, identification of lymph node involvement during the intervention might affect the extent of the resection and lead to perform a lobectomy rather than segmentectomy. Thus, intraoperative frozen section analysis of removed lymph nodes during segmentectomy has been advocated (17). In many centers however, it is not possible or at least too time consuming to perform several a frozen section on all lymph nodes. On the other hand, if only one or two lymph nodes can be sent, it is not obvious which one should be tested. Therefore, the identification of the SLN would be extremely useful in VATS segmentectomy. But the role of this concept in lung surgery has yet to be explored and to be established

Nevertheless, NIR image-guided SLN with intraoperative peri-tumoral ICG injection is described by Ito *et al.* (18). The success rate of SLN identification varies from 80.3% to 89% and seems to depend on the ICG dose (19). According to Gilmore *et al.*, 100% of SLNs were detected if 1,000 µg of ICG or greater was injected, dissolved in human serum albumin (20). In this study, in patients with an identification of SLNs, the false-negative rate was of 0%. Interestingly, 27% of patients had positive N2-nodes only confirming the effectiveness of NIR imaging to identify skip metastasis.

NIR imaging during VATS segmentectomy is helpful for the identification of the ISP and might allow to identify the SLN. It could thus improve the quality of oncological resections. However, the impact of these procedures on patient survival is not established.

NIR imaging for thoracoscopic esophagectomy

As compared to open esophagectomy, minimally invasive esophagectomy is considered safe with equivalent oncologic outcome at 3 years (21). However, anastomotic leakage (AL) after esophagectomy remains an important factor of morbidity and mortality. The prevalence of AL varies from 5% to 25% (22-24). In colorectal surgery, NIR imaging with ICG allows to assess the vascular supply of gastrointestinal anastomoses and is associated with improved anastomotic healing (25). Similarly, Ohi *et al.* reported 120 patients undergoing esophagectomy, 72.5% of whom had a minimally invasive approach. They showed a reduction of postoperative AL from 14.7% in the non-ICG group to 1.7% in the ICG group (26). They demonstrated that the absence of NIR imaging was an independent risk factor for postoperative AL with a hazard ratio of 9.07 (P=0.0098). Knowing that AL has a negative impact on long-term survival, NIR imaging could decrease early and late mortality after esophagectomy. Observational studies are now necessary to evaluate the impact in long term of NIR imaging in esophageal cancer.

The use of ICG for lymphadenectomy in esophageal cancer is described in three studies (27-29). The success rate of SLN identification varies from 60% to 100%. In the study of Yuasa *et al.*, one patient over four had a false-negative SLN (27). In the study of Schlottmann *et al.*, the SLN were correctly identified in all three patients who presented nodal involvement (29). Although the feasibility to detect SLN has been demonstrated, its usefulness has to be established.

Perspective of NIR imaging for reconstruction by VATS

Complex resections by VATS can be associated with complex reconstructions such as bronchoplasty. Although sleeve lobectomy is technically challenging by VATS, its feasibility is clearly demonstrated in several case series. Interestingly, no AL was reported, including in the largest case series with 38 patients (3). Nevertheless, the use of NIR imaging could help to assess the vascular supply of the bronchial anastomosis to avoid technical failure (30). However, at our knowledge, no study exists about the use of ICG in sleeve lobectomy.

More debatable in VATS procedures, the use of NIR imaging can be used to assess the muscle flap vascularization (31). Some authors reported extended parietal resections or pneumonectomy by VATS. Therefore, it is probably feasible to perform a pneumonectomy with a covered bronchial stump with intercostal flap by VATS. However, this technique seems to be far-fetched and useless as compared to an open technique.

In conclusion, NIR imaging in thoracoscopy could be helpful for resection and for reconstruction in complex procedures. However, the evidence of its benefit in short and long term has to be established with observational studies.

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Footnote

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

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