Review Comments

Comment 1: SLNs, NIRF, ICG - there is no decoding in the text, only in the abstract.
Reply 1: We have decoded SLNs, NIRF, ICG in the text. Please check the revised manuscript.

Comment 2: The text of the article does not indicate a method for searching for articles.
Reply 2: Electronic databases were systematically searched via MEDLINE/PubMed from inception to 1 August 2019. The following medical subject headings were searched: “indocyanine green (or ICG)” and “thoracic surgery”, “indocyanine green (or ICG)” and “pulmonary nodule”, “indocyanine green (or ICG)” and “pulmonary segment”, “indocyanine green (or ICG)” and “gastroesophageal anastomosis”, “indocyanine green (or ICG)” and “pulmonary bulla”, “indocyanine green (or ICG)” and “thoracic duct”, “indocyanine green (or ICG)” and “sentinel lymph node”. We almost select the latest 5-years literatures about ICG NIRF technology used in thoracic surgery to guarantee the advancement of our review paper. According to the reviewers, we add most significant articles in our manuscript.

Comment 3: ICG was initially used as a simple dye, not a fluorescent agent. And in
some of the cited works, a very large dose of ICG is used, which allows visualizing the
accumulation of the drug without any fluorescence. This should be noted especially.
Pulmonary nodule localization is a moot point. Better for liver cancer metastases, and
for primary cancer is bad. Very large doses up to 5 mg/kg (300 mg).

Reply 3: According to toxicity studies, 5.0 mg/kg ICG intravenous injection was quite
safe and permissible. (Fox IJ, Wood EH. Indocyanine green: physical and physiologic

In He’s study (He K, Zhou J, Yang F, et al. Near-infrared Intraoperative Imaging of
Thoracic Sympathetic Nerves: From Preclinical Study to Clinical Trial. Theranostics
2018; 8: 304-13.), for patients’ safety reasons, they referred to several studies in tumor
identification for pulmonary nodules and brain tumors and then chose the ICG
concentration of 5 mg/kg. These studies were:

Judy RP, Keating JJ, Dejesus EM, Jiang JX, Okusanya OT, Nie S, et al. Quantification
of tumor fluorescence during intraoperative optical cancer imaging. Sci Rep-Uk. 2015;
5: 16208.


Near-Infrared Optical Imaging Can Localize Gadolinium-Enhancing Gliomas During


Comment 4: The authors do not analyze the dose of injected ICG.

Reply 4: We have analyzed the dose of injected ICG in some sections, now we are adding the dose of injected ICG in other sections, please check in the manuscript.

Comment 5: Describing the shortcomings in determining the intersegmentary boundary when performing a segmentectomy, the author does not quite clearly describe the methodology for determining the intersegmentary boundary using fluorescence. The following is a description of the difference when using the method of one and two wavelengths. At the same time, it is not clear what the difference in methods is. Again, very large doses of 3.0 mg / kg -200 mg.

Reply 5: We added the methodology for determining the intersegmentary boundary using fluorescence in this section. In Kasai’s study, although the dose of ICG was very large, there were no perioperative or postoperative complications caused by infrared thoracoscopy with ICG when using either the 2-wavelength method or the 1-wavelength method.

Clinical application of ICG in determining the intersegmentary boundary can be divided into positive imaging and negative imaging. The positive imaging is ligating the
proximal artery of the target pulmonary segment and injecting ICG into the distal artery of the target pulmonary segment, then the target pulmonary segment shows fluorescence. Negative imaging is ligating the proximal artery of the target pulmonary segment and then injecting ICG into the central vein, so the lung tissue outside the target pulmonary segment shows fluorescence.

Kasai et al. ligated the dominant pulmonary artery and then observed the lung using an infrared thoracoscope after indocyanine green (ICG) intravenous injection. The 2-wavelength infrared thoracoscope irradiation and detection were conducted at 940 and 805 nm, respectively, and the images were projected based on the difference of the two reflected wavelengths. ICG absorbs 805 nm wavelength light, and the ICG distribution area appears blue against a white background. On the other hand, the 1-wavelength infrared thoracoscope irradiation and detection were conducted at 780 and 830 nm, respectively. The area stained with ICG shows fluorescence.

Comment 6: "Tracing sentinel lymph nodes - the choice of adjuvant therapy". Not this, but the need for lymph node dissection. 1 ml of ICG which concentration?

Reply 6: We have revised this section according to the comment. Sentinel lymph nodes (SLNs) dissection has become an integral part of the scale of LNs dissection for solid malignancies (such as breast cancer, malignant melanoma, etc.). Gilmore et al. assessed the safety and feasibility of NIR imaging using ICG (3.8 μg) for SLN identification in NSCLC in 29 patients. After 5 to 20 minutes, the lymph nodes showed successfully.
Comment 7: The feasibility of determining bullas and nerve structures using green indocyanin is debatable.

Reply 7: Not more studies talk about the application of ICG in determining bullas and nerve structures, but these reports are in some famous journals (such as Ann Thorac Surg, J Thorac Cardiovasc Surg, Journal of Cardiothoracic Surgery) and showing ICG real-time fluorescein imaging technology can do helpful in these sections from animal model to the clinic. So we think using ICG to determine bullas and nerve structures is feasible.

Comment 8: Hardware features are not discussed in any way.

Reply 8: We add hardware features in the “Introduction”.

Comment 9: Are there any drawbacks to this technique?

Reply 9: There are some drawbacks of this technique. We have discussed in the manuscript.

Comment 10: The article describes many positive results of using indocyanin green, but issues requiring improvement are not raised for discussion. Perhaps the article lacks illustrative material. There are other articles that describe some sections more broadly.

Reply 10: Our article describes the application of indocyanin green in some sections, and we have added some issues of this technique in the manuscript.