Peer Review File

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Reviewer A

Comment 1: Goal: *In this study, we present a review of the clinical benefits of fluorescence imaging guided liver surgery and demonstrate some practical tips.* In general, they have reached their goal, but I miss their real tips.

Reply 1: According to the suggestion of reviewer 1 and reviewer 2, we inserted the following two sentences.

We inserted one sentence to page 6, line 18～page7,line 1 and to page 7, line3～5.

The optimal timing and dose of ICG administration for this use have not yet been proved. ICG administration on the day before surgery in patients with decreased liver function should be avoided to reduce incidence of false-positives and background liver fluorescence.

We inserted another sentence to page 9, line 15～17

In laparoscopic hepatectomy, we usually use a fluorescent imaging system to fuse images from the macroscopic view and the near-infrared ray view on a single monitor and the mode of monitoring could be switched with one button.

Comment 2: during analysis on hepatic tumors it is restricted to HCC, and worldwide use of ICG in metastases is not mentioned.

Reply 2:

We really appreciate important comments by the reviewer. According to the reviewer's suggestion, the following sentences were added in the revised manuscript.

page 6, line 12～13.

ICG fluorescence imaging system is worldwide used to detect hepatocellular carcinoma (HCC) and liver metastases,

page 6, line 15～16.

The ICG fluorescence pattern of HCC and liver metastases is different.

Comment 3: The use in laparoscopy and disadvantages are well mentioned, but preferably not in one paragraph.

Reply 3:

According to the reviewer's comment, the following sentence previously located in page 6, line 1～3 was moved to page 6 ,line 13～15.

this technique is especially useful for identifying subcapsular tumors during laparoscopic surgery because visual inspection and palpation of tumors are limited compared with open hepatectomy.

Comment 4：The use of ICG cholangiography for lap cholecystectomy can be mentioned in the introduction, but is not a real part of this article about liver surgery.

Reply 4:

According to the reviewer's suggestion, the following sentence previously located in page 7, line 3～6 was moved to page 5, line 69～89.

Recently, Lehrskov et al. reported that fluorescence cholangiography was comparable to X-ray fluoroscopic cholangiography in terms of visualization of the critical junction during laparoscopic cholecystectomy.

Comment 5: Skip the line on *Conventional indigo carmine injection*

Reply 5:

We thank the reviewer for the suggestion. The following sentence was deleted according to the reviewer's comment.

Conventional indigo carmine injection does not enable visualization of the intersegmental plane during the liver resection because the dye immediately disappears after injection

Comment 6: Replace fig 4b for a better one.

Reply 6:

We really appreciate the helpful comment. However, we thought the figure 4b suitable to demonstrate the usage of ICG during liver transection, and unfortunately no better photo was found for this aim.

Reviewer B

Detection of hepatic tumors

Comment 1: Please describe that the optimal timing and dose of ICG administration for this use have not yet been proved, and, basically, ICG administration on the day before surgery in patients with decreased liver function should be avoided to reduce incidence of false-positives and background liver fluorescence.

Reply 1:

We really appreciate the insightful comments by the reviewer. According to the suggestions of reviewer 1 and reviewer 2, we inserted the following sentences to page 6, line 18～page7,line 1 and to page 7, line3～5.

The optimal timing and dose of ICG administration for this use have not yet been proved. ICG administration on the day before surgery in patients with decreased liver function should be avoided to reduce incidence of false-positives and background liver fluorescence.

Comment 2: The authors should also comment on how to manage newly-detected lesions by fluorescence imaging. Because of the relatively-high incidence of false positives, additional resection of these lesions should be recommended only when the other diagnostic modalities (re-evaluation of preoperative images, especially MR imaging, palpation/visual inspection, and/or IOUS) also support a possibility of malignancy.

Reply 2:

According to the reviewer's comment, we inserted the sentence to page 7, line 18～page 8, line 3.

For this reason, additional resection of these lesions should be recommended only when the other diagnostic modalities (re-evaluation of preoperative images, especially MRI, palpation/visual inspection, and/or intraoperative ultrasonography) also support a possibility of malignancy.

ICG cholangiography

Comment 1: Fluorescence images of the bile ducts can be obtained not only by intravenous injection but also by intrabiliary direct injection of ICG solution (J Am Coll

Surg 2009;208:e1-4).

Reply 1:

According to the reviewer's comment, we inserted the following sentence to page 8, line 15～18, and added an article in the Reference.

Ishizawa et.al. reported intravenous injection of 2.5mg ICG can also provide with fluorescent images of biliary tract without cannulation of the bile duct.

Reference

Ishizawa T, Tamura S, Masuda K, et al. Intraoperative fluorescent cholangiography using indocyanine green: a biliary road map for safe surgery. J Am Coll Surg. 2009; 208:e1-4.

Comment 2: Regarding the former technique, a recent report of the international multicenter RCT (Ann Surg 2019;270:992-999.)

Reply 2:

According to the reviewer's comment, we inserted the sentence to page 8, line 13～15, and added an article in Reference.

In 2019, an international multicenter randomized trial proved that ICG cholangiography was superior to white light alone when visualizing extrahepatic biliary structures.

Reference

Dip F, LoMenzo E, Sarotto L, et al. Randomized Trial of Near-infrared Incisionless Fluorescent Cholangiography. Ann Surg. 2019;270:992-9.

Comment 3: Should also be introduced in this manuscript. Ref. 12 is not "Ann Surg" but "Arch Surg".

Reply 3:

We Corrected "Ann Surg" to "Arch Surg".

Visualization of hepatic segments

Comment 1: Please describe significance of "anatomic resection (segmentectomy)" in terms of oncology (resection of potential intrasegmental metastasis of HCC reducing a risk of postoperative recurrence).

Reply 1:

According to the reviewer's comment, we inserted the sentence to page 9, line 14～15, and added an article in Reference.

Anatomical resection is based on a theory to eradicate portal venous tumor extension and intrasegmental metastasis of HCC.

Reference

Zhong XP, Zhang YF, Mei J, et al. Anatomical versus Non-anatomical Resection for Hepatocellular Carcinoma with Microscope Vascular Invasion: A Propensity Score Matching Analysis. J Cancer. 2019;10:3950-7

Comment 2: Please describe technical aspects especially in laparoscopic settings.

Reply 2:

According to the comments of reviewer 1 and reviewer 2, we inserted the following sentence to page 9, line 15～17.

In laparoscopic hepatectomy, we usually use a fluorescent imaging system to fuse images from the macroscopic view and the near-infrared ray view on a single monitor and the mode of monitoring could be switched with one button.