Title: Usefulness of Colonic Tattooing using Indocyanine green in Patients with Colorectal tumors

Dear editor,

Thank you for meticulous review of our manuscript and valuable comments. The manuscript has been reviewed and appropriate changes have been made following the helpful comments of the reviewers. The following is the point-by-point response to the comments.

English

As our manuscript language quality evaluation is B, we have given AJE, one of the companies mentioned in " The Revision Policies of BPG for Article ", an English proofreading.

Reviewer A

Specific Comments to Authors: This is a well-written study on the use of ICG to mark colorectal cancer. However, it was already known in current literature that tattooing is useful in minimally invasive surgery. A comparative study with a control group of no-tattooing tumors could be useless. Otherwise an observational study on safety and efficacy of ICG could be useful.

As the reviewer says, the marking of the lesion in laparoscopic surgery of colon cancer is not a new topic. However, **most studies have used ICG in less than 40 patients, there is no comparative study of the effect of preoperative tattooing using ICG**. Furthermore, there are no studies that compared differences in tattooed and non-tattooed groups using ICG with regard to staging and the surgical methods.

As a limitation of the single-institute study, we did not compare tattooing methods using various agents, but we compared them with non-tattooing group to demonstrate their role as a tattooing agent of ICG.

Reviewer B

The paper is interesting and has merits to be accepted after minor revision. Minor concerns: Please check the spelling throughout the manuscript.

1. **In Abstract - Aim: I suggest that 'beneficial' to be replaced with 'feasible'.**

* After revision, the paragraph reads as follows:

4 page, "abstract" section of the manuscript

A) It has been replaced by the recommended word.

To prove that tattooing using indocyanine green (ICG) is feasible in laparoscopic surgery of colon tumor.

2. **In Abstract - results: delta should be explained. The difference for Hb and Alb is not 'little' in my opinion.**

4 page, "abstract: methods" section of the manuscript

A1) We explained delta in methods section.

* After revision, the paragraph reads as follows:

"Between the groups, the changes in (Delta (Δ), preoperative - postoperative) the hemoglobin and albumin levels, operation time, hospital stay, oral ingestion period, transfusion, and perioperative complications were compared."

4 page, "abstract: results" section of the manuscript

A2) we removed the word "little"

Δ Hemoglobin (*0.78±0.76 vs. 2.2±1.18*g/dL, *P <0.001*) and Δ albumin (0.41±0.44 vs. 1.08±0.39g/dL, P <0.001) levels in the TG showed little difference.

* After revision, the paragraph reads as follows:

The Δ hemoglobin (0.78±0.76 vs. 2.2±1.18g/dL, P <0.01) and Δ albumin (0.41±0.44 vs. 1.08±0.39 g/dL, P <0.01) levels were lower in the TG. ~~(showed little difference.)~~

3. **How can be explained the difference in Albumin? If not, please remove from abstract, and discuss it in Discussions.**

A) We removed the words and revised some sentence in discussion.

4 page, "abstract: results" section of the manuscript

Δ Hemoglobin (*0.78±0.76 vs. 2.2±1.18*g/dL, *P <0.001*) and Δ albumin (0.41±0.44 vs. 1.08±0.39g/dL, P <0.001) levels in the TG. ~~(showed little difference.)~~

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The Δ hemoglobin (0.78±0.76 vs. 2.2±1.18g/dL, P <0.01) and Δ albumin (0.41±0.44 vs. 1.08±0.39 g/dL, P <0.01) levels were lower in the TG. ~~(showed little difference.)~~

13 page, "Discussion" section of the manuscript

Statistical analysis showed that TG had a favorable effect, such as shortened operation time, decreased blood and albumin loss, fewer hospital days, and decreased complications in early stages of the tumor.

* After revision, the paragraph reads as follows:

Statistical analysis showed that TG had a favorable effect, such as shortened operation time, decreased blood and albumin loss, fewer hospital days, and decreased complications in the N0 tumor group of the tumor.

the ~~difference in~~ blood loss expressed by Delta Hb (0.78 ± 0.7 vs. 2.28 ± 1.1 g / dL, P <0.001) and Alb (0.34 ± 0.4 vs 1.10 ± 0.3 g / dL, P <0.001) respectively low.

* After revision, the paragraph reads as follows:

The blood loss expressed by Delta Hb (0.78 ± 0.7 vs. 2.28 ± 1.1 g / dL, P <0.001) and Alb (0.34 ± 0.4 vs 1.10 ± 0.3 g / dL, P <0.001) was low.

4. In Core tip: That ICG has fewer complications that India ink is not a conclusion from the present study. Please remove.

A) We removed the sentence.

5 page, "Core tip" section of the manuscript

As minimally invasive surgery becoming the main trend, endoscopic tattooing of colonic lesions became important. ~~Tattooing with ICG has~~

~~fewer complications than India ink.~~ Colonoscopic tattooing using ICG was performed in this study.

* After revision, the paragraph reads as follows:

As minimally invasive surgery becomes the main trend, endoscopic tattooing of colonic lesions became has become important. Colonoscopic tattooing using ICG was performed in this study.

5. **Division of Gastroenterology of the Internal Medicine Department, isn't it?**

2 page of the manuscript

Division of Gastroenterology, Department of Internal Medicine, Chungnam National University Hospital, Chungnam National University college of Medicine, Daejeon, South Korea

A) It is used as the official name of our hospital organization.

If it does not matter, we'd like to write it like above.

6. **In Methods: The two groups (stage 0, I, IIa, IIb, IIc) should be named as N0. In my opinion is not very correct as early stage versus advanced stage, as a T4N0M0 may be significant difficult to be resected laparoscopically.**

A) We have changed the name to 'N0 group' and 'N1 or N2 group'.

4 page, "Results" section of the manuscript

On comparison of patients with early and advanced cancer stages, early-stage colon cancer patients had better results for operation time, hospital stay, oral ingestion period, Δ hemoglobin, and Δ albumin than did advanced stage patients.

* After revision, the paragraph reads as follows:

On comparison of patients with in the 'N0' and 'N1 or N2' groups, the N0 colon cancer group had a better results for operation time, length of hospital stay, oral ingestion period, Δ hemoglobin, and Δ albumin results than those of did the N1 or N2 group.

4 page, "Conclusion" section of the manuscript

Preoperative tattooing with ICG is useful for laparoscopic colectomy, especially in

early-stage colon cancer and LAR.

* After revision, the paragraph reads as follows:

Preoperative tattooing with ICG is useful for laparoscopic colectomy, especially in the N0 colon cancer group and LAR.

5 page, "core tip" section of the manuscript

This resulted in a reduction in operation time, a reduction in blood loss, and a reduction in the number of hospital days in patients with early stage disease.

* After revision, the paragraph reads as follows:

Resulting in a reduction in the operation time, a reduction in blood loss, and a reduction in the number of hospital days in patients with in the N0 group.

7 page, "Methods" section of the manuscript

Tumor stage was determined according to AJCC 7th edition. Stage 0, I, IIa, IIb, IIc were classified as early stage (N0) and Stage IIIa, IIIb, IIIc as advanced stage (N1 or N2).

* After revision, the paragraph reads as follows:

Tumor stage was determined according to AJCC 7th edition. Stage 0, I, IIa, IIb, IIc were classified as the N0 group and Stage IIIa, IIIb, IIIc as the N1 or N2 group.

10 page, "Results" section of the manuscript

We compared the perioperative clinical data of the carcinoma group, except the adenoma group (n=41), by early and advanced group according to stage. (Table 3) The early stage group was defined as stage 0, I, IIa, IIb, IIc (n=239), and the advanced group was defined as IIIa, IIIb, IIIc (n = 62). The early stage group showed similar results to the whole group.

* After revision, the paragraph reads as follows:

We compared the perioperative clinical data of the carcinoma group, except the adenoma group (n=41), by 'N0' and 'N1 or N2' group according to stage. (Table 3) The N0 group was defined as stage 0, I, IIa, IIb, and IIc (n=239),

and the N1 or N2 group was defined as stage IIIa, IIIb, and IIIc (n = 62). The N0 group showed similar results as the whole group.

13 page, "Discussion" section of the manuscript

To compensate for the difference in the operation time due to lymph node dissection in the advanced stage, Stage 0, I, IIa, IIb, IIc were classified as early stage and Stage IIIa, IIIb, IIIc as advanced stage. The TG and NTG were compared in early stage and advanced stage, respectively. Statistical analysis showed that TG had a favorable effect, such as shortened operation time, decreased blood and albumin loss, fewer hospital days, and decreased complications in early stages of the tumor. This is because lesions with a small tumor size or those that are less invasion are not well recognized during laparoscopic surgery.

* After revision, the paragraph reads as follows:

To compensate for the difference in the operation time due to lymph node dissection in the advanced stage, Stage 0, I, IIa, and IIb, IIc were classified as the N0 group and Stage IIIa, IIIb, and IIIc as the N1 or N2 group. The TG and NTG were compared between the 'N0' and 'N1 or N2' group, respectively. Statistical analysis showed that TG had a favorable effect, such as shortened operation time, decreased blood and albumin loss, fewer hospital days, and decreased complications, in the N0 tumor. This is because lesions with a small tumor size or those that are less invasive are not well recognized during laparoscopic surgery.

14 page, "Discussion" section of the manuscript

Therefore, if tattooing is done within a reasonable time, preoperative tattooing with ICG is useful for laparoscopic colectomy, especially for early stage colon cancer and LAR.

* After revision, the paragraph reads as follows:

Therefore, if tattooing is done within a reasonable time, preoperative tattooing with ICG is useful for laparoscopic colectomy, especially for the N0 group of colon cancer and LAR.

16 page, "Research methods" section of the manuscript

To compensate for the difference in the operation time due to lymph node dissection in the advanced stage, lymph node positive and negative groups were compared.

* After revision, the paragraph reads as follows:

To compensate for the difference in the operation time due to lymph node dissection in the advanced stage, lymph node positive (N1 or N2) and negative (N0) groups were compared.

16 page, "Research conclusions" section of the manuscript

Tattooing using ICG is a simple and effective method with few complications and can be used in laparoscopic colon surgery. Especially in early stage colon cancer and LAR group.

* After revision, the paragraph reads as follows:

Tattooing using ICG is a simple and effective method with few complications and can be used in laparoscopic colon surgery. Especially in N0 colon cancer and LAR group.

25 page, "Table 3" section of the manuscript

Staging		**TG (N=102)**	**NTG (N=199)**	**P value**
Early (Stage 0 + I +IIa + IIb +IIc)	Operation time(minutes)	172.70 ± 48.87	190.34 ± 60.18	0.025
	Delta Hb	0.86 ± 0.79	2.16 ± 1.16	<0.001
(N = 239)	Delta Alb	0.40 ± 0.47	1.07 ± 0.39	<0.001
	Hospital stay (Days)	9.37 ± 2.91	11.53 ± 8.56	0.005
	Oral intake (Days)	1.49 ± 0.87	2.68 ± 1.16	<0.001
Advanced	Operation time (minutes)	177.91 ± 56.74	195.69 ± 64.59	0.278

(Stage IIIa +IIIb +IIIc)	Delta Hb	0.50 ± 0.71	2.05 ± 1.27	<0.001
(N = 62)	Delta Alb	0.39 ± 0.41	1.06 ± 0.41	<0.001
	Hospital stay (Days)	10.74 ± 5.00	12.23 ± 8.53	0.449
	Oral intake (Days)	1.83 ± 1.23	3.31 ± 3.62	0.064

* After revision, the paragraph reads as follows:

Staging		**TG (N=102)**	**NTG (N=199)**	**P value**
N0 group (Stage 0 + I +IIa + IIb +IIc)	Operation time(minutes)	172.70 ± 48.87	190.34 ± 60.18	0.025
	Delta Hb	0.86 ± 0.79	2.16 ± 1.16	<0.001
(N = 239)	Delta Alb	0.40 ± 0.47	1.07 ± 0.39	<0.001
	Hospital stay (Days)	9.37 ± 2.91	11.53 ± 8.56	0.005
	Oral intake (Days)	1.49 ± 0.87	2.68 ± 1.16	<0.001
N1 or N2 group	Operation time (minutes)	177.91 ± 56.74	195.69 ± 64.59	0.278
(Stage IIIa +IIIb +IIIc)	Delta Hb	0.50 ± 0.71	2.05 ± 1.27	<0.001

(N = 62)	Delta Alb	0.39 ± 0.41	1.06 ± 0.41	<0.001
	Hospital stay (Days)	10.74 ± 5.00	12.23 ± 8.53	0.449
	Oral intake (Days)	1.83 ± 1.23	3.31 ± 3.62	0.064

MEMO 1.

Please make duplication checking between this manuscript and the published articles by others and then revise the manuscript.

A) This manuscript has not been published (except in the form of an abstract or as part of a published lecture or academic thesis) or presented elsewhere in part or in entirety and is not under consideration by another journal.

MEMO 2.

Please rearrange all the authors' affiliations with Department, University or Institute, City, Postcode, Country, etc. (without any symbol or figure like * or 1, postcode must be there)

Such as: full name, address

A) It has been corrected.

MEMO 3.

Please distinguish between the title of the article series. Three levels of subtitles are allowed: (1) First subtitle: All in bold and capital; (2) Second subtitle: All in bold and italic; and (3) Third subtitle: All in bold.

A) I corrected the titles

MEMO 4.

Statistical significance is expressed as aP < 0.05, bP < 0.01 (P > 0.05 usually does not need to be denoted). If there are other series of P values, cP < 0.05 and dP < 0.01 are used, and a third series of P values is expressed as eP < 0.05 and fP < 0.01.

A) Except for the example of expressing no statistical significance (for example, p = 0.08) All values are edited.

MEMO 5.

Please check and confirm that there are no repeated references!

A) I confirmed it clearly.

We would like to express our appreciation to the reviewers and editor for spending time and effort to improve our manuscript. Your suggestions were valuable to help us strengthen our work.

Again, thank you for your consideration. I look forward to hearing from you.

Sincerely.