

Format for ANSWERING REVIEWERS

16th of August 2015

Dear Editor,

Please find enclosed the edited manuscript and a CD disk containing an electronic copy of the full-text manuscript in Word format (file name LakatosPLWJG2429 .doc).

Title: Comparison of percutaneous radiofrequency ablation and CyberKnife® for initial solitary hepatocellular carcinoma

Author: Kazue Shiozawa, Manabu Watanabe, Takashi Ikehara, Yasushi Matsukiyo, Michio Kogame, Yui Kishimoto, Yusuke Okubo, Hiroyuki Makino, Nobuhiro Tsukamoto, Yoshinori Igarashi, Yasukiyo Sumino

Manuscript No: 21312

The manuscript has been improved according to the suggestions of reviewers:

1. Format has been updated.
2. Revision has been made according to the suggestions of the reviewer.
3. We changed the title according to the reviewers.
4. We added Yusuke Okubo as one of authors with author contributions.

Reviewed by 00182833

1. Surely, there are small number of patients targeted for in this study. Therefore, we assumed this manuscript as a pilot study. We added 'A pilot study' in the title. Also we mentioned it as one of the limitations in the discussion.
2. We added the exclusion and inclusion criteria clearly from page 6 line 26 to page 7 line 2.
3. We've mentioned about heterogeneity of both group as one of the limitations in the discussion.
4. We mentioned the types of adverse event in the CK group at **Result adverse event** from page 11 line 11.
5. The cost performance of CyberKnife® is higher in approximately 2 times than RFA treatment in Japan. We mentioned about it in the **Discussion** (from page 15 line 29 to page 16 line 1) according to your suggestion.
6. We added the treatment for the recurrence at **Result outcomes** (from page 10 line 31 to page 11 line 6) according to your suggestion.

Reviewed by 03253495

1. Surely, follow-up time of this study is too short to determine an advantage of two treatments. We deleted Figure 3 and mentioned it as one of limitations on page 15 line 23 to 25. We added just 'A pilot study' in the title.
2. We cited the 2 papers you suggested in the discussion on page 13 line 29 and reference.
3. We've mentioned about heterogeneity of inclusion criteria of both group as one of the limitations in the discussion on page 15 line 19 to line 23.
4. We corrected the diagnostic criteria of HCC based on the new guidelines on AASLD and added the reference.
5. We corrected the definition of intrahepatic distant recurrence on page 9 line 10 to 13 according to your advice. After the correction, the patient number of intrahepatic distant recurrence was the same.
6. The median length of follow-up periods in the RFA and CK groups were 561 days and 379 days, respectively. We corrected from the mean to the median about the follow-up time on page 10 line 5 to 6, and we changed Table 1.

Reviewed by 03015689

- a) Surely, you are right. Therefore, we assumed this manuscript as a pilot study. We added 'A pilot study' in the title. Also we mentioned it as one of the limitations in the discussion.
- b) Unfortunately, if we describe the heterogeneous inclusion criteria of both groups in the abstract, the maximum number

of letters is exceeded. So we mentioned it in the text in detail.

c) 1. Surely, you are right. We mentioned the problem you suggested as one of limitations in discussion on page 15 line 22 to 23.

2. We agree with you. We've mentioned about heterogeneity of inclusion criteria of both group as one of the limitations in the discussion on page 15 line 19 to 21.

3, 4. We showed about small sample size on this study as limitation in the discussion.

5. We corrected the diagnostic criteria of HCC based on the new guidelines on AASLD according to your suggestion.

6. Surely, the radiological criterion for relapse can't be accurately obtained by echography only. We deleted gray-scale US for assessment of the recurrence on page 9.

7. The subjects were 73 patients with just initial solitary HCC (no previous HCC treatment), excluded comorbidity like serious or life-threatening disease.

8. You are right. But we think that it is easy to understand the present text.

d) 1. We mentioned the types of adverse event in the CK group in **Result adverse event**. Especially, we paid attention to Child-Pugh score after each treatment. We could not mention detail adverse events due to small number size.

2. We agree with you. Follow-up time of this study is too short to determine an advantage of two treatments. We deleted Figure 3 and mentioned it as one of limitations on page 15 line 23 to 25. We added just 'A pilot study' in the title.

e) You are absolutely right. However, we should focus on the efficacy, utility and adverse events of only CyberKnife® treatment for initial (primary) HCC, it is important to compare CyberKnife® with RFA in HCC algorithm (strategy) in the future. We think this study is important as a pilot study in future prospective study.

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

Kazue Shiozawa, MD, PhD
Division of Gastroenterology
and Hepatology, Department
of Internal Medicine,
Toho University Medical Center,
Omori Hospital
6-11-1, Omorinishi, Ota-ku,
Tokyo 143-8541, Japan
Fax: +81-3-3763-8542

Manabu Watanabe, MD, PhD
Division of Gastroenterology
and Hepatology, Department
of Internal Medicine
Toho University Medical Center,
Omori Hospital
6-11-1, Omorinishi, Ota-ku
Tokyo 143-8541, Japan
manabu62@med.toho-u.ac.jp