

Cover letter

Dr. Lian-Sheng Ma

President and Company Editor-in-Chief

World Journal of Radiology

March , 2014

Dear Dr. Ma,

We wish to submit our revised manuscript **entitled** “Incorporating GSA-SPECT into CT-based dose-volume histograms for advanced hepatocellular carcinoma radiotherapy” for consideration for publication as a Review in the *World Journal of Radiology*.

Author

Shintaro Shirai, Morio Sato, Yasutaka Noda, Yoshitaka Kumayama, Noritaka Shimizu

Name of Journal *World Journal of Radiology*

Manuscript NO: ESPS Manuscript NO: 8386

In accordance with the comment of the reviewers, the grammar and syntax of the manuscript have been checked by a native-English-speaking medical editor. A point-by-point response to the reviewer was conducted: the red sentences are the revised ones.

We revised the original title entitled “Utility of additional GSA-SPECT information to CT based dose volume histogram in the radiotherapy for advanced hepatocellular

carcinoma with liver cirrhosis” into the revised one in accordance with the requirements of 12 words of *World Journal of Radiology*.

1. This manuscript has been improved according to the suggestion of reviewers.

In accordance with the comment of the reviewers, the grammar and syntax of the manuscript have been checked by a native-English-speaking medical editor. A point-by-point response to the reviewer was conducted: the red sentences are the revised ones.

2. Revision has been made according to the suggestions of the reviewer.

Reviewer #1

The paper is of great interest as it depicts a new RT technique/planning for HCC treatment with good 2 years survival in advanced disease. Unfortunately, the paper results reader-unfriendly and necessitates a thorough language revision by a mother tongue, before it can be considered for review.

We wish to thank you for this comment. In accordance with the comment of the reviewers, the grammar and syntax of the manuscript have been checked by a native-English-speaking medical editor.

Reviewer #2

It is an interesting and useful study. However, there are issues with the way the manuscript has been composed. It will require improvement in grammar and sentence structures before it can be accepted.

We wish to thank you for this comment. In accordance with the comment of the reviewers, the grammar and syntax of the manuscript have been checked by a native-English-speaking medical editor.

Reviewer #3

#1 I was quite confusing the way the paragraphs were listed to build up the review. Why did the Authors begin with combination therapy with TACE instead of details of the technique.

Because this article is not an original article but an invited review article, we did not comply with a usual writing style. This review presents a summary of our experience of using GSA-SPECT for 3DRT of hepatocellular carcinoma.

#2 In my opinion, after the introduction, methods should follow and thereafter the results in HCC subpopulations should be listed. In addition I would be pleased to read more about clinical selection of these patients; for example were the patient excluded from systemic therapy with Sorafenib and why? More information about costs would be welcome

This article was documented from a view point of radiation oncologist who provides three-dimensional radiotherapy to HCC with portal tumor thrombus (PVTT). We emphasized the concept of functional liver for radiotherapy to prevent adverse effects. All the patients were asked to provide radiotherapy from surgeon and/or hepatologists because of the presence of PVTT. The administration of Sorafenib was limited to liver function of Child-Pugh A classification and the cost of Sorafenib, approximately 6000 dollars per month compels the financial burden to the patients. Surgical hepatic lobectomy was not scheduled because of the presence of intrahepatic metastatic in the other lobe. Namely, treatment of surgery and internal medicine were out of indication for medical and social reasons. We added the following sentences in the text.

“All the patients in this series were asked to provide radiotherapy from surgeon and/or hepatologists because of the presence of PVTT. The administration of

Sorafenib was limited to liver function of Child-Pugh A classification and the cost of Sorafenib, approximately 6000 dollars per month compels the financial burden to the patients. Surgical hepatic lobectomy was not scheduled because of the presence of intrahepatic metastatic in the other lobe. Namely, treatment of surgery and internal medicine were out of indication for medical and social reasons.”

#3 Another unclear poin: how many patients in each HCC subgroup have been treated with this method?

The patient number of HCC subgroup of HCC > 14cm, HCC 5-14 cm and < 5 cm was documented in the text as follows.

“In 12 patients who received SPECT-B-3DCRT, the local tumor control rate was 78.6% and the 2-year survival rate was 33.3%, without serious adverse effects (Figure 5).”

“We treated 26 patients with HCCs of 5-14 cm with PVTT, leading to the control rate 92.2 % of the PVTT and, 1-year and 2-year survival rate of 44.4 % and 30 %, respectively [10].”

“Regrettably, we encountered no patient with HCC < 5 cm with PVTT [10, 11]. Then, we described the content of radiotherapy for HCC < 5cm with referring the other manuscripts.”

3.References and typesetting were confirmed to be correct.

We deeply appreciate your offer for publishing this article in the *World Journal of Radiology*.

Yours sincerely,

Morio Sato MD

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