November 12, 2021

Dr. Dennis A Bloomfield
Editor-in-Chief
World Journal of Clinical Cases

Dear Dr. Bloomfield:

Thank you very much for inviting us to resubmit our manuscript, '**Two cases of hepatocellular carcinoma effective stereotactic body radiotherapy using Gold Anchor and the Synchrony system: A case report** (Manuscript No:71627).' The reviewers and editor provided excellent suggestions and guidance, and we have revised the manuscript accordingly. We believe that the reviewers' suggestions have helped us to substantially improve the quality of the manuscript.
We sincerely hope that the reviewers' and editors' concerns have been sufficiently addressed and would like to request that the revised manuscript again be considered for publication in the *World Journal of Clinical Cases*.

Respectfully yours,

Sakue Masuda, MD
Department of Gastroenterology
Shonan Kamakura General Hospital
1370-1 Okamoto, Kamakura, Kanagawa 247-8533, Japan
Email: sakue.masuda@tokushukai.jp

RESPONSE TO REVIEWER #1:

I would like to congratulate the authors on this manuscript which is well written and quite topical. Some minor comments about language editing

1. Page 8 line 2-3 "The contrast stained the HCC in early phase and washed out in the late phase" should be changes to 'contrast-enhanced'
2. Page14 Line 24: "invasive, highly accurate, and can deliver a large dose to HCC". Suggest adding "of radiation" so that the line reads invasive, highly accurate, and can deliver a large dose of radiation to HCC. 3.

Response: Thank you for raising these issues. We have made the required corrections.

RESPONSE TO REVIEWER #2:

Briefly: The authors presented two patients (1 patient with alcoholic liver disease and the other is HBV related liver disease) with hepatocellular carcinoma who had received multimodality treatment but soon had an elevation in PIVKA II levels. Gold anchor is a marker for determining the fine margins of the tumor and it guides stereotactic body radiation. Both cases had complete response to the treatment. The manuscript is well written and the flow of logic is perfect. I believe it will contribute to the literature,

Response: Thank you very much for your commendation.

RESPONSE TO REVIEWER #3:

This article report that 2 patients with liver cancer who were difficult to control by surgical resection, radiofrequency ablation, TACE and radiochemotherapy have achieved satisfactory clinical results using SBRT combined with GA and Synchrony system treatment, This has a positive guiding role in exploring new radiotherapy programs for liver cancer, and also provides clinical support for radiotherapy to become the fourth local therapy for HCC.

1. The description of the research background is not sufficient. Therefore, it is recommended to supplement the application status of SBRT.

Response: Thank you for your suggestion. We have accordingly added the following text to page 5 (lines 8–9):

"However, with SBRT, it can be difficult to track tumors in the liver due to respiratory motion management (RMM)[8]. SBRT with RMM is becoming more common; however, RMM is often performed with breath-holding or fixation of the trunk. For a more focused and accurate delivery of SBRT, fiducial markers are used to locate a tumor in the liver[9]."

It is now common practice to use SBRT rather than conventional RT for HCC in hospitals where SBRT is available.
The indications for radiotherapy in HCC guidelines are not standardized. The reasons for the use of RT in the present cases had been described on page 9 (line 29) – page 10 (line 3) as follows:

The reason for choosing radiotherapy in our cases was that they showed local recurrence and were refractory to surgery, TACE, or chemotherapy; in addition, RFA was difficult because, in the first case, the recurrence was close to the inferior vena cava, whereas in the second case, it was close to the left branch of the portal vein.

2. It is recommended to briefly describe the specific conditions of the surviving lesions before SBRT treatment? Such as: quantity and size, etc.

Response: We have accordingly added the size of the HCC before SBRT treatment to page 6 (line 18) and page 8 (line 5).

3. The discussion part lacks in-depth analysis.
1) What is the definition of high dose? What is the basis for the use of radiation dose in the article?

Response: We have added the following text to page 10 (lines 5–8) to clarify these points:

"A large dose of radiation is typically defined as one over 2 Gy. SBRT delivers extremely precise high doses in a limited number of treatment fractions (usually 3-6 fractions at >5 Gy per fraction) over a treatment course of 1-2 wk[8]."

2) It is recommended to supplement related complications about the use of SBRT with GA and the Synchrony system for the treatment of liver cancer and analyze the causes.

Response: We have tried to make the complications part stand out. We have also added that Radixact itself has no specific complications. To this purpose, we have now added the following text to page 10 (lines 23–24):

"There are no complications specific to Radixact™, but specific complications associated with SBRT and GA should be considered."

GA complications are described on page 10 (line 24) – page 11 (line 12).
SBRT complications are described on page 11 (line 24) – page 12 (line 8).

3) What are the limitations of the treatment in this article?

Response: We have added the following text to page 15 (lines 6–9):

"As described above, SBRT with GA and the Synchrony system can be considered a useful fourth local therapy for HCC. However, the extent of irradiation is limited by the patients' liver function; in the literature, most patients treated with SBRT have Child-Pugh A disease and limited number of lesions (often <3 tumors) [32]."

4.It is recommended to follow up to observe the long-term efficacy of this 2 patients, such as survival time, whether recurrence within one year, etc.

Response: We have added the long-term follow-up findings in the 2 patients demonstrating the efficacy of treatment to page 7 (lines 1–2) and page 8 (lines 19–21).

5. Some of the cited documents are outdated, it is recommended to I cite recent literature.

Response: We have updated the list of references to address your concerns. Accordingly, reference 1, shown below, has been deleted, and reference 2 has been cited in its place on page 11 (line 29).

1 **Ingold JA,** Reed GB, Kaplan HS, Bagshaw MA. Radiation hepatitis. *Am J Roentgenol Radium Ther Nucl Med* 1965; **93:** 200-208 [PMID: 14243011]

2 **Chen CP**. Role of radiotherapy in the treatment of hepatocellular carcinoma. *J Clin Transl Hepatol* 2019; **7:** 183-190 [PMID: 31293919 PMCID: PMC6609847 DOI: 10.14218/JCTH.2018.00060]