
List of Responses

Dear Editors and Reviewers:

Thank you for your letter and for the reviewers' comments concerning our manuscript entitled "Efficacy and safety of CT-guided microwave ablation with fine needle assisted puncture positioning technique for hepatocellular carcinoma" (ID: 70902). Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches. We have studied comments carefully and have made correction which we hope meet with approval. Revised portion are marked in red in the paper. The grammar, spelling and other places modified by a native English-speaking editor are not marked in red. The main corrections in the paper and the responds to the reviewer's comments are as flowing:

Responds to the reviewer's comments:

Reviewer #1:

1. Please show the rationale for setting the cut-off value of AFP to 400 ng/mL.

Response: A recent study of 609 patients included in four randomized controlled trials showed that AFP, as a categorical variable with a cut-off value of 400 ng/ml, could be used as a predictor of the efficacy in advanced HCC (Regmi P, et al. Efficacy and safety of sorafenib plus hepatic arterial infusion chemotherapy for advanced hepatocellular carcinoma. *Surg Oncol.* 2021;39:101663). In another study that included 756 patients to evaluate the recurrence pattern after surgery, multivariate analysis showed that AFP, as a categorical variable with a cut-off value of 400 ng/ml,

was highly correlated with the risk of recurrence after surgery (Liang L, et al. Association of postoperative biomarker response with recurrence and survival in patients with hepatocellular carcinoma and high alpha-fetoprotein expressions (>400 ng/ml). *J Hepatocell Carcinoma*. 2021;8:103-118). In a recent retrospective study of 1490 patients with HCC, the treatment modalities were liver transplantation, RFA / PEI, TACE, sorafenib and best supportive care. The results showed that AFP with a cut-off value of 400 ng/ml had a significant impact on survival irrespective of treatment received (Bhatti ABH, et al. Clinical Profile and Treatment of Hepatocellular Carcinoma: A Single-Center Experience. *South Asian J Cancer*. 2021;10(2):76-80). Therefore, this study set the cut-off value of AFP variable to 400 ng/mL.

2. I think the CT image is upside down in Figure 3.

Response: First three sub-images in Figure 3 is a suite of image in a patient with HCC undergoing microwave ablation in prone position, in order to make the comparison more intuitive, the MRI image of follow-up is placed upside down.

3. How about the analysis of overall survival between two groups?

Response: In the last follow-up, only 6 of a total of 124 patients were dead, it is difficult to draw more reliable conclusions about overall survival. Considering the Reviewer's suggestion, we added the analysis of overall survival in the paragraph of *Survival and Recurrence Outcome*.

4. You mentioned "the FNP technique used in CT-guided MWA in the current study may improve outcomes in terms of LTP, RFS and procedure-related

complications for HCC, and FNP technique was independently associated with good LTP and RFS” . Can you say the same result in radiofrequency ablation for HCC?

Response: We conclude that FNP technology used in CT guided MWA may improve the prognosis of LTP, RFS and procedure- related complications for HCC. The conclusion is based on CT guided microwave ablation procedure. Therefore, the same conclusion may not be reached in radiofrequency ablation for HCC. In the discussion of this paper, it is mentioned that the microwave electrode needle will produce artifacts in CT scanning, which is different from our previous application of RFA, which is also one of the factors that prompted us to carry out this study. The fine needle without artifact in CT scanning as a mark is helpful to the reasonable MWA electrode needle placement.

Whether the same conclusion can be reached in radiofrequency ablation is an interesting topic. Although it is not the research content of this paper, it is very helpful for our future study.

Special thanks to you for your good comments.

Reviewer #2: This is a well-conducted and well-reported retrospective study comparing FNP technique and conventional puncture technique in CT-guided MWA. In my opinion results are interesting and deserve publication. One general comment: the Introduction and the Discussion can be seen as too long. can the Authors reconsider their length, and maybe shorten these sections a bit? very minor: reference #1, is it correct to cite an Erratum?

Response: We have made appropriately deleted the Introduction and the Discussion according to the Reviewer's comments.

Special thanks to you for your good comments.

Reviewer #3: The manuscript describes a useful technique during liver tumor ablation, used to mark a target under US guidance, akin to fiducial placement for SBRT. In challenging locations such as near diaphragm, this technique can help. However, I do not believe you could draw many conclusions from a comparative study, as ablation probe placement skill is largely operator dependent, location and lesion size play a major role. Ability to paralyze the patient under general anesthesia during lesion's targeting and most importantly the use of CT-fluoroscopy are not addressed by the manuscript.

Response: It is really true as Reviewer suggested that ablation probe placement skill is largely operator dependent, location and lesion size play a major role. Since the tumor size and location are comparable between the two groups at baseline, the difference of ablation skill proficiency of operators is very important,

Because the description of the proficiency of ablation technology of the two groups of patients in the manuscript is not clear enough, the impact of the researcher's operation level on the results in a single center study with a small sample has to be worrying. The operators of all TACE and MWA procedures were belong to the same attending physician team in this study, the two chief operators have been working together for more than 15 years, so the impact of the researcher's operation level on the results is little. Therefore, considering the Reviewer's suggestion, we add a

description of the operators in two groups with similar technical proficiency background in the fourth paragraph of the part of PATIENTS AND METHODS.

In this study, general anesthesia was not used in microwave ablation procedures, but only local anesthesia and analgesics was given. The patient is awake in microwave ablation procedures. So the ability to paralyze the patient was not evaluated. However, considering that the suggestions of reviewers are very helpful, we added that the patient is awake in microwave ablation procedures. Aconsidering to the Reviewer's suggestion, we added the use of CT-fluoroscopy in the paragraph of The Microwave Ablation Puncture Technique.

We tried our best to improve the manuscript and made some changes in the manuscript. These changes will not influence the content and framework of the paper. And we marked the major changes in red in revised paper.

We appreciate for Editors/Reviewers' warm work earnestly, and hope that the correction will meet with approval.

Once again, thank you very much for your comments and suggestions.

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April 15, 2022