

March 16, 2017

Dear editor,

Thank you so much for carefully reviewing our manuscript (ID: 33014). We found all of the reviewers' comments to be extremely important and helpful, and we have revised and updated our manuscript according to the comments and the Guidelines/Requirements.

Below is the point-by-point response to the reviewers' comments.

Review 1: "Two major points should need to be mention here: 1. How to adjust the liver volumetric evaluation before resection? 2. In the literatures, what about the lower limited ICG test and Child's classification can be accept for central lobe resection?"

Answer: We thank the reviewer's valuable suggestion. Liver function evaluation is very important for patients with HCC. We added discussion about liver function measurement and Indocyanine Green (ICG) clearance test in the section of "THREE-DEMENSIONAL (3D) IMAGING RECONSTRUCTION IN PREOPERATIVE EVALUATION". In previous reports, individual resection ranges can be selected according to tumor location and liver function, including central resection (removal of segments IV, V, and VIII), right anterior sectorectomy (removal of segments V and VIII), segment IV resection, caudate lobe resection, or non-anatomical resection. For patients without enough liver function reserve, central lobe resection is not commonly recommended.

Review 2: "In this article, the authors provided a comprehensive and updated review on the importance of centrally located HCC. Based on the functional

approach, this article meets the journal's scope in general. More importantly, the review article covers the shortage of updated review article of centrally located HCC, which will be broadly interesting to researchers this field. However, the manuscript is poorly written and the manuscript should be revised by a native speaker before publication.”

Answer: Thank you for your positive comments. The authors, Rao A., Vu V. and Xu L. are native speakers. They have critically reviewed and revised the manuscript substantially to polish the language.

Review 3: “Nice overview of the subject.”

Answer: Thank you for the positive comment.

Review 4: “This is a review article on Management of centrally located hepatocellular carcinoma. Although management of this disease is complex, this review article does not address all of the treatment options specially radiofrequency assisted resection. This manuscript does not add anything new to the exiting literature.”

Answer: Thank you for the reviewer’s valuable suggestion. Centrally located HCC is a special type of liver cancer. The management of centrally located HCC has evolved profoundly over the past years. This review focuses the recent development of the management of centrally located HCC, especially in recent five years. To reflect upon this main point, we searched through the related literatures again, and as suggested by the reviewer, we added the discussion about radiofrequency-assisted resection in the section of “SURGICAL DETERMINATION AND RESECTION MARGIN”. We also deleted some

obscure words and changed the title to “management of centrally located HCC: update 2016”.

Review 5: “The manuscript entitled Management of Centrally Located Hepatocellular Carcinoma: Development and Challenges by Wei-Bo Yu et al, is an interesting review. However there are problems with the language which need to be corrected.”

Answer: Thank you for the positive comments. The authors, Rao A., Vu V. and Xu L. are native speakers. They have critically reviewed and revised the manuscript substantially to improve English writing.

All changes are highlighted in the revised manuscript. Thank you very much for your consideration!

Sincerely yours,

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