

Dear Editor and Reviewers,

Thank you very much for your valuable comments and suggestions on our manuscript.

Enclosed, please find our copy of the revised manuscript entitled “Radiomics for the detection of microvascular invasion in hepatocellular carcinoma”. Amendments and changes were made as suggested by the previous reviewers. We hope the revised version will now be suitable for publication in the *World Journal of Gastroenterology*.

Our point-to-point response to the reviewers is enclosed in this letter.

We thank you for your continuing consideration and look forward to hearing from you soon.

Thank you and best regards,

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Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors:

The authors presented a review focusing on the topic: 'Radiomics for the detection of microvascular invasion in hepatocellular carcinoma'. MVI is a significant prognostic factor, carrying with potential clinical relevance. And a mount of evidence showed that radiomics is predictive of MVI status. Before publication, I suggest the author should still address some issues.

1.Title:Ok 2.Language: the paper needs further polish. Some confusing sentences hinder better understanding of this review. 3.I suggest the authors add several references of conventional imaging features for predicting MVI without using radiomics, such as MRI/CT/US. And please discuss the potential benefit of radiomics in comparison with conventional imaging modalities. 4. Also it would be helpful for authors to list a table encompassing significant literatures regarding radiomics for MVI prediction in each section. The table would be more concise and informative for readers to understand.

Response: *We thank the reviewer for their positive comments.*

-The manuscript has been revised and polished by a native English-speaking language editor, and the language certificate has been provided in PDF format. According to the reviewers' comments, we added several references of conventional imaging features for predicting MVI without using radiomics in the introduction part, and further introduced the potential benefits of radiomics. We have added corresponding contents and highlighted them in the article. Meanwhile, in Table 1, we list the significant literature regarding radiomics for MVI prediction in each section. Meanwhile, we have added a column of imaging modalities to show the corresponding sections more clearly.

Reviewer #2:

Scientific Quality: Grade A (Excellent)

Language Quality: Grade A (Priority publishing)

Conclusion: Minor revision

Specific Comments to Authors:

As previously reported, microvascular invasion (MVI) is closely related to recurrence in postoperative HCC and is a major topic in the HCC treatment setting. MVI is assessed primarily through pathological and immunohistochemical analysis of postoperative tissue samples being needle biopsy the only method to accurately confirm the diagnosis before surgery but it is limited by suboptimal sensitivity since biopsy may cause false negatives. In this interesting review, the authors addressed radiomics as non-invasive tool to preoperative predict HCC-MVI status by delineating the tumor and or a certain distance from the surface of tumor to extracting features. They discuss the application of radiomics based on various imaging modalities in preoperative evaluation of HCC-MVI and explores the future research directions for facilitate the clinical translation of radiomics. The review is of interest and of current clinical relevance. However, in my opinion some important literature data are lacking and should be discussed to improve the clinical significance.

-MRI-BASED RADIOMICS: the authors stated that "MRI provides many additional imaging sequences that are helpful in the diagnosis of HCC " and that "and enhanced scan by combined use of some extracellular and hepatocyte contrast agents, such as gadoxetic-acid that has the ability to distinguish relatively small and subtle lesions through low signal in the hepatobiliary stage (HBP)". In this regard, it would be useful to recall that a combination of MR parameters can be useful for the early diagnosis of small hepatocellular carcinoma (HCC). For example, it has previously reported that double hypointensity in the portal/venous and hepatobiliary phases can be

considered a MRI pattern, highly suggestive of hypovascular hepatocellular carcinoma (which is very difficult to diagnose by imaging) as previously reported (Impact of gadoxetic acid (Gd-EOB-DTPA)-enhanced magnetic resonance on the non-invasive diagnosis of small hepatocellular carcinoma: a prospective study. *Aliment Pharmacol Ther.* 2013;37(3):355-63). - Another topic worth mentioning is the difficult imaging characterization of recurrent HCC nodules due to the potential different imaging features of recurrent nodules. It is well known that in cirrhosis primary and recurrent nodules (10-30 mm nodules after a previously treated hepatocellular carcinoma) may display variations in enhancement pattern, as previously reported (Characterization of primary and recurrent nodules in liver cirrhosis using contrast-enhanced ultrasound: Which vascular criteria should be adopted? *Ultraschall in der Medizin* 2013;34:280-287). The authors should discuss that, in this setting, radiomics may be useful to better characterize recurrent nodules. - A last point I would suggest to discuss is the potential role in the differential diagnosis of liver nodules in patients with chronic liver diseases (thank to additional imaging parameters), for example in distinguish some difficult-to-characterize focal liver lesion such as macronodular hepatic tuberculosis which can be misdiagnosed as HCC according to only LI-RADS criteria as recently reported (Contrast-enhanced ultrasound LI-RADS LR-5 in hepatic tuberculosis: Case report and literature review of imaging features; *Gastroenterology Insights* 2021; Volume 12, Issue 117; Yang C, Liu X, Ling W, Song B, Liu F. Primary isolated hepatic tuberculosis mimicking small hepatocellular carcinoma. *Medicine* 2020;99:e22580).

Response: *We thank the reviewer for their positive comments.*

-As the reviewer said, the combination of MRI multi parameters can contribute to the early diagnosis of small HCC. Similar to multiple sequences, radiomics based on MRI with multiple sequences and parameters can provide more possibilities for the prediction of MVI. We have revised and highlighted it in the MRI-BASED

RADIOMICS section. Indeed, the imaging manifestations of liver nodules in patients with chronic liver disease are complex and diverse, such as primary and recurrent nodules of liver cirrhosis and tuberculous nodules. We believe through collecting a large number of targeted nodules (specific and various nodules) and based on radiomics, these nodules would be predicted and identified. We have revised and highlighted it in the future direction section.

EDITORIAL OFFICE'S COMMENTS

Authors must revise the manuscript according to the Editorial Office's comments and suggestions, which are listed below:

(1) Science editor:

- to address all the points raised by the reviewers.

Language Quality: Grade B (Minor language polishing)

Scientific Quality: Transfer to another BPG Journal

Response: *We thank the editor for comments of our manuscript.*

-We have revised the paper according to the points raised by the reviewers, and the manuscript has been polished by a native English-speaking language editor. We hope the revised version will now be suitable for publication in the World Journal of Gastroenterology, and we do not consider other journals.

(2) Company editor-in-chief:

I have reviewed the Peer-Review Report, the full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Gastroenterology, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its

revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors. Please provide decomposable Figures (in which all components are movable and editable), organize them into a single PowerPoint file. Please authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content.

Response: *We thank the editor for positive comments of our manuscript.*

-We have provided the figures in the PPT file and standard three-line tables according to the suggestions of the Editor. In addition, the text has been amended according to the Editor's suggestions and corresponding requirements of the journal, and all the revisions made have been highlighted in the final version of the manuscript.