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PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 74196

Title: Radiomic Analysis Based on Multi-phase MRI to Predict Preoperatively Microvascular Invasion in Hepatocellular Carcinoma

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05497413
Position: Peer Reviewer
Academic degree: PhD
Professional title: Academic Research
Reviewer's Country/Territory: New Zealand
Author's Country/Territory: China

Manuscript submission date: 2021-12-24

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-12-25 15:40

Reviewer performed review: 2022-01-04 10:23

Review time: 9 Days and 18 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[ ] Yes [Y] No

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Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Yueming Li et al. developed a radiomic analysis model based on preoperative magnetic resonance imaging (MRI) data to predict MVI in HCC. The overall research is relatively complete, but I have a few questions that I would like to discuss with the author. 1. In other articles, the identification methods of most independent predictors are univariate and multivariate COX regression analysis, and the author uses univariate and multivariate logistic regression analysis to identify. I hope the author can explain the advantages of using logistic regression analysis. 2. The description of the method part is not specific, and the reader cannot repeat it completely. 3. The author uses R software, but the specific method and R package are not cited. 4. The results of independent prognostic factors should be visualized with pictures. 5. The results of the 5-fold cross-validation should also be displayed with pictures. 6. The author only constructed a model based on 113 patients. The model was not verified by external independent data. I am very worried about its accuracy and whether it can be applied to all patients. 7. Part of the picture results can be merged, instead of putting a small picture in a whole figure. 8. The language part of the article still needs some polishing.

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Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03739641
Position: Editorial Board
Academic degree: PhD
Professional title: Nurse, Professor
Reviewer's Country/Territory: Japan
Author's Country/Territory: China

Manuscript submission date: 2021-12-24

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-01-19 01:00

Reviewer performed review: 2022-01-23 09:24

Review time: 4 Days and 8 Hours

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [Y] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Re-review	[ ] Yes [Y] No

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Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

I am applicated to review your valuable manuscript. I hope that some comments may be helpful to improve your manuscript. Your sample size was 113 including 73 MVI (+) cases and 40 MVI (-) cases. In such case, only seven variables allow to enter to multivariate logistic analysis to detect the risk factor to MVI (+) which may contribute to worse disease-free survival for cases. Readers may be understandable if you add logical explanation about your multivariate analysis process. Thank you and best regards.

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Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03699961
Position: Associate Editor
Academic degree: MD, PhD
Professional title: Professor
Reviewer's Country/Territory: Japan
Author's Country/Territory: China

Manuscript submission date: 2021-12-24

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-01-19 13:58

Reviewer performed review: 2022-01-24 14:54

Review time: 5 Days

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [Y] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No

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Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Title: Radiomic Analysis Based on Multi-phase MRI to Predict Preoperatively Microvascular Invasion in Hepatocellular Carcinoma. Yueming Li, Yuemin Zhu, Lanmei Gao, et al. 1) General Comments In this manuscript, the authors aimed to show the higher accuracy of an algorithm using most discriminant factors (MDF), which are created by image texture analysis using MaZda software as 101 features and are statistically refined into 30 features, in prediction of microvascular invasion (MVI) comparing with a regular image diagnosis by radiologists. Basically, this manuscript is consisting of statistical analyses and MRI images. The statistical methods should be described in detail. The MRI images should be presented to show the usefulness of MDF. The followings are several concerns that the authors may wish to consider: 2) Specific comments Major concerns: 1. In Radiomic analysis of Methods section, the authors described that the useful features were selected among 101 features in each sequence using algorithms, i.e., mutual information (MI), Fisher coefficient (Fisher) and classification error probability, which was combined with average correlation coefficients (POE + ACC and PA). These combinations led to the 30 highest discriminative power features in each sequence for further analysis. It is difficult, however, how the authors selected the 30 highest discriminants and calculated a probability from the 30 discriminants in combination. What is the POE + ACC and PA? Please explain the methods in detail and discuss what are expected to be the major determinants of MVI from the point of MDF. 2. Histogram features are included in the 101 features that were used to develop MDF consisting of 30 features. Why were histogram features separately subjected for the validation study? Please describe the

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reason to pick up histogram features. Furthermore, it would be helpful to understand the effect of MDF on the prediction of MVI that the authors present MRI images at AP and PVP for the cases with MVI+ and MVI-, which show similar histogram features but different MDF. 3. The major purpose of this study is to show the higher accuracy of an algorithm using MDF in prediction of MVI comparing with a regular image diagnosis by radiologists. I believe that histogram features are considered to be what radiologists get from the information to reach their diagnosis. However, I am not sure that histogram features actually involve the information just enough for the diagnosis by radiologists. The efficacy of the algorithm should be directly compared with the diagnosis that was made by radiologists. Minor concerns: 1.In image analyses, the largest cross-sectional area was evaluated for MVI. Then, which section was evaluated in histology for MVI?

2. Original T2WI should be presented without the coloration showing ROI.

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RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 74196

Title: Radiomic Analysis Based on Multi-phase MRI to Predict Preoperatively Microvascular Invasion in Hepatocellular Carcinoma

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03699961

Position: Associate Editor

Academic degree: MD, PhD

Professional title: Professor

Reviewer's Country/Territory: Japan

Author's Country/Territory: China

Manuscript submission date: 2021-12-24

Reviewer chosen by: Jia-Ru Fan

Reviewer accepted review: 2022-03-25 23:53

Reviewer performed review: 2022-03-26 07:33

Review time: 7 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [Y] Major revision [ ] Rejection
Peer-reviewer	Peer-Review: [Y] Anonymous [ ] Onymous

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statements	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Title: Effects of Targeted-edited Oncogenic IGF-1R with Specific-sgRNA on Biological Behaviors of HepG2 Cells. Min Yao, Yin Cai, Zhi-Jun Wu, et al. 1) General Comments In this manuscript, the authors explored the expressions of insulin-like growth factor-1 receptor (IGF-1R) and P-glycoprotein (P-gp) in hepatocellular carcinoma (HCC), surrounding liver tissues, and sera to show the important biological roles in hepatocarcinogenesis, HCC progression, and therapeutic managements. After editing the target sequence using Crispr/Cas9 system, cell proliferation, apoptosis, cell cycle arrest, migration, and invasion were quantitatively evaluated in a hepatoma cell line. Furthermore, the synergistic effects on cell growth of the IGF-1R editing and anti-cancer agents were investigated. Although the strategies were straightforward, data presentation is insufficient. Novel evidence is scarce. There is no direct evidence suggesting the conclusion that IGF-1R gene is a potential modulator to reverse multidrug resistance (MDR) in HCC cells. The followings are several concerns that the authors may wish to consider: 2) Specific comments Major concerns: 1. Because the crucial roles of IGF-1R in hepatocarcinogenesis, HCC progression, and therapeutic managements have been reported as the authors mentioned, all the results presented in this manuscript are similar with the evidence that have been reported in the literature except for the synergistic effects on cell growth of the IGF-1R editing and anti-cancer agents. Although the authors expected that the synergistic growth inhibitory effects are achieved by reversing MDR character of HCC specifically through the function of P-gp, there is no direct evidence suggesting a molecular link neither between IGF-1R and MDR nor between IGF-1R and P-gp. Without the direct evidence suggesting two molecules, it is difficult to draw the conclusion. 2. In comparisons among three or

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more groups, I believe the authors would perform statistics using ANOVA first and follow post hoc tests to see the probabilities in a specific combination. Unfortunately, however, there are no explanation for post hoc test. Only one probability is presented and is unclear if it is for ANOVA or for one of specific combinations. Furthermore, the chi-square values and probabilities are not consistent with my calculation. For example, "Differentiation Group" of IGF-1R in Table 2 shows chi-square value of 4.699 and probability of 0.030, which are calculated as 7.131 and 0.0076, respectively, using GraphPad Prism 8 software. In addition, TNM stage and other factors such as tumor size and number are confounding each other. They should not be analyzed together. In summary, statistical methods and results should be checked again and presented more precisely. Minor concerns: 1. Many typos, poor English expressions, careless mistakes of referencing, and so on. Carefully rewrite and edit English. 2. In "Editing IGF-IR with cell proliferation inhibition" paragraph of Result section, the relative ratio of IGF-1R to β-actin expression of Western bolting in the control group was reported as 31.22 ± 0.13. Is it correct? 3. In "Effects of edited IGF-IR on the biological features of HepG2 cells" paragraph of Result section, the actual numbers of apoptotic cells should be described. 4. There is not description for Figure 3C at all. 5. In "Synergistic effect of sgRNA with anti-cancer drugs" paragraph of Result section, the corresponding table should not be Table 3. It should be Table 4.