

**Dear Professor Lian-Sheng Ma,**  
**Founder and Chief Executive Officer,**

On behalf of co-authors, we thank you very much for considering a revised version of our manuscript “A Radiomics Model Based on Preoperative Gadoteric Acid-Enhanced MRI for Predicting Liver Failure” (Manuscript ID: 51459), which we wish to be considered for publication in *World Journal of Gastroenterology*. We thank the reviewers for the kind comments and suggestions. We have thoroughly corrected the manuscript based on editor and reviewers’ comments. As below, we listed the changes, and provided point-by-point responses to the comments. The changes we made to the text are highlighted in red.

We do hope that the revised manuscript can be judged as acceptable for publication in *World Journal of Gastroenterology*. If any more responses are considered to be necessary, please let me know.

Looking forward to hearing from you soon.

Best regards,

Jun Shen

No. 107 Yanjiang Road West

Department of Radiology, Sun Yat-Sen Memorial Hospital

Sun Yat-Sen University,

Guangzhou, 510120

Guangdong, P.R.China

Telephone: (8620) 8133-2702

Fax: (8620) 8133-2702

E-mail: shenjun@mail.sysu.edu.cn

## Point-by-point Response

### Reply to reviewers

#### Comment 1 How significant or necessary is the addition of the ICG-15 measurement?

Response: Thank you for your comment. The ICG clearance test is a very important method to evaluate liver function in clinical daily work<sup>[1]</sup>. Our results also showed that ICG-R15 was an independent risk factors for liver failure. Combining ICG-R15 with radiomics signature achieved an AUC as high as 0.894 for predicting liver failure, which is significantly higher than that of radiomics signature alone. These results suggest the importance of ICG-R15, which we have mentioned in the Introduction and Discussion sections.

[1] Zipprich A, Kuss O, Rogowski S, Kleber G, Lotterer E, Seufferlein T, Fleig WE, Dollinger MM. Incorporating indocyanin green clearance into the Model for End Stage Liver Disease (MELD-ICG) improves prognostic accuracy in intermediate to advanced cirrhosis. *Gut* 2010; 59: 963-968.

#### Comment 2 What happened to the patients that developed postoperative liver failure?

**Also, was it a sustained type of liver failure or merely immediately postop?**

Response: We have added the prognosis of those patients who developed postoperative liver failure to the Results section. The added texts are highlighted in red.

*Revised manuscript* (page 11, line 1-3): “Among 15 patients with liver failure, 3 of them had a sustained type of liver failure and died, while 12 of them developed liver failure immediately after surgery and recovered after proper treatment.”

#### Comment 3 How do the authors propose to use their model in the clinical setting, ie what would it change in terms of the patients' treatment plan?

Response: Thanks for this comment. We believe that the radiomics model proposed in our study can be used as an alternative biomarker for preoperative liver function assessment. It can be used in combination with ICG-R15 to improve the ability to predict postoperative liver failure when surgery is planned for a cirrhotic patient with HCC. If there is a high risk of postoperative liver failure, some locoregional treatments including percutaneous ethanol injection (PEI), radiofrequency ablation (RFA), trans-arterial chemoembolization (TACE) and radioembolization rather than major hepatectomy would be applied for cirrhotic patients with HCC<sup>[2]</sup>. In addition, if a patient has uncertain results of ICG test, the radiomics model can be used alternatively to predict the risk of postoperative live failure. We have added this information to the Discussion section of revised manuscript. The added texts are highlighted in red.

[2] Bruix J, Sherman M. Management of hepatocellular carcinoma: an update. *Hepatology* 2011; 53: 1020-1022.

*Revised manuscript* (page 15, line 19-22, page 16, line 1-4): “For example, it can be used in combination with ICG-R15 to improve the ability to predict postoperative liver failure when surgery is planned for a cirrhotic patient with HCC. If there is a high risk of post-operative liver failure, major hepatectomy should be avoided and some locoregional treatments such as percutaneous ethanol injection, radiofrequency ablation, trans-arterial chemoembolization and radioembolization can be applied for this patient. In addition, if a patient has uncertain results of ICG test, such as a patient with severe jaundice, the radiomics model can be used alternatively to predict the risk of postoperative live failure<sup>[33]</sup>.”

**Comment 4 Have the authors compared their model with other models evaluating post operative hepatic failure?**

Response: Thanks for your comment. We have compared our model with several model reportedly previously. Amber. et al have used several texture features derived from preoperative CT images to predict postoperative liver failure, but it's a preliminary study incorporating simple statistics analysis<sup>[3]</sup>. Wimber. et al showed that the measurement of relative liver enhancement (RLE) on hepatobiliary phase images of gadoxetic acid-enhanced magnetic resonance (MR) imaging can allow preoperative assessment of the risk of liver failure after major liver resection with an AUC of 0.948<sup>[4]</sup>. However, they had a small number of patients with liver failure ( $n = 3$ ). We have added this information to the Discussion section of revised manuscript. The added texts are highlighted in red.

[3] Simpson AL, Adams LB, Allen PJ, et al. Texture analysis of preoperative CT images for prediction of postoperative hepatic insufficiency: a preliminary study. *J Am Coll Surg* 2015; 220: 339-346.

[4] Wibmer A, Prusa AM, Nolz R, Gruenberger T, Schindl M, Ba-Ssalamah A. Liver failure after major liver resection: risk assessment by using preoperative Gadoxetic acid-enhanced 3-T MR imaging. *Radiology* 2013; 269: 777-786.

*Revised manuscript* (page 15, line 6-14): "Previously, several texture features derived from preoperative CT images has also been proposed to predict postoperative liver failure<sup>[16]</sup>. However, this study has a small number of patients ( $n = 36$ ) and no predictive model was built<sup>[16]</sup>. In addition, the measurement of relative liver enhancement on hepatobiliary phase images of gadoxetic acid-enhanced magnetic resonance (MR) imaging has been shown to be able to preoperatively assess the risk of liver failure after major liver resection with an

AUC of 0.948<sup>[9]</sup>. However, only a small number of patients with liver failure ( $n = 3$ ) was included in this study. The value of relative liver enhancement should be further validated by a large cohort study.”