

## **Responses to Reviewer**

**Reviewer:** CA 19-9

**Response:** Thank you for your comment. I have corrected this error. The recommended revision was made on page 2, line 11.

**Reviewer:** Describe at first occurrence

**Response:** Thank you for your comment. I have changed DL radiomics to deep learning-based radiomics. The recommended revision was made on page 2, line 11.

**Reviewer:** AUC: Area under the ROC curve

**Response:** Thank you for your comment. I have changed area under the receiver to Area under the ROC curve.

**Reviewer:** Should highlight the comparison of 3 models for both entities, using AUC/c-indices:

1. ER - clinical vs radiomics vs clinical + radiomics
2. OS - clinical vs radiomics vs clinical + radiomics

**Response:** Thank you for your comment. The DL radiomics model for predicting ER showed satisfactory clinical benefits (AUC 0.819, 0.568 in the training and testing

cohorts), similar to clinical model (AUC 0.580, 0.520 in the training and testing cohorts,  $p > 0.05$ ). This is ER - clinical vs radiomics.

The clinical+DL radiomics model and the DL radiomics model outperformed the clinical model in the training and testing cohorts (all  $p < 0.001$ ). This is OS - clinical vs radiomics vs clinical + radiomics.

**Reviewer:** Need to be specific

**Response:** Thank you for your comment. I have rewritten the sentence. The DL radiomics model for predicting ER showed satisfactory clinical benefits (AUC 0.819, 0.568 in the training and testing cohorts), similar to clinical model (AUC 0.580, 0.520 in the training and testing cohorts,  $p > 0.05$ ). The recommended revision was made on page 3, line 10-12.

**Reviewer:** Add zero before decimal. 0.05

**Response:** Thank you for your comment. Thank you for your comment. I have rewritten the sentence. The DL radiomics model for predicting ER showed satisfactory clinical benefits (AUC 0.819, 0.568 in the training and testing cohorts), similar to clinical model (AUC 0.580, 0.520 in the training and testing cohorts,  $p > 0.05$ ). The recommended revision was made on page 3, line 10-12.

**Reviewer:** There are few, such as:

1. Ma QP, et al Dynamic contrast-enhanced ultrasound radiomics for hepatocellular carcinoma recurrence prediction after thermal ablation. *Molecular Imaging and Biology*. 2021 Aug;23(4):572-85.

2. Liu F, et al. Deep learning radiomics based on contrast-enhanced ultrasound might optimize curative treatments for very-early or early-stage hepatocellular carcinoma patients. *Liver Cancer*. 2020;9(4):397-413.

**Response:** Thank you for your comment. These articles were not indicated the postoperative recurrence and prognosis of HCC using DL radiomics with ultrasonographic and CEUS images. But in order not to be misunderstood, I deleted the sentence.

**Reviewer:** screened

**Response:** Thank you for your comment. I have changed recruited to screened. The recommended revision was made on page 6, line 1.

**Reviewer:** Full form?

**Response:** Thank you for your comment. Thank you for your comment. I have rewritten the sentence. World Federation for Ultrasound in Medicine and Biology (WFUMB)-European Federation of Societies for Ultrasound in Medicine and Biology

(EFSUMB) and CEUS Liver Imaging Reporting and Data System(LI-RADS) . The recommended revision was made on page 6, line 11-13.

**Reviewer:** Provide calibration graphs in supplementary material

**Response:** Thank you for your comment. Thank you for your comment, but the prognosis model does not have the calibration graphs.

**Reviewer:** Provide a list of radiomic features analyzed. Also provide a list of ranked features (could be provided in supplementary material).

**Response:** Thank you for your comment. Thank you for your comment, but deep learning-based radiomic feature is similar to black box, without specific features.

**Reviewer:** Different models

**Response:** Thank you for your comment. I have changed difference model to different model. The recommended revision was made on page 9, line 4.

**Reviewer:** which

**Response:** Thank you for your comment. I have changed whom to which. The recommended revision was made on page 9, line 16.

**Reviewer:** Add some of the basic demographics of full group like age/gender/commonest primary etiology here.

**Response:** Thank you for your comment. Mean age of 414 patients was 53.00 (45.00-60.00) years, 375(90.6) male. The recommended revision was made on page 9, line 17-18.

**Reviewer:** Does that mean arterial phase? Why not venous phase as venous washout is more characteristic of HCC, while arterial enhancement could be seen in regenerative nodules as well.

**Response:** Thank you for your comment. Thank you for your comments. Select peak contrast intensities of CEUS images for analysis in our study. Although venous washout is more characteristic of HCC, it is difficult to determine which frame is the most significant for venous washout, and it may become more washout with the extension of observation time.

**Reviewer:** Why there was significant drop in test cohort?

**Response:** Thanks for your comments, we tried to improve the accuracy in the test cohort, but the results were not ideal.

**Reviewer:** What does this mean?

**Response:** Thanks for your comments, it means satellite lesions of HCC.

**Reviewer:** Does that mean dependent and independent variables?

**Response:** Thanks for your comments, it means constant and dependent variable.

**Reviewer:** Below par

**Response:** Thanks for your comments, we tried to improve the accuracy in the test cohort, but the results were not ideal.

**Reviewer:** At time of resection? Were they part of resection or not? It is obvious if satellite nodules are left behind, one would have early recurrence of tumor. As such, the tumor was not completely cured by resection. Such patients should have been excluded.

**Response:** Thank you for your comment, we mean that the satellite lesion was found by ultrasound before resection.

**Reviewer:** Interestingly, these tumor markers are not related with primary liver cancer, then why they were done and how could they be related with survival in HCC?

**Response:** Thank you for your comment, because carcinoembryonic antigen, ruminal antigen 125, and ruminal antigen 19-9 are the indicators of preoperative tumor markers in patients. Due to the possible selection bias in our population, these indicators were related to survival in HCC in our analysis. It is worthy of further study whether the results of tumor markers can be improved or decreased by removing these tumor markers.

**Reviewer:** 95%CI and p value in text does not match with data in Table 3, where it is 0.4 1.03, p=0.07

**Response:** Thank k you for your comment, it is my handwriting error.

**Reviewer:** Very high %

**Response:** Thank you for your comment. It's me. This is a very high percentage of HCC patients in our study.

**Reviewer:** Pre resection?? Does this mean cirrhotic liver?

**Response:** Thanks for your review, we mean sonicated the lesion seen with unsmooth Margins.

**Reviewer:** Does not match with the information provided in main text

**Response:** Thank k you for your comment, it is my handwriting error.