



## PEER-REVIEW REPORT

**Name of journal:** *World Journal of Gastroenterology*

**Manuscript NO:** 74110

**Title:** Radiomics Signatures and Nomogram of Gd-EOB-DTPA Enhanced MRI for Preoperative Prediction of Microvascular Invasion in Small Hepatocellular Carcinoma: A Multi-Center and Prospective Validation Study

**Provenance and peer review:** Unsolicited Manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 00028182

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Associate Professor, Doctor

**Reviewer's Country/Territory:** Italy

**Author's Country/Territory:** China

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<b>Scientific quality</b>	<input checked="" type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection



<b>Re-review</b>	[ <input checked="" type="checkbox"/> ] Yes [ <input type="checkbox"/> ] No
<b>Peer-reviewer statements</b>	Peer-Review: [ <input checked="" type="checkbox"/> ] Anonymous [ <input type="checkbox"/> ] Onymous Conflicts-of-Interest: [ <input type="checkbox"/> ] Yes [ <input checked="" type="checkbox"/> ] No

### **SPECIFIC COMMENTS TO AUTHORS**

It is well known that pre-operative assessment of microvascular invasion (MVI) is a relevant issue as it is closely related to recurrence in postoperative HCC and is a major topic in the HCC treatment setting. Currently, 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 multicenter study, the authors aimed to develop and validate radiomics scores and nomogram of Gd-EOB-DTPA enhanced MRI for preoperative prediction of MVI in small HCC (sHCC). The study evaluated retrospectively 221 patients, 94 external and 100 prospective patients with postoperative pathological diagnosis of sHCC. Radiomics models of Gd-EOB-DTPA enhanced MRI and diffusion weighted images (DWI) were constructed and validated by machine learning. A prediction model was developed using multivariable logistic regression analysis which included: radiomics scores, radiologic features and alpha-fetoprotein (AFP) level. The radiomics nomogram was analyzed based on its discrimination ability, calibration, and clinical usefulness. The radiomics nomogram was validated by external independent cohort data. Predictive capability was assessed using the areas under the receiver operating characteristic curve (AUC). They found that pathological examination confirmed MVI in 64 (28.9%), 22 (23.4%) and 16 (16.0%) of 221, 94 and 100 patients. AFP, tumor size, nonsmooth tumor margin, incomplete capsule and peritumoral hypointensity on hepatobiliary phases (HBP) had poor diagnostic value for MVI of sHCC. A total of 1409 quantitative imaging



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features were extracted. The classifier of Logistic regression (LR) was the best machine learning method, the radiomics scores of HBP and DWI had the great diagnostic efficiency for prediction of MVI, in the testing set and validation set the AUC of HBP was 0.979, 0.970 and 0.803, the AUC of DWI was 0.971, 0.816 and 0.801 ( $P < 0.05$ ). The radiomics and clinic combine nomogram model exhibited good calibration and discrimination in the testing and two external validation cohorts (C-index of HBP and DWI was 0.971, 0.912, 0.808 and 0.970, 0.843, 0.869, respectively). They concluded that machine learning with LR classifier has the best radiomics score in HBP and DWI. The developed radiomics nomogram as a noninvasive preoperative prediction method shows favorable predictive accuracy for evaluate MVI in sHCC. The study is of interest and of current clinical relevance. However, in my opinion some issue deserve further details and important literature data are lacking and should be discussed to improve the clinical significance. - it is well know that imaging diagnostic features (and non-invasive diagnosis) of HCC are validated only in patient with underlying cirrhosis. Please describe in details characteristics and etiology of underlying liver disease of study population (how many had cirrhosis and how many were non-cirrhotic?). - As the major finding of the study is that the radiomics signatures of HBP and DWI can further improve the ability to predict MVI, I would suggest to recall in discussion that such a approach of a combination of MR parameters has already previously reported as a useful tool 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 regarded a MRI pattern, highly suggestive of hypovascular hepatocellular carcinoma (which is vey 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



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difficult imaging characterization of recurrent HCC nodules due to the potential different imaging features of recurrent nodules. It is well know 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. Thus in such a setting, the proposed radiomic approach could be of major clinical interest.



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<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection



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<b>Re-review</b>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

the idea is good