

Editorial for “Three-Dimensional Multifrequency MR Elastography for Microvascular Invasion and Prognosis Assessment in Hepatocellular Carcinoma”

The prognosis of individuals with hepatocellular carcinoma (HCC), the most prevalent primary liver malignancy, is closely linked to the aggressiveness and recurrence of the tumor. The occurrence of complications after surgery continues to be a major and persistent challenge.¹

MR elastography (MRE) employs a modified phase-contrast imaging sequence, combined with the use of an external driver to transmit mechanical vibrations to the tissues, to identify propagating shear waves within the liver. This technique allows the assessment of a substantial portion of the liver and provides information on multiple mechanical properties associated with various pathophysiological states. Due to substantial progress in MR technology, MRE has proven to be a precise noninvasive diagnostic method for detecting and monitoring various liver diseases.^{1–3} MRE imaging could serve as a valuable tool for staging malignancy and predict disease prognosis.^{1,4}

In this complex prospective JMRI study,⁵ the authors create nomograms that incorporate biomechanical properties assessed through three-dimensional (3D) multifrequency MRE to predict microvascular invasion (MVI) and recurrence-free survival (RFS) of HCC. One hundred and fifty patients suffering from HCC were included in the study. Surgically resected liver specimens were used for pathological evaluation. Multifrequency wavenumber recovery maps, indicating the shear wave speed (c) and phase angle (φ), were generated using a 1.5T equipment, in addition to the routine mp-MRI protocol at 3.0T.

As results, the inclusion of tumor c improved the diagnostic performance of mp-MRI (AUC increased from 0.81 to 0.86; $P = 0.04$) in MVI detection. The tumor c emerged as an independent predictor of MVI and liver c as an independent predictor of RFS. For patients identified as MVI-positive by the 3D multifrequency MRE model, RFS was shorter compared to those identified as MVI-negative. This 3D multifrequency MRE study, including lower frequencies (~ 30 –

60 Hz) beyond the more widespread 60 Hz single-frequency approach, clearly demonstrated a decrease in stiffness when MVI is present. A recent review performed by Liang et al presents other studies reporting contrary results.⁴ This discrepancy between studies can be explained by considering the wide range of responses that soft biological tissues exhibit to different excitation frequencies. Stiffness measured at higher frequencies tends to be more sensitive to the accumulation of extracellular matrix and fibrosis. While lower frequencies, in the range of 30–40 Hz, may provide sensitivity to processes occurring in aggressive cancer.³ Furthermore, different ROI positioning methods significantly affect HCC tumor stiffness measurements.⁶ This study benefits from using a 3D technique since had been demonstrated that 3D reconstruction provides better spatial resolution and a higher signal-to-noise ratio.³ 3D MRE holds a precision advantage over its 2D counterpart, mainly because it can capture shear wave propagation in three directions as opposed to a single plane in 2D. This capability allows for better visualization of shear wave dynamics within complex organs. Stiffness values derived from 3D MRE are typically lower than those obtained through 2D. To enhance diagnostic accuracy, future research efforts should concentrate on establishing robust thresholds for the interpretation of 3D MRE.³

One important limitation is the fact that this study focused on participants with HCC who had viral hepatitis. Hence, modifications to the model developed for MVI prediction may be necessary for individuals with HCC who also have a history of conditions such as alcoholic liver disease or drug-induced liver disease.³

Considering that not all patients are candidates for surgery and obtaining pathology, and acknowledging the invasive nature of biopsies, these results may enhance the practical applicability of MRE for prognostic purposes. This technique could aid clinicians in choosing appropriate active clinical treatments by providing a non-invasive solution for

diagnosing and predicting the prognosis of MVI and RFS of the patients.

Funding Information

RGN received support from Fundação para a Ciência e Tecnologia through LARSyS funding (10.54499/LA/P/0083/2020 and 10.54499/UIDP/50009/2020).

Nuno Adubeiro, MSc, PhD

Department of Radiology, School of Health of Porto/Polytechnic Institute of Porto (ESS/IPP), Porto, Portugal
EPIUnit, Institute of Public Health, University of Porto, Porto, Portugal
Laboratory for Integrative and Translational Research in Population Health (ITR), Porto, Portugal
E-mail: nca@eu.ipp.pt

Rita G. Nunes, PhD

Institute for Systems and Robotics—Lisboa, Lisboa, Portugal
Department of Bioengineering, Instituto Superior Técnico, Universidade de Lisboa, Lisbon, Portugal

Maria Luísa Nogueira, MSc, PhD

Department of Radiology, School of Health of Porto/Polytechnic Institute of Porto (ESS/IPP), Porto, Portugal
EPIUnit, Institute of Public Health, University of Porto, Porto, Portugal
Laboratory for Integrative and Translational Research in Population Health (ITR), Porto, Portugal

References

1. Idilman IS, Li J, Yin M, Venkatesh SK. MR elastography of liver: Current status and future perspectives. *Abdom Radiol* 2020;45(11):3444-3462.
2. Li J, Venkatesh SK, Yin M. Advances in MR Elastography in liver. *Physiol Behav* 2017;176(12):139-148.
3. Pepin KM, Welle CL, Guglielmo FF, Dillman JR, Venkatesh SK. Magnetic resonance elastography of the liver: Everything you need to know to get started. *Abdom Radiol*. 2022;47(1):94-114.
4. Liang J, Ampuero J, Castell J, et al. Clinical application of magnetic resonance elastography in hepatocellular carcinoma: From diagnosis to prognosis. *Ann Hepatol* 2023;28(2):100889.
5. Liu G, Shen Z, Chong H, et al. Three-dimensional multifrequency MR elastography for microvascular invasion and prognosis assessment in hepatocellular carcinoma. *J Magn Reson Imaging* 2024;60(6):2626-2640. <https://doi.org/10.1002/jmri.29276>.
6. Liu W, Rong D, Zhu J, et al. Diagnostic accuracy of 3D magnetic resonance elastography for assessing histologic grade of hepatocellular carcinoma: Comparison of three methods for positioning region of interest. *Abdom Radiol* 2021;46(10):4601-4609.

DOI: 10.1002/jmri.29315

Level of Evidence: 5

Technical Efficacy: Stage 2