

# Letters

## Open Questions in the Assessment of Liver Fibrosis Using Real-Time Elastography

We read the recent article by Săftoiu et al. [1] on the evaluation of real-time elastography in the assessment of liver fibrosis. Although this tool is interesting, some findings remain controversial [1–3].

Real-time elastography could reveal the physical properties of the liver by indicating the degree of displacement induced by the mechanical compression of the transducer on the liver (the strain is smaller in harder tissue compared with softer tissue); the different hardness characterizes the diseased and normal tissues [4]. However, different measurement techniques of the strain have been described [1–3].

We agree with Săftoiu et al. [1] that the placement of the elastography box inside the liver shows important biases if the analysis of strain is limited to only one region of interest (ROI) because real-time elastography is based on comparing structures with different stiffness. The authors suggest that the ROI should also include the surrounding tissues (adipose tissue, diaphragm, and intercostal muscles) because of the broader range of strain [1]. In the semiquantitative assessment with the hue histogram analysis, they performed analyses of ROIs including these structures, but comparisons with the liver were not included [1].

We suggest comparing them to assess differences in the hue histogram analysis and to assess whether relative thresholds of stiffness could be determined for the surrounding tissues and the normal or diseased liver. Because real-time elastography has been validated for studying stiffness of tissues other than liver, such as breast [5], thyroid [6], and prostate gland [7], the more complex structure of the liver could require the revision of thresholds that reflect degrees of displacement representative of softer or harder liver tissues. Hue histogram analysis could be used to identify these thresholds and to train the software to display stiffness as a scaled gradient of color optimized for the

range of stiffness expected in the liver. This could then allow the recognition of diseased and normal liver tissues by their different hardness, represented on an adapted grading scale of colors.

However, the principle is interesting given that the hue histogram analysis of normal tissues (liver and surrounding tissues) would produce a normal gaussian distribution in which the harder tissues fall into the left side of the histogram. When significant liver fibrosis is observed, the distribution would be skewed toward the left side of the histogram because of the increased hardness of the liver.

In any case, the time delay between the patient visit and learning the results of the hue histogram analysis would be a limit because of the additional computer-based analysis required. Therefore, we have asked the manufacturer of the real-time elastography instrument (EUB 8500, Hitachi Medical Systems) to upgrade the software to include this functionality.

Meanwhile, at the request of the manufacturer, we compared ROIs corresponding to structures localized in the liver with different degrees of displacement, such as the highly elastic right branch of the hepatic vein and the liver tissue of interest. This “strain ratio” could be a reliable parameter immediately calculated by the software, avoiding further computer analyses. It could allow assessments of liver fibrosis on the basis of the principle that the harder the liver, the higher the corresponding ratio.

The reliability of real-time elastography is certainly crucial [1]. Our data also show significant intraobserver variability and lack of interobserver agreement. This limited reliability is still more significant when we consider that intraobserver variability was about 40% in the acquisition of the single compared ROIs, even though they were acquired according to standardized procedures, centering them 3 cm below the Glisson’s capsule and assessing them only if three consistent series of color-coded elastography frames were obtained.

This suggests that the hue histogram analysis might exhibit low reproducibility because of the inability of the sonologist to obtain consistent acquisitions. Although we asked the manufacturers to build modified transducers (3.5–5-MHz), adapted on miniconvex that provide better windows for propagating the elastic wave through the intercostal spaces to the required depth in the liver; the degree of compression remains a significant bias because it is not easily reproducible, either by a single sonologist (whether in the same examination or in different sessions) or by different workers. The strain is therefore not easily standardized.

Lastly, as suggested [1], we compared real-time elastography with transient elastography, a noninvasive tool recently validated for the assessment of liver fibrosis [8]. Our data show that transient elastography exhibited better reproducibility compared with real-time elastography. Moreover, real-time elastography failed to identify the stages of fibrosis with the expected accuracy, whereas transient elastography identified them well.

In conclusion, although at the limits of current modules, the promise of obtaining reconstructions of heterogeneous damage related to liver fibrosis (by means of assessments of every liver segment) [1, 3] suggests further investigation to improve the reliability of the real-time elastography assessment of liver fibrosis.

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