Magnetic resonance elastography measurements of viscosity: a novel biomarker for human hepatic tumor malignancy?

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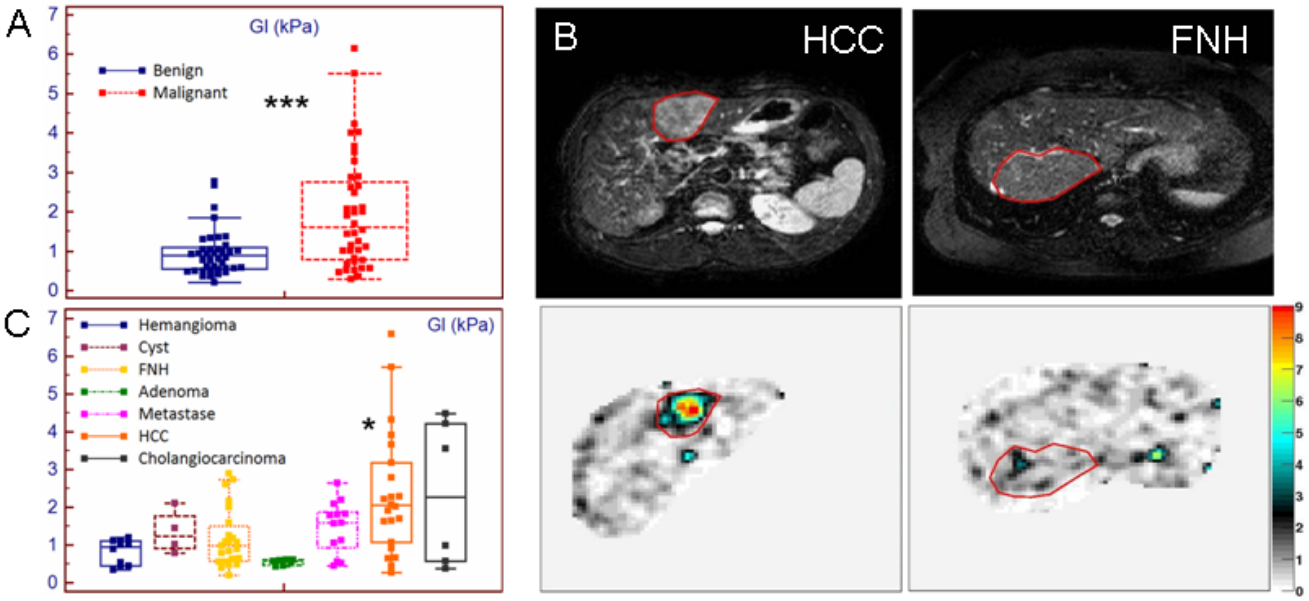
Introduction:
The accurate determination of the degree of malignancy of a tumor remains a clinical challenge, especially if the invasiveness of the diagnosis method is of concern. Benign and malignant lesions are known to possess different microstructural properties (such as the organisation of their vasculature, the state of the extracellular matrix or their proliferative potential) which can affect their overall mechanical properties [1]. To determine if magnetic resonance elastography (MRE) could represent a novel non-invasive diagnosis tool, tissue elasticity (Gd) and viscosity (Gl) measurements were conducted in a cohort of 76 patients with histologically confirmed hepatic lesions.

Material and methods:
MR imaging sessions were conducted on a 1.5T Philips clinical MRI system (Philips Medical Systems, Best, The Netherlands). In addition to routine morphological acquisitions, consenting patients (n = 76) were subjected to conventional dynamic contrast-enhanced (DCE) imaging as well as MRE. The study included both benign (10 hemangiomas, 4 cysts, 23 FNH and 5 adenomas) and malignant (13 metastases, 19 HCC and 5 hepatocholangiocarcinomas) hepatic tumors. For MRE, acoustic waves (50 Hz) were produced by a transducer located on the right flank of the patient, and synchronous motion-encoding bipolar gradients were added to a spin-echo sequence with EPI readout (TR/TE = 560/40 ms, field of view of 320 × 320 mm^2 for a 80 × 80 matrix and 7 transverse slices of 4 mm in thickness) to encode 3 orthogonal displacement maps in phase images. Total data acquisition was 72secs subdivided into 6 breath holds of 12secs each. Gd and Gl maps were reconstructed by fitting a polynomial function to the displacement values under physical constraints of local mechanical isotropy and tissue incompressibility. Average Gd and Gl values were obtained from specific regions of interest (ROI) in each lesion: a "global" ROI encompassed the whole tumor, whereas a "viable tumor" ROI was positioned on the viable tumor regions presenting a maximal enhancement on the DCE images during the arterial or portal venous phase.

Results:
Malignant tumors were found to be more viscous than benign lesions (Fig. A and B), whether the global ROI ($\overline{Gl}$ = 0.99 ± 0.63 kPa for benign tumors and 1.97 ± 1.44 kPa for malignant tumors) or the viable tumor ROI were considered (0.98 ± 0.66 kPa and 2.13 ± 1.54 kPa, for benign and malignant lesions, respectively). The inclusion of cysts (a very distinctive and easily diagnosed type of lesion) in the benign subgroup did not affect the outcome of the viscosity measurements ($\overline{Gl}$= 1.02 ± 0.63 kPa) but resulted in a significant elasticity difference between benign ($\overline{Gd}$ = 2.02 ± 0.69 kPa) and malignant lesions ($\overline{Gd}$ = 2.35 ± 0.75 kPa). Gl measurements also differentiated HCC from hemangioma, FNH, adenoma and metastases (Fig. C) which was not the case for Gd (not shown).

Conclusion:
This study showed that the distinction between the elastic and the viscous components of the shear modulus brings a more complete insight on hepatic tumors than stiffness alone [2], while being in overall agreement. MRE measurement of viscosity appears to be a promising biomarker for the determination of hepatic tumor malignancy. The higher viscosity of malignant lesions, such as HCC, could be explained by their disorganized vasculature which may abnormally attenuate acoustic waves. Viscosity measurements could also be used to assist to some extent the characterization of tumor types.



A: Box plots of Gl (kPa) in global ROIs; *** $p < 0.001$; **B:** anatomical images (top) and Gl maps (kPa; bottom) for a HCC (left) and a FNH (right); **C:** Box plots of Gl (kPa) of each tumor type (* $p < 0.05$ between HCC and hemangioma/FNH/adenoma/metastases)

[1] S. Kumar and V.M. Weaver, Cancer Metastasis Rev 28: 113 (2009)
[2] S.K. Venkatesh *et al.*, Am J Roentgenol 190: 1534 (2008)