

Grading of chronic liver inflammation quantified by shear wave dispersion MR elastography: initial clinical results on 26 patients

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Purpose / Introduction: Magnetic Resonance Elastography (MRE) is a non-invasive and reliable marker of liver fibrosis[1]. However, liver fibrosis is often associated with inflammation and, until now, no definite noninvasive biomarker has been found to detect and grade inflammation in the clinical setting. Theoretical and physical considerations indicate that the microscopic tissue structures may influence not only the viscoelastic parameters, but also their evolution with varying wave frequency[2,3]. The purpose of our study is to assess the performance of wave dispersion measurement by multi-frequency MRE for the grading of liver inflammation.

Subjects and Methods: Twenty-five patients with viral hepatitis B (n=8) and C (n=17) were prospectively included in this study and underwent MRE. Liver inflammation and fibrosis were assessed with METAVIR scoring of percutaneous biopsies. MRE was carried out on a 1.5T system (Philips Healthcare, Best, The Netherlands) using a gradient-echo sequence (TR/TE=112ms/9.6ms, 1m20s acquisition time, (4mm)³ isotropic resolution, 3-directional fractional encoding at 120Hz, 8 phase offsets) with an electromagnetic actuation of simultaneous 28, 56 and 84 Hz mechanical waves to the liver. The complex-valued shear modulus was calculated by demodulation and local inversion of the linear viscoelastic 3D wave equation and converted into wavelength λ (mm) and attenuation coefficient α (mm⁻¹). The frequency dependence of each parameter (modeled by a power law) was assessed as the exponent parameter, γ_λ and γ_α . ANOVA and ROC analysis were performed for statistical analysis, with $P \leq 0.05$ considered as significance threshold.

Results: The only statistically significant parameters for grading liver inflammation were the wavelength $\lambda_{(84\text{Hz})}$ and the exponent of the wavelength, γ_λ . As expected, $\lambda_{(84\text{Hz})}$ increased with progressive inflammatory activity (stiffening of the liver) while the exponent parameter γ_λ decreased with inflammation (Fig. 1). For γ_λ , ANOVA was positive ($p < 0.01$) with positive post-test for A0 vs. A2. When pooling A0 and A1 patients vs. A2 and A3 patients, the area under the ROC curve was 95% ($P < 0.0001$), with a 100% sensitivity and 85% specificity for a cut-off value of $\gamma_\lambda = -0.43$ (Fig. 2) which largely outperformed the corresponding area for the wavelength $\lambda_{(84\text{Hz})}$ yielding only 73% ! When examining subgroups of patients with the same fibrosis stage, the decrease in γ_λ as a function of inflammation grade was still systematically observed (Fig. 3) although no statistical significance was obtained due to the limited number of patients, i.e.

F1: $\langle \gamma_\lambda \rangle = -0.27 \pm 0.08$ (A0, n = 3), $\langle \gamma_\lambda \rangle = -0.33 \pm 0.05$ (A1, n = 9)
F2: $\langle \gamma_\lambda \rangle = -0.33 \pm 0$ (A1, n = 1), $\langle \gamma_\lambda \rangle = -0.45 \pm 0.03$ (A2, n = 2)
F3: $\langle \gamma_\lambda \rangle = -0.43 \pm 0.07$ (A1, n = 4), $\langle \gamma_\lambda \rangle = -0.51 \pm 0.01$ (A2, n = 2) $\langle \gamma_\lambda \rangle = -0.53 \pm 0$ (A3, n = 1)

Discussion/Conclusion: The frequency response of λ proved to be sensitive and specific in distinguishing between mild (A0/A1) and severe (A2/A3) inflammation grades. This response was also observed independently from the fibrosis stage. Our results demonstrate that γ_λ has the potential to be a novel noninvasive biomarker for liver inflammation with important clinical implications.

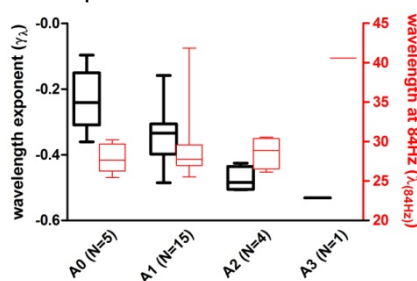


Fig. 1: Wavelength exponent values (black) and wavelength at 84Hz (red) for different inflammation grades. γ_λ decreases with inflammation grades.

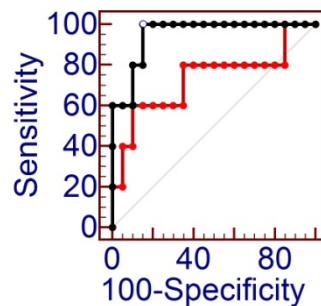


Fig. 2: ROC curve for the determination of A0-A1 vs. A2-A3 using $\lambda_{(84\text{Hz})}$ (red) or γ_λ (black). High sensitivity and specificity is attainable on a wide range of threshold values.

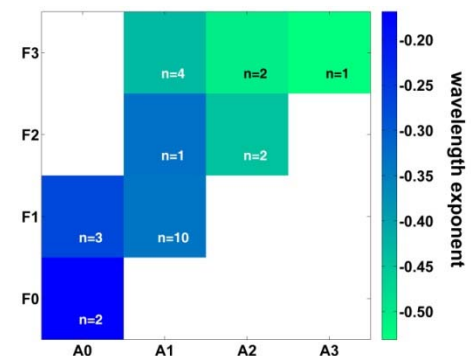


Fig. 3: Wavelength exponent vs. inflammation grade, represented for given fibrosis stages. The exponent is seen to vary with inflammation even in fixed fibrosis stages.

- [1] Huwart L. 2008, Gastroenterology 135:32-40
 [2] Holm S. 2010, JASA 127:542-8
 [3] Asbach P. 2010, Radiology 257:80-86