Separate assessment of fibrosis, steatosis and inflammation: Multi-parametric imaging of chronic liver diseases

Sabrina Doblas[1], Helena S Leitao[1,2], Philippe Garteiser[1], Gaspard d'Assignies[1,3], Feryel Mouri[4], Valérie Vilgrain[1,3], Ralph Sinkus[1], Carlos FGC Geraldes[2], and Bernard E Van Beers[1,3]

[1]U773-CRB3, INSERM, Paris, France, [2]Center for Neuroscience and Cell Biology, University of Coimbra, Coimbra, Portugal, [3]Radiology Department, Beaujon University Hospital, Clichy, France, [4]Hepatology Department, Beaujon University Hospital, Clichy, France

Purpose: Magnetic resonance elastography (MRE) and diffusion-weighted imaging (DWI) have both been proposed as non-invasive alternatives to liver biopsy to assess hepatic fibrosis. Due to an extensive fibrotic remodelling of the extracellular matrix, advanced fibrosis stages generally present restricted water diffusion [1] and increased stiffness [2]. However, steatosis and inflammation often coexist with fibrosis and these confounding factors could potentially bias the evaluation of hepatic mechanical and diffusion properties [3, 4]. The purpose of this study is to establish the influence of steatosis and inflammation on the measurement of viscoelastic parameters and diffusion coefficients in the assessment of hepatic fibrosis.

Subjects and Methods: Fifty-eight non-cirrhotic patients with chronic viral hepatitis B (n = 26) and C (n = 32) were included in this prospective study. They underwent MR imaging including MRE and DWI at 1.5T, followed by percutaneous liver biopsy for METAVIR scoring and steatosis grading. MRE acquisition used a spin-echo scheme (TE/TR = 40ms/320ms, 4mm resolution) with 100 Hz motion-encoding gradients applied consecutively in 3 directions and 4 phase offsets. 50 Hz mechanical waves were applied to the liver by a transducer positioned on the right flank of the patient. DWI acquisition was performed using a spin-echo sequence with EPI readout (TE/TR = 56/300 ms, 4mm resolution, b= 150, 300, 500 s/mm^2). The following viscoelastic parameters were determined using a local inversion of the linear viscoelastic complex 3D wave equation: the stiffness G_{abs} (kPa), the wave propagation coefficient β (mm^{-1}) and the wave attenuation coefficient α (mm^{-1}). The pure diffusion coefficient D was calculated by fitting the normalized signal intensity to a mono-exponential model. Univariate Spearman rank correlations (rho), multiple regression coefficients (RC) and ROC curve analysis (AUROC) were used for statistical analysis.

Results: Patients with a high level of liver inflammation exhibited a lower β and a higher G_{abs} than A0A1 patients, with moderate correlation (β_{A3}=0.16±0.03 mm^{-1} vs β_{A0}=0.2±0.02 mm^{-1}, p=0.04, rho=-0.27; G_{absA3}=3.66±1.3 kPa vs G_{absA0}=2.2±0.44 kPa, p=0.007, rho=0.35). Correlations were also found between fibrosis and G_{abs}, β and D, with an increase in G_{abs} (p=0.0004; rho=0.45; *Fig. 1*), a decrease in β (p=0.0012; rho=-0.42) and a decrease in D (p=0.03; rho=-0.29) in patients with significant fibrosis (F ≥ 2). Patients with > 33% steatosis had significantly lower D than non-steatotic patients or patients with mild steatosis (D_{S0S1}=1.19±0.2 ×10^{-3} mm^2/s vs D_{S2S3}=0.98±0.16 ×10^{-3} mm^2/s, p = 0.0002, rho=-0.47, *Fig. 2*), and D and steatosis were even more strongly correlated in the absence of fibrosis (p=0.0008, rho=-0.55). No correlation was found between α and fibrosis, steatosis or inflammation. Multiple regression analysis identified fibrosis as the main variable dictating G_{abs} behaviour (p=0.001, RC=0.51) with an additional mild influence of steatosis (p=0.047, RC=-0.4). However, F0F1 vs F2F3 discrimination was similar whether steatotic patients were included or not in the ROC curve analysis ($AUROC_{Gabs}$ = 0.782 and 0.77, resp., *Fig. 3*). β was tightly linked to fibrosis (p=0.0006, RC=-0.44) and was independent from steatosis and inflammation. Steatosis was found to mostly influence the diffusion coefficient D (p = 0.0003), which was not affected by either fibrosis or inflammation.

Conclusion: The viscoelastic parameters were predominantly influenced by fibrosis and slightly by steatosis. As revealed by the multivariate analysis, inflammation did not affect them, and any difference seen between A0A1 and A2A3 patients was certainly due to the underlying fibrosis stage. The diffusion coefficient was greatly affected by steatosis, fibrosis being a secondary factor for this parameter. This shows the usefulness of a multiparametric approach to tissue assessment when several pathological states coexist.

References

[1] Lewin M *et al.* 2007 *Hepatology* 46: 658
[2] Huwart L *et al.* 2008 *Gastroenterology* 135: 32
[3] Bonekamp S *et al.* 2011 *J Clin Gastroenterol* 45: 885
[4] Leitao HS *et al.* 2012 *Eur Radiol*

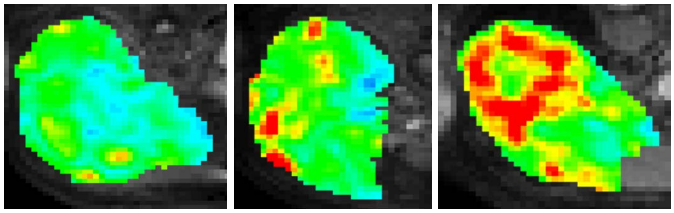

Fig. 1: G_{abs} (kPa) maps for patients A0F0-S70%, A1F2-S10% and A1F3-S40%

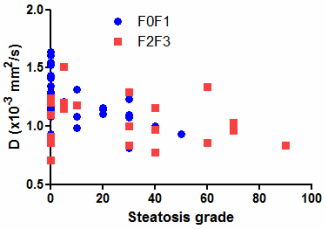

Fig. 2: D was negatively correlated to steatosis grade

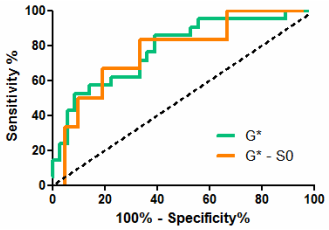

Fig. 3: Discrimination between F0F1 and F2F3 was similar whether steatotic patients were included or not.