Distinction between non-advanced and advanced liver fibrosis: Comparison between MR DCE imaging and T2-corrected IVIM at 3.0T.

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Introduction
Lever fibrosis is an important cause of mortality and morbidity in patients with chronic liver diseases and cirrhosis, end-stage of fibrosis, involve 15,000 and 40,000 deaths per year in France and in USA respectively (1,2). Reversible aspect of liver fibrosis has been recognized, and more effective treatment strategies have emerged. Nevertheless these latter require an early detection and a clinical follow-up of liver fibrosis. While liver biopsy is the gold standard for the diagnosis of chronic liver diseases, inherent risk, interobserver variability and sampling errors makes liver biopsy unusable for the clinical follow up. Thus, there is a real clinical need in the development of non-invasive methods for liver fibrosis assessment. At 1.5 T, human in-vivo studies have demonstrated that liver perfusion imaging using a MR dynamic contrast enhanced method (MR-DCE) has the potential to detect and assess vascular modifications associated to liver fibrosis (3,4). On another hand, intra-voxel incoherent motion imaging (IVIM) has been proposed to asses liver fibrosis (5). This technique was able to separate two kind of diffusion: the pure molecular diffusion and the perfusion-related diffusion. Our objective was to combine IVIM with perfusion imaging using a MR-DCE technique at 3.0 T and evaluate this protocol for fibrosis severity assessment on a prospective study including patients with chronic liver diseases. Through this study, perfusion-related diffusion parameters given by IVIM and quantitative perfusion parameters given by MR-DCE imaging were compared.

Materials and Methods
Subjects: Twenty two subjects (10 W, 12 M; mean age: 43.8 ± 14.6 years; mean weight: 74.3 ± 15.9 Kg) with chronic liver diseases were prospectively enrolled.

Liver fibrosis was histologically quantified with METAVIR and Brunt or CRN quantification in patients with viral hepatitis and NAFLD respectively.

Liver perfusion was assessed with a T1-weighted contrast enhanced sequence with a 3D T2-prepared T1-weighted spoiled gradient echo technique with temporal resolution of 1.8 s. Temporal evolution of contrast uptake was fitted to mono-exponential or bi-exponential functions. Temporal resolution was 1.8 s. Dynamic acquisition was performed with a 3D LAVA sequence employing the auto-calibrating reconstruction for cartesian imaging with an accelerating factor of 3. Acquisition parameters were: TR/TE, 1.9/0.8 ms; 9° flip angle; 128 × 160 acquisition matrix (2562 rebuilding); 480 mm² FOV; 2/3 partial K-space filling. 24 cm slab thickness including 48 coronal slices of 5 mm thickness rebuilt with a ZIP 2 interpolation algorithm. Temporal resolution was 1.8 s. Dynamic acquisition started simultaneously with contrast medium injection (Multihance, Bracco s.p.a, Milano, Italy) and lasted 180 s in free-breathing. Injection rate was 6.0 mL/sec and posology was 0.2 mL.Kg⁻¹. IVIM was performed using a single-shot SE-EPI sequence, in free breathing, with 12 b-values (0-10-20-40-60-80-100-200-300-400-600-800 s·mm⁻²) and a weighted signal averaging procedure (2 to 9 signal accumulations according to b-values). Three orthogonal diffusion gradients were sequentially applied. A 2000 ms TR, 54 ms minimum TE; 21 axial slices of 8 mm thick; 400 × 300 mm² FOV; 128 × 96 acquisition matrix (256² rebuilding) were used. Scan duration was 5'12".

Images processing: First, a dedicated algorithm was used to quantify perfusion parameters. It included an image registration procedure based on an affine averaging procedure (2 to 9 signal accumulations according to b-values). Three orthogonal diffusion gradients were sequentially applied. A 2000 ms TR, 54 ms minimum TE; 21 axial slices of 8 mm thick; 400 × 300 mm² FOV; 128 × 96 acquisition matrix (256² rebuilding) were used. Scan duration was 5'12".

Discussion
Perfusion parameter variations confirm the existence of hemodynamic changes associated with fibrous damage. Parameter modifications are consistent with previous results obtained at 1.5 T (4). The deposition of extracellular matrix components in liver fibrosis restricts the pure molecular diffusion as illustrated by Dslow values differences between non-advanced and advanced fibrosis. As suggested by the correlations between Dfast and total perfusion or portal perfusion, Dfast reflects the hemodynamic changes, in particular the decrease of portal perfusion induced by fibrosis. As showed by Dfast-values differences between NAFLD and chronic hepatitis for the group with no fibrosis, fat vesicles in NAFLD also restrict pure molecular diffusion. Even if this double contribution to molecular diffusion restriction did not affect the relevance of this parameter to evaluate fibrosis severity in this study, fat overload has to be taking into account with IVIM since it may constitute a confounding factor for fibrosis evaluation. In the present case, histology-confirmed fat overload did not modified perfusion parameters-values. All these issues suggest that the combination of IVIM with MR DCE imaging do not bring additional information to assess liver fibrosis. Indeed, perfusion parameters given by MR-DCE imaging alone are already relevant to evaluate fibrosis severity. Nevertheless, T2-corrected IVIM could be a useful injection-free alternative to distinguish between non-advanced and advanced fibrosis.

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