INTRAVOXEL INCOHERENT MOTION DIFFUSION-WEIGHTED IMAGING FOR DETECTION OF LIVER FIBROSIS IN HCV: COMPARISON OF FOUR SEQUENCES

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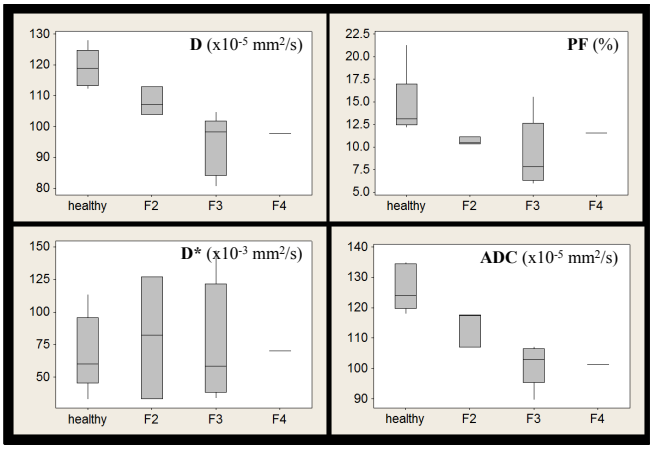
Introduction: Non invasive detection of liver fibrosis and longitudinal assessment after antiviral therapy are urgent clinical needs in chronic hepatitis C virus infection (HCV). Intravoxel Incoherent Motion (IVIM) Diffusion-weighted imaging (DWI) is a promising tool for detection of liver fibrosis and cirrhosis [1-2] as it provides estimates of microscopic tissue water diffusion, which is impaired by excessive collagen distribution in fibrosis, along with decreased blood perfusion in fibrosis. The goal of this study was to evaluate IVIM DWI, using monopolar (MP) vs. bipolar (BP) diffusion encoding gradients, and respiratory triggered (RT) vs. free breathing (FB) acquisition schemes in terms of diagnostic performance for fibrosis detection and reproducibility.

Methods: This prospective study was IRB approved and all subjects were consented. 19 subjects (6 healthy, 13 HCV with liver fibrosis diagnosed on biopsy, M/F 14/5, mean age 46 y) underwent two MRI exams (max. 2 weeks between scans) including IVIM with 4 different sequences: FB-BP, FB-MP, RT-BP and RT-MP. 16 b-values (0 to 800 mm^2/s) were sampled in the coronal plane at 1.5T (Siemens Avanto) using a fat suppressed interleaved 2D SSEPI acquisition with resolution of 2.9x2.3x8 mm^3, TR 3000 (FB)-1 respiratory cycle (RT)/TE 63ms (MP) or 73ms (BP), GRAPPA=2. ROIs were drawn on 5 consecutive slices centered on the portal vein in the liver parenchyma. Fitting of the bi-exponential IVIM decay, using a Bayesian method [3], yielded the true Diffusion coefficient (D), Perfusion Fraction (PF), and pseudo-diffusion coefficient (D*). Additionally a mono-exponential fit using all 16 b-values yielded the Apparent Diffusion Coefficient (ADC). Liver biopsy was performed in the HCV group.

Table 1	FB Bipolar			FB Monopolar			RT Bipolar			RT Monopolar		
	Normal	Fibrosis	p*	Normal	Fibrosis	p*	Normal	Fibrosis	p*	Normal	Fibrosis	p*
D	119.3 ± 6.3	99.2 ± 9.9	**0.0003**	114.1 ± 11	99.3 ± 8.9	**0.022**	115.4 ± 7.6	102.5 ± 9.8	**0.009**	104.0 ± 6.5	99.3 ± 9.2	0.238
PF	14.6 ± 3.5	9.9 ± 2.9	**0.022**	14.3 ± 2.9	10.6 ± 3.2	**0.046**	14.7 ± 4.8	9.2 ± 2.5	**0.037**	16.6 ± 7.2	10.3 ± 3.6	0.088
D*	68.0 ± 29.4	77.0 ± 40.5	0.627	53.0 ± 30.0	56.8 ± 24.0	0.781	57.3 ± 20.1	71.9 ± 26.9	0.212	45.5 ± 16.1	67.8 ± 25.2	**0.039**
ADC	126.0 ±7.5	105.6 ± 8.6	**0.0004**	124.2 ± 10.8	105.7 ± 7.3	**0.007**	122.9 ± 7.1	106.9 ± 10.0	**0.002**	113.7 ± 5.1	104.8 ± 9.9	**0.022**

Mean ± SD values of IVIM DWI parameters for the healthy and fibrotic groups, for the four sequences tested. *Paired t-test (significant p values are bolded), D and ADC ($x10^{-5}$ mm^2/s), PF (%), D* ($x10^{-3}$ mm^2/s).

Results: The following distribution of fibrosis was observed in HCV: F2 (n=4), F3 (n=6), F4 (n=3). For all sequences D, PF and ADC were significantly lower for HCV patients than for healthy subjects **(Table 1)**. This trend was also observed within the fibrotic group, as the fibrosis scores increased from F2 to F4 **(Fig.)**. In addition, D, PF and ADC showed good to excellent reproducibility for all 4 sequences **(Table 2)**. D* did not vary significantly between groups and was generally poorly reproducible, except for RT-MP. FB-MP was found to give the most reproducible results and FB-BP was best able to differentiate the healthy and fibrosis groups.



Boxplots of D, PF, D* and ADC for the FB-BP acquisition

Discussion: In previous studies on IVIM in liver cirrhosis, Luciani et al.[1] have reported a decrease in ADC and D* in cirrhosis, while Patel et al.[2] have reported a decrease in D, PF, D* and ADC. Our study differs in that it aims at detecting liver fibrosis. Liver fibrosis is associated with excessive collagen deposition, which tends to restrict water diffusion and to decrease the vascular volume within sinusoids, both effects that could account for a decrease in D and PF. The decrease in ADC is a result of the combined decrease in D and PF. This preliminary study has shown that IVIM of the liver has acceptable to excellent reproducibility and is able to differentiate healthy and fibrotic liver especially when a FB-BP acquisition scheme is used. This shows good promise for a non-invasive diagnosis of liver fibrosis using DWI. Further studies are needed, with a larger number of patients spanning the fibrosis stages F0 to F4 in order to assess the performance of the technique within the fibrotic population.

Table 2	D	PF	D*	ADC
FB BP	9.2	34.7	63.2	11.0
FB MP	4.2	6.9	20.0	3.3
RT BP	7.7	18.3	37.4	7.9
RT MP	8.6	22.0	36.1	6.8

Reproducibility (CV, in %) of the 4 different DWI sequences

References

1. Luciani et al., Radiology 2008 249:891-899
2. Patel et al., JMRI 2010, 31:589-600
3. Koh and Collins. AJR 2011; 196:1351–1361

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