Intravoxel Incoherent Motion MR Imaging showed lower pure molecular diffusion in fibrotic livers: a report of preliminary results

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Introduction: Prior studies suggested that liver fibrosis may be associated with progressive restriction of diffusion motion because of the increase in connective tissue associated with liver fibrosis. It is also well accepted that liver fibrosis/cirrhosis is associated with reduced liver perfusion [1-3]. Le Bihan et al [4] demonstrated that both pure molecular diffusion and microcirculation, or blood perfusion, can be distinguished by using intravoxel incoherent motion (IVIM)-based DW imaging, provided that multiple b values to encompass both low b values (<200 sec/mm^2) and high b values (>200 sec/ mm^2) are used. In biologic tissues, IVIM includes microcirculation of blood in the capillary network, which is also called perfusion. The signal attenuation is according to the Formula (1) $SI = SI_0[(1-f)\cdot\exp^{-b\cdot D} + f\cdot\exp^{-b\cdot D*}]$, where S is the mean signal intensity, f is the fraction of the diffusion linked to microcirculation, D is the diffusion parameter representing pure molecular diffusion (slow component of diffusion), and $D*$ is the diffusion parameter representing incoherent microcirculation within the voxel (perfusion-related diffusion, or fast component of diffusion). Considering that $D*$ is significantly greater than D [4], its influence on signal decay can be neglected for b factors greater than 200 sec/mm^2. With the D value determined by using Equation, f and $D*$ values can be calculated by using a nonlinear regression algorithm based on Formula 1. This current study report the preliminary results of IVIM evaluation of 11 healthy volunteers and 11 liver fibrosis subjects.

Material and Methods: The study was approved by the local research and ethics committee and informed consent was obtained before commencement of the study. 11 healthy volunteers (5 female, 6 male; mean age: 32-yrs old; range 21-47-yrs old) and 11 patients (1 female, 10 male; mean age: 32-yrs old; range 22-43-yrs old) with histopathologically proved liver fibrosis were included. The IVIM DW imaging sequence was applied with a 1.5-T MR imaging system (Philips Healthcare). The sequence was based on standard single-shot DW spin echo-planar imaging, with 10 b values of 10, 20, 40, 60, 80, 100, 150, 200, 400, 800 sec/mm^2 respectively. The IVIM DW imaging sequence was respiratory gated, which resulted in an average repetition time of 1500 msec, and TE was 63. Slice thickness =7mm. NEX=2. All regression algorithms were implemented with software (MatLab; Mathworks, Natick, Mass), which allowed the extraction of parametric maps representing f, D, and $D*$ parameters, which were fitted on a pixel-by pixel basis. Avoiding artifacts and blood vessel, one ROI was manually placed on the b=0 sec/mm^2 DWI image (see Fig.1) obtained with software (Matlab). The mean D, $D*$, and f parameters derived from the pixel-by-pixel analysis was computed.
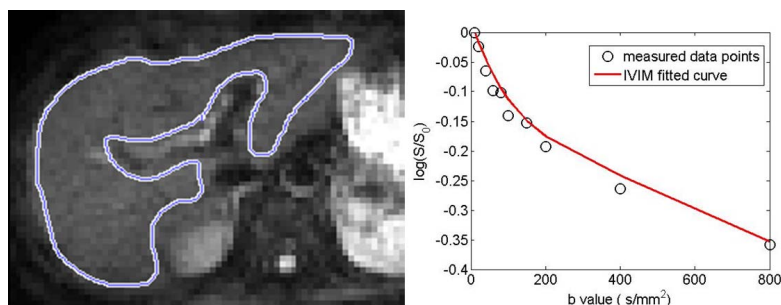

Fig.1, The placement of ROI on the b=0 DWI image (left) and the corresponding IVIM fitted curve of measured signal decay (right).The ROI was placed over the whole liver, avoided the artifact and blood vessel.

Table.1, The D, D*, and f parameters measured in healthy volunteers and patients liver. Data are means ± standard deviations. #: by Mann Whitney U test.

Results: All curves of signal-intensity decrease demonstrated biexponential type decay as expected, whether the measurements were obtained in the healthy liver group or in the liver fibrosis group (Fig 1). The mean D, $D*$, and f parameters measured in healthy volunteers and patients liver were listed in Table1. The D value in patients was significantly lower than that in healthy subjects (p=0.013). The f value was also lower in the patients, though statistical significance was not reached (p=0.066).

Parameters	Volunteers	Patients	p-value#
D ($\times 10^{-3}$ mm^2/sec)	1.10 ± 0.18	0.90 ± 0.16	0.013
f	0.22 ± 0.11	0.14 ± 0.06	0.066
$D*$ ($\times 10^{-3}$ mm^2/sec)	10.46 ± 3.47	14.39 ± 5.08	0.066

Discussion: On the basis of the IVIM theory, Luciani et al [5] studied patients with documented liver cirrhosis (METAVIR score F4 liver fibrosis, n=12) and healthy liver group (n=25). They reported the D ($\times 10^{-3}$ mm^2/sec) value and the f (%) were 1.10±0.7 and 27.0 respectively in the healthy liver group, which are quite similar to our current study. Interestingly, while Luciani et al [5] reported there was no difference in D value and f between the healthy livers and the cirrhotic livers (p=0.4 for D and 0.07 for f with the cirrhotic livers higher), our results demonstrated both D value and f were lower in the cirrhotic livers compared with the healthy livers, which can be explained by that liver fibrosis is associated with progressive restriction of diffusion motion because of the increase in connective tissue, and liver fibrosis is associated with reduced liver perfusion. On the other hand, our results showed there was no significant difference of $D*$ value between the healthy livers and the fibrotic livers. Luciani et al [5] reported $D*$ was reduced in the cirrhotic livers, though their f value was higher in the cirrhotic livers. In larger data sample from patients with type 2 diabetes with and without liver steatosis (n=108), Guiu et al [6] reported that both D and $D*$ are significantly decreased in steatosis. It is surprising that while we obtained similar values of D and f to Luciani et al's results, the $D*$ value is much lower in our studies. Acutally the $D*$ value in our study is similar to a recently experimental study performed on rat liver [7]. Andreou et al. [8] reported showed good to moderate measurement reproducibility of D, while with unsatisfactory measurement reproducibility for $D*$ of liver. They suggested efforts to improve measurement reproducibility of IVIM parameters should be explored.

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