Intravoxel Incoherent Motion (IVIM)*: A Potential Application in Cirrhosis Assessment

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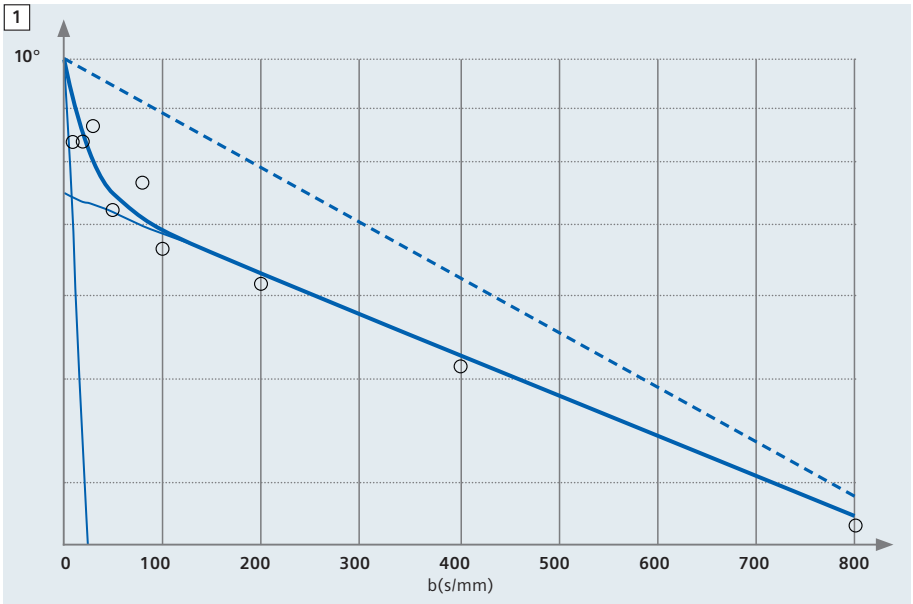
Introduction

In 1988 Le Bihan et al. [1] defined intravoxel incoherent motion (IVIM) as the microscopic translational motions that occur in each image voxel in Magnetic Resonance (MR) imaging. In biological tissues these motions include molecular diffusion of water and microcirculation of blood in the capillary network. Microcirculation of the blood in capillary network, also called "perfusion", can also be considered as an incoherent motion since the capillary organization can be seen at the voxel size as random. These two phenomena account for the bi-exponential decay of the signal observed on diffusion-weighted imaging (DWI) when different diffusion b-values are applied. The IVIM sequence allows the extraction of two diffusion coefficients, one related to molecular diffusion restriction, D, another related to the tissue perfusion called D* and finally the vascular volume fraction f.

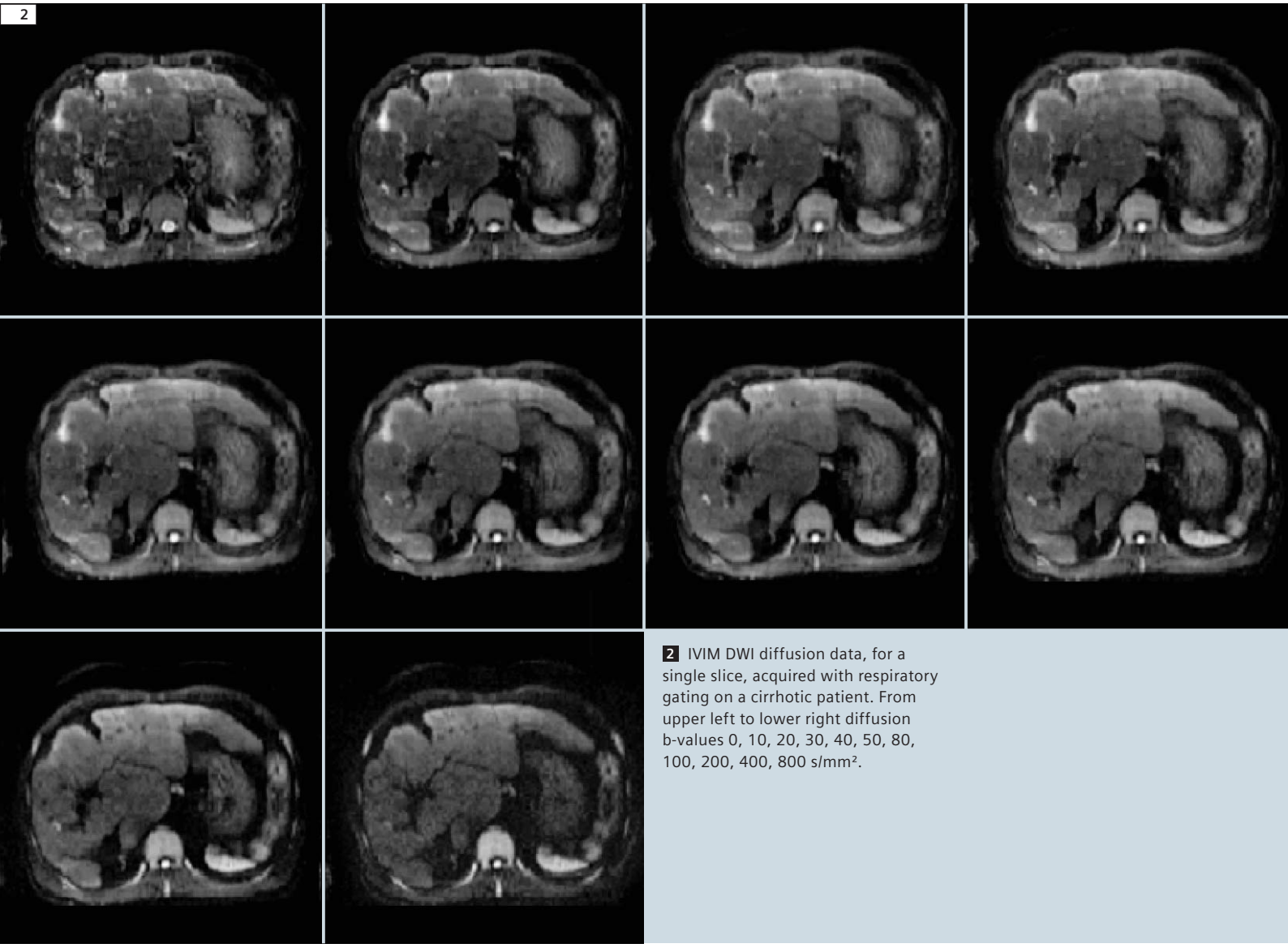
In their seminal paper Le Bihan et al. wrote: "Thoracoabdominal studies were not possible at the time of this work, due to motion artifacts and signal-to-noise ratio (SNR) considerations". The sequence used could only allow cardiac gating. Long TE was necessary to achieve the highest b-value needed for the study, while T2 relaxation in abdominal tissue is shorter than in the brain [2] leaving very low signal left. Strong gradient amplitudes could not be used because Eddy current was not sufficiently compensated on their scanner at this time.

Nowadays, diffusion-weighted (DW) Echo Planar Imaging (EPI) sequence, available on MAGNETOM MR scanners, allows both respiratory gating using a pneumatic belt, or more recently, a navigator. Eddy currents are now well compensated



1 Example of signal decay as a function of the diffusion b-values in a given voxel of a right lobe of the liver of a cirrhotic liver. Circles represent Normalized Signal, the bold solid line is the IVIM non-linear regression fit providing D, D* and f. Light solid lines represent D and D* decay curves separately. Finally the dashed line is the mono-exponential fit applied on b 0, 400, 800 s/mm², as described in [6], which provides ADC.

*WIP – Work in progress. The information about this product is preliminary. The product is under development and not commercially available in the U.S., and its future availability cannot be ensured.

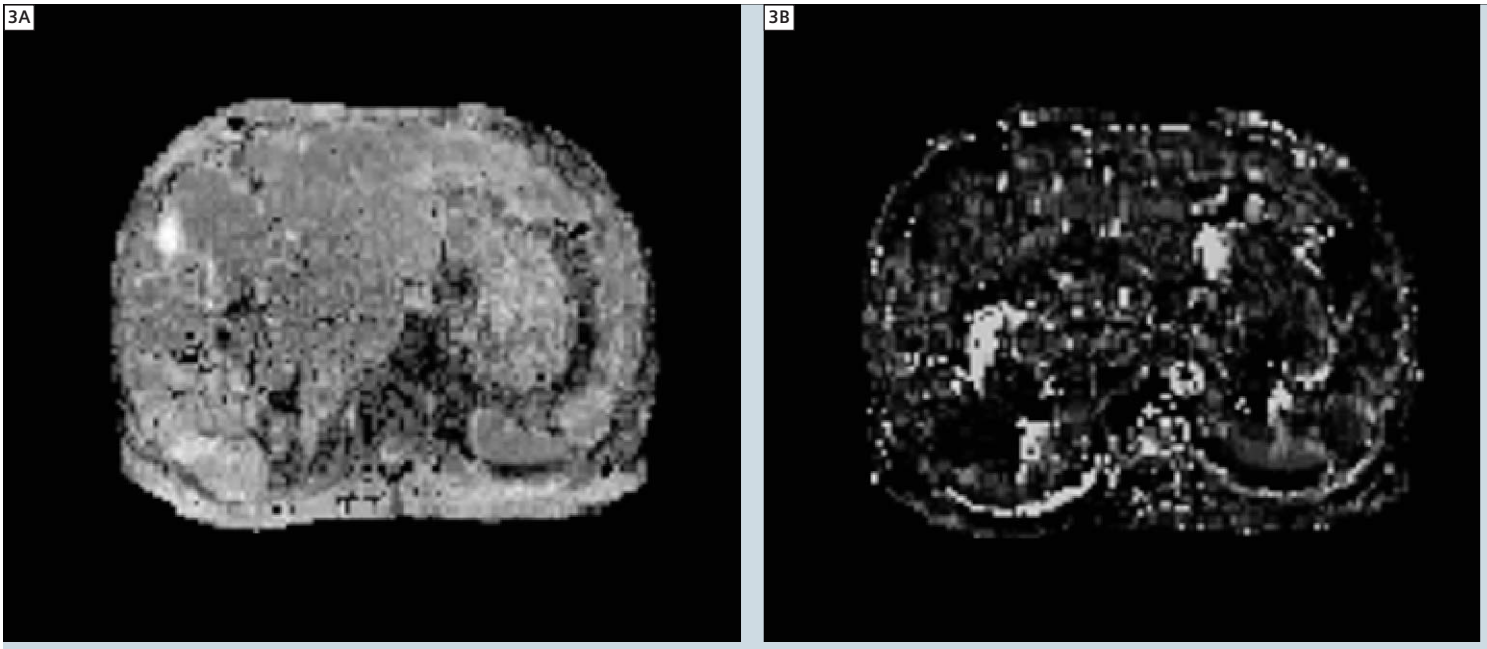


2 IVIM DWI diffusion data, for a single slice, acquired with respiratory gating on a cirrhotic patient. From upper left to lower right diffusion b-values 0, 10, 20, 30, 40, 50, 80, 100, 200, 400, 800 s/mm².

[3]. Strong gradient amplitudes can be achieved while decreasing the minimum TE reachable for DW imaging. All these evolutions now allow the application of IVIM technique to the moving organs and more particularly to the liver.
In highly perfused tissue, such as the liver, the D* component is expected to strongly affect the signal decay especially at low diffusion b-values [4]. Lemke et al. have recently shown [5] that, in the liver, the suppression of the vascular component of the signal, using Dark Blood preparation, could strongly reduce the D* contribution. These findings confirm that the vascular component has an effect on the signal decay when it is weighted by diffusion gradients.
Classic liver disease can progressively lead to diffuse fibrosis with cirrhosis as an end stage. The diagnostic of cirrhosis is based on pathological examination of a tissue sample. Functional imaging techniques using either ultrasound, or computed tomography and MR imaging have been proposed to assess and follow-up cirrhosis [6]. Recently, Luciani et al. [7] proposed the application of the IVIM-DWI technique to the assessment of cirrhotic liver with liver pathology on explanted livers taken as the reference. The preliminary results of this study are reported below.

Clinical protocol

The measurements were performed on a 1.5T Siemens MAGNETOM Avanto. Six elements of the Spine Matrix coil array embedded in the patient table and 6 ele-



3 IVIM maps for a cirrhotic patient, obtained using data presented in Fig. 2. From upper left to lower right D, D*, f, and ADC maps are respectively presented.

ments of the Body Matrix coil array were selected for optimum signal reception. The IVIM DW sequence was designed to study liver routinely. The sequence parameters were the following: FOV 300 x 250 mm², matrix 138 x 90, twelve 5 mm thick slices were acquired with 3 averages, BW 1342 Hz/px, acceleration factor 2 with *syngo* GRAPPA reconstruction. The sequence was triggered with a pneumatic respiratory belt but could also be done with a PACE (Prospective Acquisition CorrEction) navigator [9] leading to a TR ~3 sec. Ten b-values (b = 0, 10, 20, 30, 40, 50, 80, 100, 200, 400, 800 s/mm²) were applied in the 3 perpendicular directions once by scan for a TE 70 msec. TA, depending on the respiration rate, was equal to 2–3 min. The analysis was done pixel by pixel at Matlab (Mathworks, Natick, MA, USA) in two steps as described extensively in [7]. Firstly, since D* contribution can be neglected at high b-values, D was extracted using high b-values (b ≥ 200 s/mm²) and a mono-exponential fit. Secondly, a non-linear regression was applied to solve remaining parameters: f the vascular volume faction and D*. In addition an ADC measurement was calculated using b = 0, 200, 400, 800 s/mm² and a simple mono-exponential fit to compare our findings with the literature [6].

The study was approved by the Institutional Review Board of the University Hospital. The IVIM sequence was applied in addition to the routine liver MR imaging protocol. Two populations were included in the study: livers with METAVIR F4 score at the liver biopsy [8] performed within the past two months and healthy livers with no history of hepatic diseases and no evidence found during the MR exam.

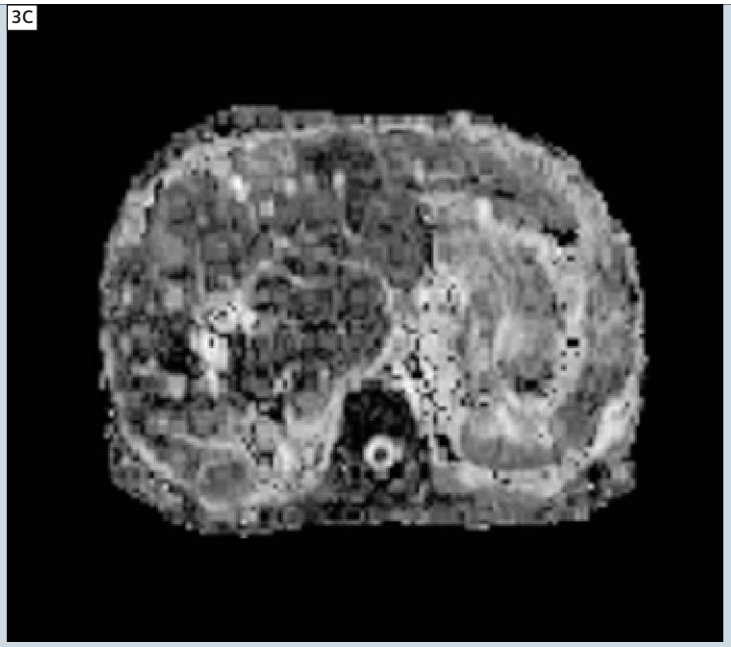
Discussion

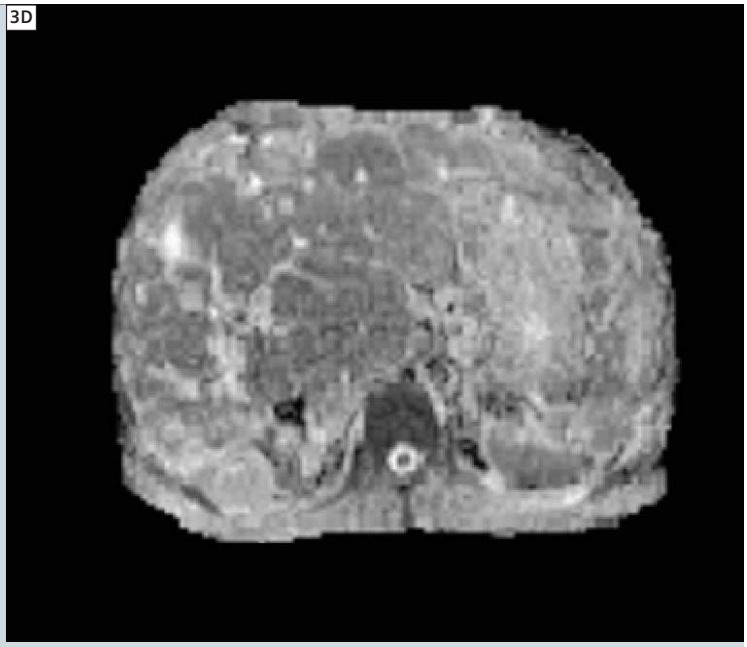
All curves of signal decrease demonstrated a bi-exponential decay whether the measurements were obtained in the healthy liver group or in the cirrhotic liver group (Fig. 1). Figure 1 also shows that the mono exponential fit usually applied does not fit well with the decay observed in liver tissue. Figures 2 and 3 show examples of diffusion maps both for healthy and cirrhotic patients. Findings show that the liver diffusion component linked to perfusion (D*) significantly decreased in the cirrhotic liver group compared the healthy liver group and could account for the reduced ADC in cirrhotic livers reported in previous studies [6] and also seen in this study (Figures 2 and 3).

It is generally accepted that liver cirrhosis is associated with reduced liver perfusion: The increased arterial flow triggered by intra-hepatic portal hypertension in liver fibrosis is insufficient to compensate for the reduced portal flow [10]. For Moreno et al. [10, 11], the mean portal flow in healthy subjects was 20.9 ± 4.1 ml/min/kg as opposed to 6.5 ± 5.6 ml/min/kg in patients with cirrhosis. This could explain the observed decay of D* in cirrhotic livers.

ADC was found comparable to the literature for healthy and cirrhotic groups. ADC was significantly higher than D both in the healthy liver group and in the cirrhotic liver group.

Results of IVIM DW imaging suggest that the diffusion component related to the molecular displacement (D) does not differ significantly between cirrhotic and healthy livers. Similar findings have already been reported by Yamada et al. [4], who found that D was significantly lower than ADC, thus suggesting that





differences reported in ADC between patients with cirrhosis and healthy patients were mainly related to the perfusion component of liver diffusion. Therefore, even if the study is preliminary and limited, it is clear that the IVIM model seems to be more properly designed to accurately fit the diffusion behavior of liver tissue (Fig. 1). It shows also that the assessment of D* may potentially be considered as a surrogate marker of capillary liver perfusion especially and could be a good indicator of the fibrosis disease. Further investigations are expected to confirm its potential to discriminate liver fibrosis.

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