Liver diffusion/perfusion using biexponential analysis with 30 b-values

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Introduction: Diffusion Weighted Imaging (DWI) is growing in clinical applications in MR imaging evaluation of the abdomen. The measurement of random molecular motion is the basis of DWI. Each substance has a diffusivity (D) defined by the formula $D = r_{rms}^2/6t$, which provides a measure of the distance traveled by a molecule in a given time. When there are no physical barriers to molecular motion, the diffusion is unrestricted and D is high, but when physical barriers are present the diffusion is restricted.

To measure diffusivity correctly, confounding effects need to be addressed. Not all molecular motion in tissues is random. Transport of molecules across cell membranes and within cells has been reported as contributing to changes seen on DWI. Capillary flow, or perfusion, is believed to introduce a fast diffusion component in liver in addition to the slower, random diffusion of molecules (1–3). Another known confound for diffusion measurements is the approach to longitudinal steady-state, which can take one or more excitations to establish (4). The signal is always much higher on the first excitation than on subsequent ones. If a b = 0 image is acquired on the first excitation and a b > 0 image is acquired on the second excitation, then it may appear that the tissue is extremely sensitive to b-value. It is possible this effect is a confound for measurements of fast diffusing components in liver. The purpose of this study is to investigate and measure perfusion and equilibration effects in DWI of the liver.

Methods: This prospective, pilot study was performed on 4 healthy subjects using a 3.0T GE scanner. A DWI spin echo EPI sequence was used with water excitation, TR 1500 ms, TE 55 ms, matrix 128x160 and 30 b-values acquired in a single 45 sec breath-hold, as follows: 0, 0, 0, 0, 0.6, 0.8, 1.1, 1.4, 1.9, 2.5, 3.3, 4.4, 5.9, 7.8, 10.4, 13.8, 18.3, 24.4, 32.4, 43.2, 57.4, 76.4, 102, 135, 180, 239, 318, 424, 564 & 750 sec/mm^2. No "dummy" excitations were used. Crusher gradients around the 180° RF pulse give an intrinsic b-value of around 2 sec/mm^2 for this sequence so the actual b-values are slightly higher than the listed values. The sequence was repeated approximately every 10 minutes for 90 minutes, with subjects eating an *ad lib* meal after the second repetition to alter the perfusion rate in the liver (2). The maximal increase of hepatic blood flow is expected approximately 1 hour after eating (5).

Results: As shown in Figure 1, there is a 40% decrease between the first and second excitations. This that one dummy pulse is sufficient for the longitudinal equilibrium to become established. Excluding the first b = 0 data point, unconstrained biexponential curve-fitting was performed using Levenberg-Marquardt. Representative data sets are shown in Figure 2 at two time-points: pre- and 1 hour post-prandial, with best-fit curves overplotted on the data. Fitted parameters for all time-points are given in Table I. The slow and fast diffusivities and the signal fraction of the fast component are presented (mean over subjects ± standard deviation).

Discussion: To the best of our knowledge, this large number of b-values to study DWI of the liver has not been done previously. Our study confirms the need for one or more dummy pulses to achieve steady state and also finds support for fast and slow components of diffusion, consistent with intravoxel incoherent motion (1–3). The diffusivity and fraction of the fast component were measured before and after eating to increase perfusion. Results are somewhat variable, but suggest the fast fraction may increase postprandially.

Figure 1: The averaged signal across repetitions versus excitation number for the first 15 excitations.

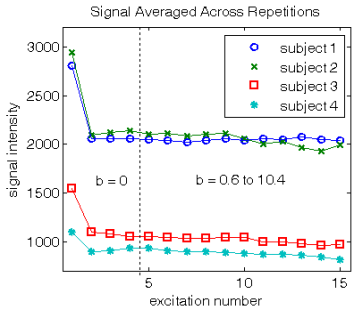

Table I: Average diffusion properties across subjects (n = 4).

Time-Point	$D_{slow} \times 10^{-3}$ (mm^2/sec)	$D_{fast} \times 10^{-3}$ (mm^2/sec)	Fraction of Fast Component
1	0.97 ± 0.21	164 ± 108	0.12 ± 0.08
2	0.90 ± 0.18	68 ± 55	0.10 ± 0.11
3	0.89 ± 0.17	379 ± 437	0.04 ± 0.05
4	0.93 ± 0.25	73 ± 57	0.24 ± 0.11
5	0.94 ± 0.23	74 ± 60	0.20 ± 0.11
6	0.82 ± 0.13	48 ± 50	0.22 ± 0.05
7	0.97 ± 0.24	197 ± 234	0.19 ± 0.05

Refs: (1) Yamada. *Radiology* 1999; 210: 617. **(2)** Hollingsworth. *NMR Biomed* 2006; 19: 231. **(3)** Le Bihan. *Radiology* 2008; 249: 748. **(4)** Shiehmorteza. *J Magn Reson Imaging* 2009; 30: 547. **(5)** Dauzat. *Eur J Appl Physiol Occup Physiol* 1994; 68: 373.

Figure 2: The signal in each subject as a function of b-value at time-points 1 and 7 (note: first excitation excluded).