The effect of ROI size and analysis technique on IVIM parameters in the liver

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Target Audience Researchers and clinicians interested in body/liver imaging and disease, with a particular interest in diffusion imaging.

Purpose The DWI signal decay as a function of b-value in the liver has been shown to be non-monoexponential[1,2,3]. The intravoxel incoherent motion (IVIM) technique was developed to model this non-monoexponential signal decay. The IVIM concept is that diffusion within *in vivo* tissue is more complex than simple random Brownian motion of water molecules and includes a faster component that might represent the microcirculation of blood through capillaries[4]. The IVIM model is biexponential (i.e. two component model) and includes terms for the fraction of received signal attributed to moving blood (perfusion fraction, f_p), the diffusion of the moving blood (pseudodiffusion, D_p), and the diffusion excluding contributions from moving blood (true molecular diffusion, D_t), (Equation 1). Once the data is collected, however, there are a number of different ways to analyze that data. The choice of ROI and method of parameter extraction can all affect the results. In this study, IVIM parameter values are compared with different ROIs and analysis techniques in order to determine which combination provides the best separation between normal volunteers and cirrhotic patients.

Methods Eight subjects with no known history of abdominal disease participated in this study. Each subject underwent two consecutive respiratory-triggered spin echo EPI DWI scans on a GE 1.5T scanner. TR varied based on subjects' breathing and ranged from 6-9s. Additional parameters were: FOV=36-50cm, TE=63.4ms, 3 orthogonal diffusion directions acquired simultaneously (3in1), b = (0, 10, 25, 50, 100, 150, 200, 400, 800) s/mm^2, slice thickness = 8 skip 2mm, and a matrix size of 192x256. Fifteen cirrhotic patients were also imaged with the same parameters, but only one DWI scan. IVIM parameters were calculated using the segmented approach and analysis methods previously published (3,4). The segmented approach takes advantage of the fact that, since $D_p >> D_t$, its effect can be neglected when b > 200 s/mm^2. Thus, the segmented method involves using only high b-values to estimate D_t and f_p. All curve-fitting analyses were performed in Matlab using a Levenberg-Marquardt algorithm (nlinfit). Poorly fit voxels, defined as voxels where the Jacobian matrix was ill-conditioned, were excluded from the analysis. Two different regions of interest (ROIs) were evaluated. Large circular ROIs with 20mm radii were drawn in three consecutive slices in the lower right lobe of the liver. In addition, smaller, 5mm radius ROIs were placed in the same slices. ROIs were placed to avoid large intrahepatic vessels. Mean and median values of each parameter were extracted on a voxelwise basis within the ROI (mean and median methods). The DWI signal was also averaged within the ROI and the averaged signal was then fitted to obtain one value for each IVIM parameter within an ROI (ROI method). Large and small ROIs were compared with a paired two-sample t-test. Normal livers were compared to cirrhotic livers with an unpaired two-sample t-test.

$$\frac{S_b}{S_0} = \left(1 - f_p\right) \cdot e^{-b \cdot D_t} + f_p \cdot e^{-b \cdot D_p} \quad (1)$$

Table 1. IVIM parameter averages

		Fractional Perfusion			Molecular Diffusion			Pseudodiffusion		
		Large	Small	P-Val	Large	Small	P-Val	Large	Small	P-Val
Mean	Normal	0.26 (0.01)	0.22 (0.01)	2e-5	1.12 (0.04)	1.12 (0.04)	NS	51.1 (3.5)	44.0 (4.1)	0.001
	Cirrhotic	0.26 (0.01)	0.23 (0.01)	3e-5	1.09 (0.04)	1.10 (0.05)	NS	30.3 (2.1)	30.0 (2.1)	NS
	P-Val	NS	NS		NS	NS		5e-6	0.002	
Median	Normal	0.25 (0.01)	0.21 (0.01)	8e-5	1.10 (0.04)	1.10 (0.04)	NS	25.1 (4.0)	24.1 (4.7)	NS
	Cirrhotic	0.24 (0.01)	0.22 (0.01)	4e-4	1.08 (0.04)	1.09 (0.05)	NS	12.8 (1.0)	13.0 (1.2)	NS
	P-Val	NS	NS		NS	NS		0.002	0.011	
ROI	Normal	0.24 (0.02)	0.20 (0.01)	5e-4	1.11 (0.04)	1.11 (0.04)	NS	96.2 (11.2)	78.2 (11.3)	0.008
	Cirrhotic	0.19 (0.02)	0.16 (0.02)	0.023	1.08 (0.04)	1.09 (0.05)	NS	49.1 (6.6)	57.9 (10.0)	NS
	P-Val	0.031	NS		NS	NS		0.001	NS	

Data is shown as mean (standard error); P-Val = p-value of two-sample t-test; NS = Not Significant.

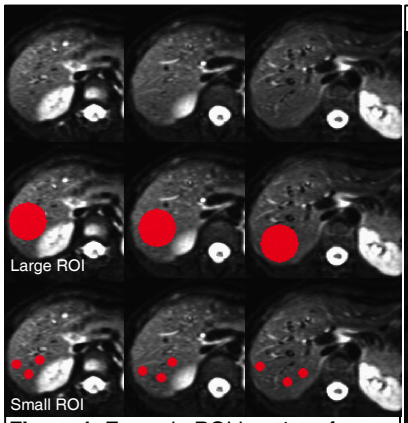

Figure 1. Example ROI locations for one representative subject.

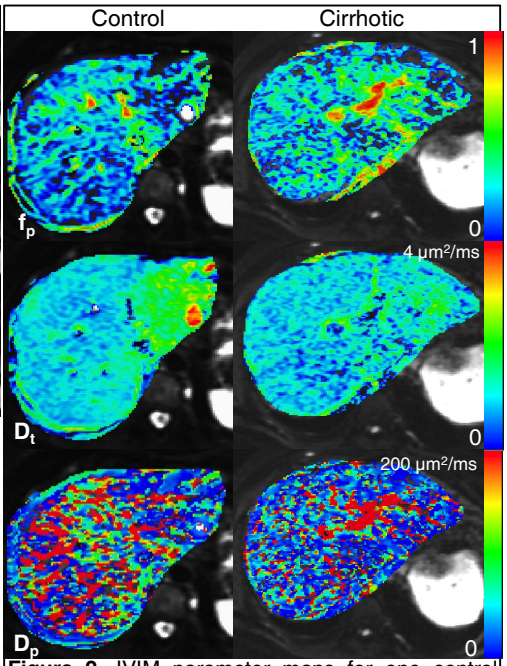

Figure 2. IVIM parameter maps for one control subject and one cirrhotic patient.

Results Results are summarized in Table 1. The f_p was higher in the large ROIs versus the small ROIs for each of the mean, median, and ROI techniques in both control subjects and cirrhotic patients. D_p was higher for the large ROI versus the small ROI for the mean and ROI techniques in the control subjects. The f_p was higher in normal livers compared to cirrhotic livers for only the large ROI, ROI method. D_p was higher in normal livers compared to cirrhotic livers for all cases except the small ROI, ROI technique. Large ROIs provided greater separation between normal and cirrhotic livers, with the lowest p-value being seen for the large ROI, mean technique (P = 5e-6). Example ROIs are shown in Figure 1, and example parametric maps for one control subject and cirrhotic patient are shown in Figure 2. Finally, D_p varied substantially depending on analysis technique with the ROI technique resulting in the highest D_p and median technique the lowest.

Discussion Higher values were found for the perfusion-related IVIM parameters for the large ROIs compared to the small ROIs. This is likely due to the fact that large hepatic vessels could not be completely avoided due to the size of the large ROIs. In general, there was a greater separation between normal and cirrhotic livers using the large ROIs compared to the small ROIs. This may be caused by alterations in flow in large intrahepatic vessels between normal livers and cirrhotic livers increasing the differences between the two groups. Two parameters (f_p and D_p) were significantly different between normal and cirrhotic livers for the large ROI, ROI technique. However, in general, parameters extracted with the ROI technique were more variable than the mean and median techniques. This may be due to the way the parameters are extracted for the voxelwise versus ROI techniques. The voxelwise techniques implicitly exclude noisy voxels, as those voxels were most likely to be poorly fit. The ROI technique did not exclude any voxels for the total signal average.

Conclusion The choice of ROI and analysis technique can affect IVIM parameter values. Parameters extracted from large ROIs provided the best separation between normal and cirrhotic livers.

References 1. Luciani A et al. *Radiology*. 249(3):891-9, 2008. 2. Patel J et al. *JMRI*. 31:589-600, 2010. 3. Guiu B et al. *Radiology*. 265(1):96-103, 2012. 4. Le Bihan D et al. *Radiology*. 168:497-505, 1988.