Spatially constrained model of body Diffusion-Weighted MRI signal decay increases precision of parameter estimates

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Introduction: Diffusion-weighted MRI (DW-MRI) of the body is a non-invasive imaging technique sensitive to the incoherent motion of water molecules inside the area of interest. A model for low b-factor range (< 1000 s/mm^2) incorporates a combination of a slow diffusion component associated with the Brownian motion of water molecules, and a fast diffusion component associated with the bulk motion of water within micro-capillaries. This so-called, intra-voxel incoherent motion (IVIM) model is characterized using a slow diffusion coefficient (*D*) and a fast pseudo-diffusion coefficient (*D**) for the exponential two decay rates and the fractional contribution (*f*) of the micro-capillary component (1).

However, the Incoherent Motion (IM) is a property of the tissue, not of the voxels, and does not stop at voxel boundaries. In homogeneous regions, it extends beyond voxel boundaries, and these properties change at changes in tissue microstructure and macrostructure, not at the voxel boundaries. We propose therefore to drop the dependency on the voxel structure, and to refer to the Incoherent Motion generating the signal arising from multiple connected voxels. In particular, we introduce a new model of DW-MRI signal decay (IM-MRI) in which the parameters of the two exponential decays at one voxel depend on the parameters of the two exponential decay model at all of the adjacent voxels by introducing a spatial homogeneity prior. Our new IM model is therefore extending the original Intra Voxel Incoherent Motion (IVIM) model by considering the same model of Incoherent Motion but not limited to voxel boundaries (2).

Essentially, our IM model produces estimates of IVIM parameters for all voxels simultaneously, rather than solving for each voxel independently. As a result, we increase the reliability of the parameter estimates from the DW-MRI data without acquiring additional data or losing spatial sensitivity. The goal of this work was to assess the improvement in the precision of Incoherent Motion parameter estimates by using our novel spatially constrained IM model compared to the traditional IVIM model.

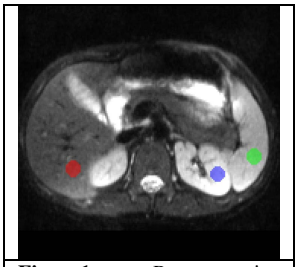

Fig. 1: Representative example of the regions of interest used to analyze the fit quality overlaid on the DW-MRI image with b-value=5 s/mm^2

Materials and Methods:

We obtained DW-MRI images of 30 subjects - 18 males and 12 females with a mean age of 14.7 (range 5-24, std 4.5) that underwent MRI studies due to suspected inflammatory bowel disease between Sep. 2010 and Sep. 2011. Radiological findings of the study subjects' abdominal organs (i.e., liver, kidneys and spleen) were normal. We carried out MR imaging studies of the abdomen using a 1.5-T unit (Magnetom Avanto, Siemens Medical Solutions, Erlangen, Germany) with a body-matrix coil and a spine array coil for signal reception. Free-breathing single-shot echo-planar imaging was performed using the following parameters: repetition time/echo time (TR/TE) = 6800/59 ms; SPAIR fat suppression; matrix size = 192×156; field of view = 300×260 mm; number of excitations = 1; slice thickness/gap = 5 mm/0.5 mm; 40 axial slices; 8 b-values = 5,50,100,200,270,400,600,800 s/mm^2. A tetrahedral gradient scheme was used to acquire 4 successive images at each b-value with an overall scan acquisition time of 4 min. Diffusion trace-weighted images at each b-value were generated using geometric averages of the images acquired in each diffusion sensitization direction.

We estimated the model parameters from the in-vivo DW-MRI data for each voxel using both the independent voxel-wise IVIM model and our spatially constrained IM model with the "fusion bootstrap moves" optimization technique (2).

We calculated the averaged model parameter values obtained using the two different models over three regions of interest (ROI) - each manually annotated; in the liver, the spleen, and the kidney (Fig. 1). We determined whether there was a statistically significant difference between the average model parameter values estimated with the different estimation methods with a two-tailed, paired Student's t-test, with p<.05 indicating a significant difference.

We calculated the precision of the parameter estimates by means of the coefficient of variation (CV) of the parameter estimates at each voxel in the IVIM and IM maps of each patient using model-based wild-bootstrap analysis (3). For each patient, we averaged the CV values over the same, three ROIs mentioned above. We examined the statistical significance of the difference in the precision of the parameter estimates for the IVIM and IM models using a two-tailed paired Student's t-test with p<.05 as indicating a significant difference. We performed the statistical analyses with standard statistical software (Matlab® R2010b; The MathWorks, Natick, MA, USA).

Table 1: Incoherent Motion model parameters values (mean, std) for each organ as calculated using the IVIM and the IM models.

		D		D*		F	
		mean	std	mean	std	mean	std
Liver	IVIM	1.02	0.32	41.22	26.58	0.25	0.10
	IM	0.95	0.26	34.43	36.22	0.28	0.10
	p-value	**0.0011**		**0.0254**		**<0.001**	
Spleen	IVIM	0.91	0.56	20.74	18.25	0.10	0.08
	IM	0.82	0.37	21.04	31.44	0.13	0.09
	p-value	**0.0297**		0.9470		**0.0045**	
Kidney	IVIM	1.76	0.32	23.58	26.72	0.19	0.12
	IM	1.73	0.30	21.82	30.16	0.21	0.12
	p-value	**0.0152**		0.1371		**0.0082**	

Results: Table 1 summarizes the average values of the incoherent motion parameters for each organ's ROI, as estimated by the four methods along with the level of significance of the difference (two-tailed paired Student's t-test, N=30, p<0.05). Fig. 2 depicts the bar plots of the CV over the 30 subjects for the incoherent motion parameters. Our IM model reduced the CV of the D* parameter estimates by 43%; the CV of the f parameter estimates by 37%; and the CV of the D parameter by 17%. The improvement in CV was significant for all parameters (p<0.0001).

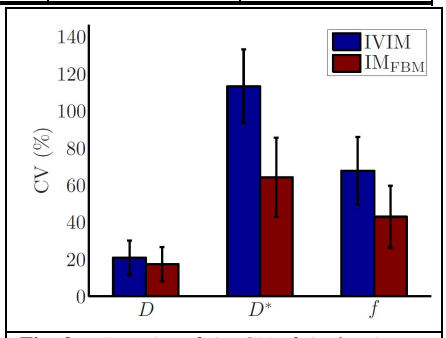

Fig. 2: Bar plot of the CV of the incoherent motion parameters as estimated from 30 patients. The CV was significantly lower (p<0.0001) when using our IM-FBM approach than when using the IVIM approach for all parameters.

Discussion: The role of incoherent motion parameters as quantitative imaging biomarkers for various clinical applications is becoming increasingly important. However, the Incoherent Motion (IM) is a property of the tissue, not of the voxels, and does not stop at voxel boundaries. In this work, we introduce a new model of DW-MRI signal decay due the incoherent motion of the water molecules which is not limited to the voxel boundaries by removing the dependency on the intra-voxel measurements (IM-MRI). We demonstrated the improvement achieved by using our IM model using *in-vivo* abdominal DW-MRI data of 30 patients. We are planning to evaluate the clinical advantage achieved by using this new model in characterizing physiological processes compared to the previously used independent voxel-wise IVIM model.

Bibliography:

1. Le Bihan D, Breton E, Lallemand D, Aubin ML, Vignaud J, Laval-Jeantet M. Separation of diffusion and perfusion in intravoxel incoherent motion MR imaging. Radiology. 1988 Aug;168(2):497-505.
2. Freiman M, Perez-Rossello JM, Callahan MJ, Voss SD, Mulkern RV, Warfield SK. Reliable assessment of perfusivity and diffusivity from diffusion imaging of the body. Med Image Comput Comput Assist Interv. 2012;15(1):1-9.
3. Davidson R, Flachaire E. The wild bootstrap, tamed at last. Journal of Econometrics. 2008;146(1):162 - 9.