The effect of white matter perfusion on diffusion MRI based microstructural tissue models

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Audience: Researchers interested in disentangling microstructural and perfusion information.

Introduction: Non-Gaussian diffusion models have a strong benefit over Gaussian diffusion modelling in that they can estimate restricted diffusion components that contain information on intracellular water [1, 2]. These models, however, do not take into account perfusion effects at the microscopic scale, as can be measured using intra-voxel incoherent motion fitting (IVIM) [3]. This causes diffusion-weighted signal attenuation at low b-values with a much higher pseudo-diffusion coefficient (D*) than the true tissue diffusion coefficient. Not taking this pseudo-diffusion into account affects the estimated diffusion parameters in these models. In this work, we show the effects of pseudo-diffusion on a microstructural diffusion model, NODDI, to elucidate unexpected model parameter estimates.

Methods: Acquisition - Two NODDI datasets (test-retest) were acquired on a healthy male subject (28 yo), both with 11 b=0-images and three shells at b=300, 700, and 2500 s/mm^2 with 8, 32, and 64 DWIs per shell, respectively. FOV of 24×24 cm was acquired with a 96×96 and 50 slices of 2.5 mm thick. SENSE=2, TE/TR = 71.7/5200 ms, and scan time of 9m58s. Additionally, an IVIM dataset was acquired with the same FOV and resolution, but with b-values of 0, 20, 40, 60, 80, 100, 125, 150, 200, 250, 500, 750, 1000 s/mm^2 (6,3,3,3,3,3,3,3,3,3,6,8,10 DWIs per b-values and NEX=2) at TE = 58 ms, in a 9m53s scan. Modelling - Motion and distortion correction was performed in ExporeDTI [4]. From both corrected NODDI datasets, three DWI subsets were extracted: i) with all data (b=0, 300, 700, 2500; ALL_1 & ALL_2); and ii) a dataset without the b=0-images (NOb0_1 & NOb0_2). The high pseudo-diffusion coefficient of blood means there is no perfusion-related signal left at b>=300 s/mm^2 so the second DWI subset is not affected by perfusion [5]. NODDI fitting was performed using the open-source Matlab NODDI toolkit [2]. For the IVIM dataset, all DWIs of each b-value were averaged to generate a single DWI. A WM mask was created based on the ADC map. An initial fit was done on the data averaged over the WM mask to initialize the voxel-wise fitting performed within the WM mask. For the voxel-wise fit, the ADC was estimated from the data with b>300 s/mm^2 and fixed when fitting the perfusion fraction (f) and D* in NiftyFit, part of NifTK [6]. Analysis - Test-retest reproducibility was calculated for three NODDI parameters (intracellular volume fraction, ficvf; isotropic volume fraction, fiso; and orientation dispersion index, ODI), for each DWI subsets (ALL & NOb0) as the coefficient of variation (CoV=σ/μ) between test and retest. Differences in estimated parameter values were determined between the ALL and NOb0 subsets, and interpreted w.r.t. the reproducibility estimates. To determine the sensitivity of NODDI volume fractions to perfusion they were correlated to IVIM-derived perfusion parameters.

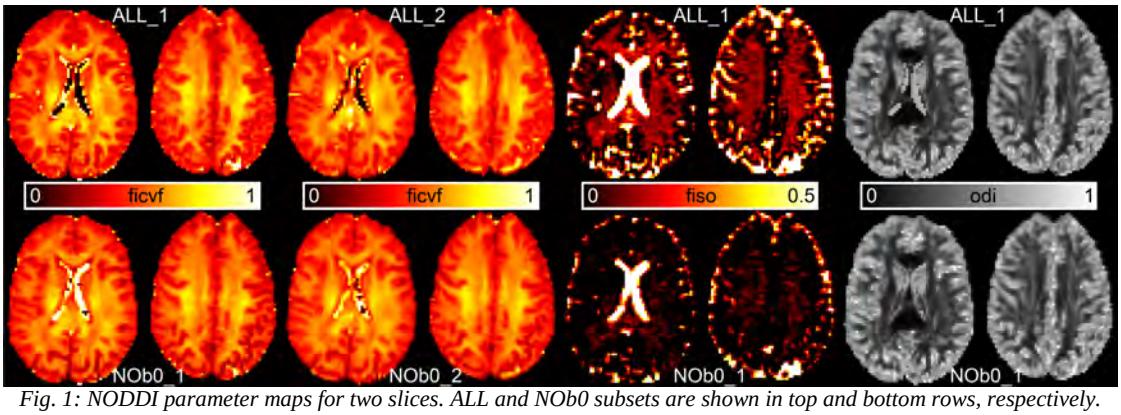

Fig. 1: NODDI parameter maps for two slices. ALL and NOb0 subsets are shown in top and bottom rows, respectively.

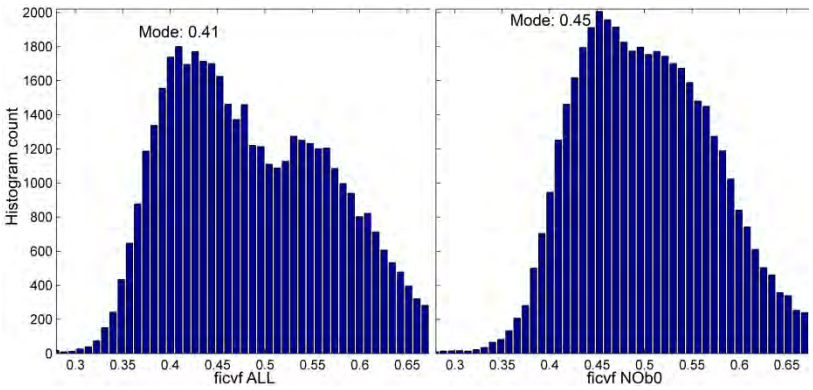

Fig. 2: Histograms of ficvf values from the ALL and NOb0 datasets in the WM.

Table 1: Coefficient of Variation between test-retest datasets

	ficvf	fiso	ODI
ALL	2.53	0.74	2.23
NOb0	2.67	0.47	2.23

Table 2: NODDI parameter values for all subsets (mean over WM)

	ficvf	fiso	ODI
ALL	0.49	0.061	0.39
NOb0	0.50	0.013	0.40

Results: Fig. 1 shows example maps of ficvf (test-retest), fiso, and ODI for two slices for both the ALL and NOb0 datasets. Reproducibility of all parameters and in all subsets is high (Table 1). Clear differences can be observed in the WM between the ALL and NOb0 datasets for values of fiso (Table 2). Closer inspection of ficvf values in the WM shows differences between the ALL and NOb0 datasets (Fig. 2). Correlation of IVIM-derived fD* values with NODDI-based isotropic diffusion in WM voxels is shown in Fig. 3, showing moderate correlation.

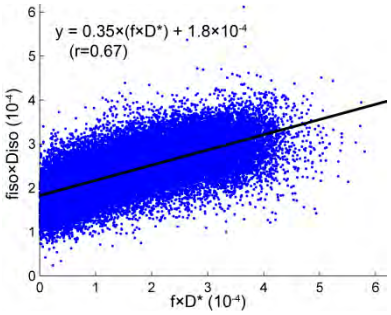

Fig. 3: Correlation between IVIM-based perfusion (f×D) and isotropic diffusion in NODDI (fiso×Diso). Here, Diso is the diffusivity of the fiso compartment (fixed at 3×10^{-3} mm/s^2).*

Discussion: Fitting the NODDI model to DWI data without b=0-images results in a five times lower isotropic compartment than with the b=0-images. Part of the high fiso in the full NODDI dataset can be explained as an effect from perfusion causing DWI signal attenuation at b<300 s/mm^2. Other factors causing non-zero fiso in WM could be the model's limitation in only modelling a single fiber population. In multi-fiber voxels the high parallel diffusivity along non-dominant fiber orientations could be misrepresented as originating from an isotropic diffusion compartment. Although Table 2 shows that the mean ficvf and ODI values within the WM are not affected by this, there is a pronounced difference in the histogram of ficvf values when not including the b=0-images. The mode of the histogram shifts significantly from 0.41 to 0.45, with a general increased presence of higher ficvf values. Whether this also partially originates from the same perfusion effects as that affect fiso is to be investigated in more detail. The effects of WM perfusion are likely to extend to other microstructural tissue models and, more generally, to other non-Gaussian diffusion MRI methods.

References: [1] Assaf et al., NeuroImage 2005:27;48-58; [2] Zhang et al., NeuroImage 2010:61;1000-16; [3] Le Bihan et al., Radiology 1988:168;497-505; [4] Leemans et al., ISMRM 2009, p3537; [5] Le Bihan, NeuroImage 2012:62;1131-6; [6] http://cmictig.cs.ucl.ac.uk/research/software