# Assessing scan-rescan reproducibility of the parameter estimates from NODDI

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**PURPOSE** This work aims to establish the scan-rescan agreement of the parameters estimated by *Neurite Orientation Dispersion and Density Imaging (NODDI)* [1], a recent diffusion MRI technique that can directly quantify microstructural indices of neurites *in vivo,* in the human brain. NODDI employs a multi-compartment model that distinguishes brain tissue into the intra- and extra-cellular compartments. It provides two key parameters, the neurite density ($v_{IC}$), which is the intra-cellular volume fraction, and the orientation dispersion index (ODI), which characterizes the orientation dispersion of the axonal and/or dendritic projections. In [1], these parameters have been demonstrated to provide more direct measures of microstructure than the standard indices from *Diffusion Tensor Imaging* (DTI) [2]. Compared to the existing multi-compartment techniques [3], NODDI has the advantage of being more clinically feasible, requiring only a two-shell protocol with a modest increase from the imaging time of DTI. With the rapid adoption of the technique in biological and clinical research, it becomes important to characterize the precision of the parameters that NODDI provides. Hence, in this work, we conduct a reproducibility study of NODDI, by assessing the scan-rescan agreement of the NODDI estimates in a group of healthy subjects. We additionally determine the reproducibility of standard DTI measures in the same subjects to provide a comparison to that of NODDI.

**METHODS** Subjects and Data Acquisition: Four healthy volunteers (2 males and 2 females) were recruited for this study. For each subject, diffusion-weight (DW) MR images were acquired on a 3T Philips scanner (Gmax = 60 mT/m), using an optimized NODDI protocol for the scanner as detailed in [1]. The NODDI protocol consists of two high-angular resolution diffusion imaging (HARDI) shells with b=711 s/mm$^2$ (30 directions) and b=2855 s/mm$^2$ (60 directions), as well as 9 b=0 volumes. Each subject was scanned in two imaging sessions separated by a week to test scan-rescan reproducibility. Standard T1-weighted anatomical scans were additionally performed during each imaging session to enable three-tissue-class segmentation to be used for tissue-specific quantification. Model Fitting: For each subject, after correcting for motion and eddy-current distortions, DW-MR images were used to fit the DTI and NODDI models. The standard DTI measures, Fractional anisotropy (FA) and mean diffusivity (MD), were determined using Camino [4]; the NODDI parameters were computed using the NODDI Matlab toolbox. Image Processing: To place each subject's parameter estimates into a common space, spatial normalization was applied to the b=0 volumes using affine image registration. Gray and white matter tissue segmentation was estimated using the anatomical scans and mapped to the corresponding b=0 volume to compute tissue-specific reproducibility of the parameter estimates. Reproducibility Analysis: The scan-rescan reproducibility of the parameter estimates were assessed with two metrics. First, we compute the Pearson's correlation coefficient of the scan and rescan estimates of each parameter. It quantifies the consistency in the rank ordering of the two sets of parameter estimates and a value close to 1 means very high consistency between the estimates. We calculate this metric separately for each subject and report its mean and standard deviation over the study cohort. Second, we compute the coefficient of variation of each parameter, which measures the scan-rescan variability of a parameter relative to its mean. It is computed voxel-wise and separately for each subject, then averaged over the voxels in a region of interest and over the entire cohort. For both metrics, the analysis was conducted separately for gray and white matter.

**RESULTS & DISCUSSION:** Figure 1 illustrates qualitatively the scan-rescan reproducibility of the NODDI parameters in the normalised space, in comparison to the standard DTI indices, for two of the subjects. The quantitative assessment results are shown in Table 1, for Pearson's Correlation Coefficient, and in Table 2, for Coefficient of Variation. Both qualitatively and quantitatively, we can observe that NODDI and DTI parameter estimates have comparable reproducibility. The correlation coefficients of the NODDI estimates are slightly lower in gray matter than in white matter. This is in part due to the parameter estimates of gray matter are clustered in a narrower numerical range than those of white matter. The coefficient of variation is significantly higher in gray matter than in white matter for both NODDI and DTI. This is likely due to poor gray matter segmentation as a result of the present choice of affine registration that does not adequately account for the nonlinear deformation between b=0 volumes to their corresponding anatomical scans. Future work will address this limitation by utilizing higher-order image registration approach for this purpose.

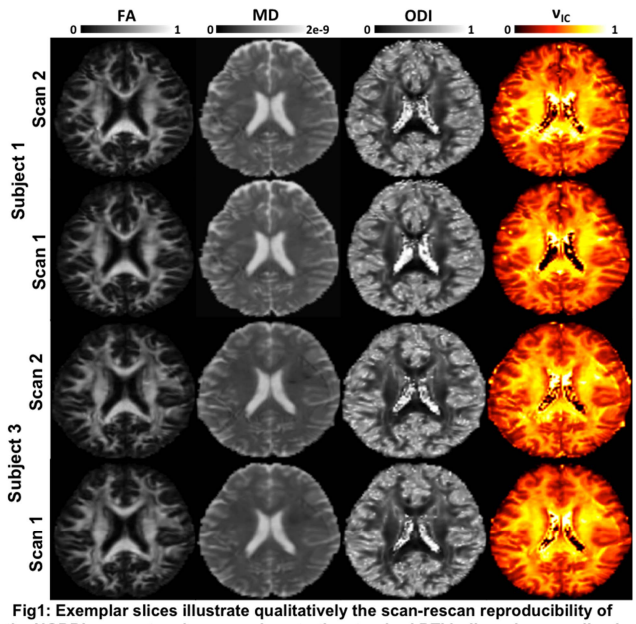


**Fig1: Exemplar slices illustrate qualitatively the scan-rescan reproducibility of the NODDI parameters in comparison to the standard DTI indices, in normalised space**

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**REFERENCES:** 1. Zhang et al, NIMG 12; 2. Basser et al, Biophysics J 94; 3. Panagiotaki et al, NIMG 12; 4. Cook et al, ISMRM 06.

| Maps | White Matter correlation coefficient | | Gray Matter correlation coefficient | |
|---|---|---|---|---|
| | Mean | Standard deviation | Mean | Standard deviation |
| $v_{ic}$ | 0.924 | 0.024 | 0.884 | 0.063 |
| ODI | 0.909 | 0.028 | 0.893 | 0.051 |
| FA | 0.962 | 0.017 | 0.945 | 0.036 |
| MD | 0.942 | 0.041 | 0.945 | 0.045 |

**Table 1: The mean and standard deviation of the Pearson's correlation coefficients of all four subjects, for the scan-rescan study for each tissue-type**

| Maps | White Matter (%) | Gray Matter (%) |
|---|---|---|
| $v_{ic}$ | 5.1393 | 9.8178 |
| ODI | 5.7193 | 8.9620 |
| FA | 4.4318 | 7.1963 |
| MD | 4.0953 | 7.0649 |

**Table 2: The coefficient of variation values for each of the parameter, for White and Gray matter regions**