An optimized protocol for neurite orientation dispersion and density imaging (NODDI) in preclinical studies

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Purpose: Neurite orientation dispersion and density imaging (NODDI) is a recent model-based diffusion MRI technique that provides more specific measures of the neurite microstructure than diffusion tensor imaging. The technique was originally designed for clinical 3T systems; an economical multi-shell diffusion protocol was developed to enable accurate estimation of NODDI parameters within a clinically-feasible acquisition window [1]. The feasibility of NODDI on high-field pre-clinical systems was recently demonstrated for mouse brain but with a lengthy acquisition of two hours[2]. A more economical acquisition is needed to enable broader uptake of the technique. This work addresses this challenge. We empirically determine the optimal protocol in this setting by comparing the accuracy and precision of NODDI parameters estimated with a broad range of protocols that differ in the number of shells, the b-values, or the number of repetitions. These protocols are extracted from a rich diffusion acquisition of 5 shells and 5 repetitions that provides the ground truth NODDI parameters.

Methods: Acquisition A wild-type mouse (6 weeks) was anesthetized with 1.5% isoflurane and scanned on a 9.4T Agilent scanner using a transmit/receive RF coil with 33mm inner diameter (Rapid Biomedical). The diffusion acquisition employed a 3-shot spin-echo EPI sequence which consisted of five shells: shell one and two: two b=0 images and 6 directions with b=308 s mm^{-2} and b=516 s mm^{-2} respectively; shell three and four: three b=0 images and 20 directions with b=740 s mm^{-2} and b=1125 s mm^{-2} respectively; shell five: four b=0 images and 30 directions with b=2112 s mm^{-2}. All the shells had the same TR (2000ms) and TE (30ms) as well as the same diffusion-encoding gradient duration δ (5.5ms) and separation Δ (9.3ms). These sequence parameters were dictated by the highest b-value that we chose according to [2]. The lower b-values were achieved by reducing the height of the diffusion-encoding gradient. The additional sequence parameters were: FOV=250x250 mm for 8 slices with 1 mm thickness and data matrix=64x64, 5 repetitions.

Data analysis The fitting was performed using the NODDI Matlab Toolbox [1] which provides the parameter maps of neurite density index (NDI) and neurite orientation dispersion index (ODI). In this analysis, two groups of protocols were created: one group consists of a three-shell combination and another group consists of a two-shell combination. In both groups, the highest b-value (b=2112) was included and all the directions available were used. For the three-shell group, four protocols were created choosing one b-value from either shell one or two and a second b-value from either shell three or four. For the two-shell group, two protocols were created choosing either shell three or four. The chosen b-values for each protocol are presented in Table 1 showing the acquisition time difference for each protocol. For each protocol the fitting was performed with either 3 or 5 repetitions. We did not include any comparison to single-shell acquisitions as it was previously demonstrated that NODDI fitting requires a minimum of two shells[1]. To evaluate the protocol performance, the statistics of the estimation bias relative to the ground truth were computed for two representative regions-of-interest, one for grey matter and the other for white matter. The region chosen for the white matter was the corpus callosum (red arrow in Fig.1) and for grey matter the thalamus (blue arrow in Fig.1).

Table 1 List of protocols evaluated showing the acquisition time differences per protocol and repetitions. The chosen b values are presented in smm-2 and the acquisition time in minutes

Protocol nº	b value	Acq.time 5rep	Acq.time 3rep
1	b=308, b=740, b=2112	66	40
2	b=516, b=1125, b=2112	66	40
3	b=308, b=1125, b=2112	66	40
4	b=516, b=740, b=2112	66	40
5	b=1125, b=2112	58	30
6	b=740, b=2112	58	30
7	All the b-values	100	60

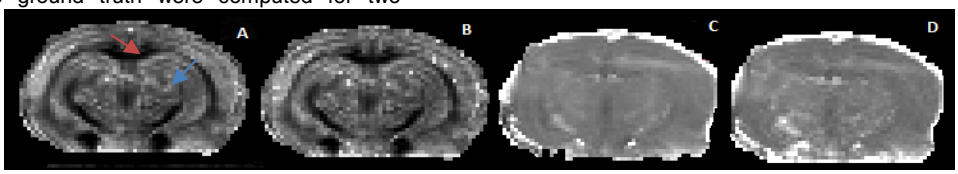

Figure 1 ODI and NDI maps from two protocols: ODI map from ground truth (A) and protocol 3-3 repetitions (B); NDI maps from ground truth (C) and protocol 3-3 repetitions (D). Red arrow: corpus callosum and blue arrow: thalamus

Results Fig. 1 shows the parameter maps of an example slice for the ground truth and protocol 3. The maps for protocol 3 are visibly noisier than those of the ground truth, which is not surprising. The analysis of the estimation errors of different protocols shows that neither the number of shells nor the choice of b values affects the accuracy of the estimation significantly. Comparing the protocols with different number of repetitions, while the average errors are similar in most cases, the variance in the errors is largest for the three-repetition protocols. Overall, the results show that all the protocols perform similarly well.

Discussion In this study, we used a rich multi-shell diffusion acquisition of a mouse brain to empirically determine an optimised protocol that provides the best trade-off between the acquisition time and the accuracy in NODDI parameter estimation. Finding such a protocol is important, especially for multi-parametric studies in which the available time for each technique is often limited. Our results suggest that it is feasible to estimate the NODDI parameters accurately with a protocol that is less than an hour by using two b-values. One limitation of the current study is that we have not applied motion and eddy-current distortion corrections. Future work will look at applying the appropriate image post-processing to mitigate these artefacts. This will likely reduce the variations observed and may support the use of data with 3 or fewer repetitions.

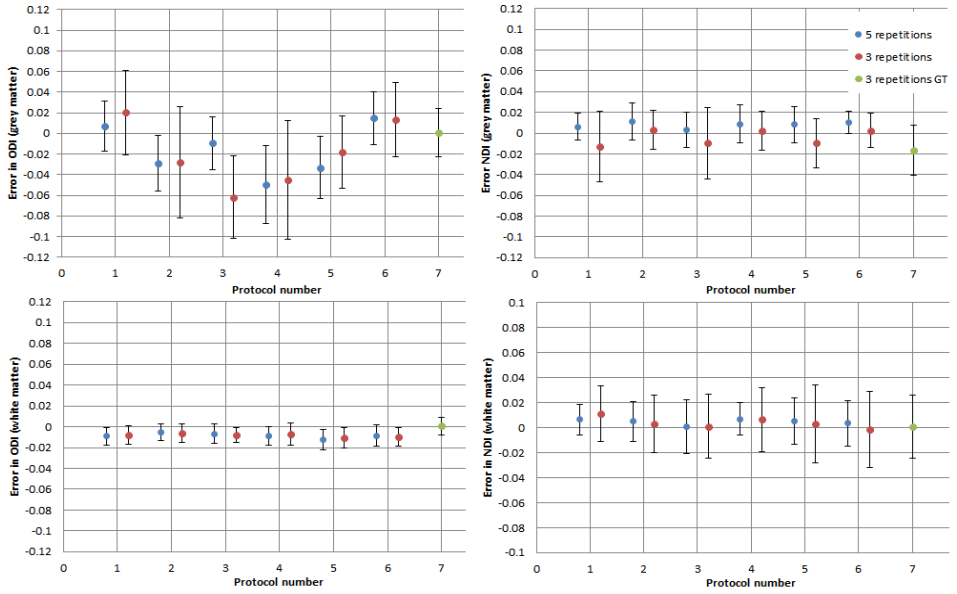

Figure 2 Mean and standard deviation of error in the NODDI estimated parameters (ODI and NDI) for protocol 1-6 against the ground truth protocol for the grey matter (on the top) and white matter (on the bottom) for 3 and 5 repetitions

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References 1. Zhang H et al. NeuroImage (NI) (2012); 61(4):1000–16. **2**. Colgan N et al. Proc ISMRM (2014); p.1942