Full Optimization of Multi-Shell Diffusion Acquisition Schemes for Advanced Microstructural Imaging

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INTRODUCTION AND TARGET: The lack of specificity of diffusion tensor MRI, mainly due to the inadequacy of the tensor model to characterise fibre orientation when there is more than one fibre population within a voxel, and its implicit assumption of there being a single tissue compartment, has leveraged the search for higher order approaches to model diffusion dynamics in tissue. Hybrid models, expressing the signal as a summation over different compartments, are particularly useful in this context, teasing apart the different contributions to diffusion anisotropy and providing more specific indices to characterize microstructure, e.g., the axonal density (AD) and the fibre orientation(s) (FO). The CHARMED model of white matter [1], the NODDI model for white and grey matter [2], the ball-and-stick model for tractography [3], as well as other models based on restricted diffusion [4], all share the need for collecting several diffusion-weighted (DW) measurements at both low and high b-values. To date, the issue of gradient scheme optimization (#directions, #measurements in each shell etc.) for multi-shell acquisitions has been only partially addressed [5,6]. Here a comprehensive optimisation of the experimental acquisition scheme is developed, optimising and comparing different approaches reported in the literature though both Monte-Carlo simulations and *in vivo* acquisitions. As a result, an optimised protocol for multi-shells acquisitions is proposed, that balances scan duration with accuracy/precision on the estimated parameters, needing only a 12 minutes acquisition for whole-brain maps of AD and FO. The protocol is addressed to all the experimenters wishing to perform advanced diffusion imaging striking the best balance between scan time and accuracy/precision.

METHODS: *In Silico:* Monte-Carlo simulations (50000 walkers, 20000 timesteps, AD=0.42, one/two FO, signal-to-noise ratios (SNR) of 23, 43 and 64) were used to produce synthetic DW data using three different acquisition schemes, shown in Fig.1a:
UNEVEN: 8 shells in which the number of gradient orientations in each shell increases with the increasing b-value (i.e., similar to [1]) where both the angular coverage of each shell and the total angular coverage (i.e., once the gradient directions in all the shells are projected onto a single shell) are maximised
EVEN: 8 shells with the same number of gradient orientations in each shell, where both angular coverage of each shell and the total angular coverage are maximised
EVENSAME: 8 shells with the same gradient orientations (i.e., similar to [3,5]), where only the angular coverage of the single shell is maximized.
200 gradient orientations (optimized and temporally ordered according to [6]) were used. For each scheme, 8 different maximum b-values are tested, ranging from bmax=2500 s/mm^2 to 11250 s/mm^2. To identify the shortest possible protocol for each scheme and for each maximum b-value, we truncate the datasets (optimally ordered) by removing one measurement at a time from the end of the acquisition, and run the analysis to calculate AD and FO. The best scheme is identified by finding the shortest possible protocol that maintains accuracy and precision for AD and FO below 5% for single fibre and below 10% for crossing fibres (for FO, accuracy and precision are calculated with respect to the largest possible error, which is 90°).
In Vivo: DW data were acquired from a healthy subject (age = 37 years), using the three schemes UNEVEN, EVEN and EVENSAME on a 3T HDx Signa (GE) MR system. Data were collected with a DW spin-echo EPI sequence with: TR/TE = 6000/122 ms, resolution 1.8x1.8x2.4 mm, matrix size 128x128x9, diffusion pulses separation/duration Δ/δ=50/43ms. The resulting AD and FO maps were compared with the full protocol. The reproducibility of the maps was assessed by repeating the acquisition three times in three different sessions. For both simulated and real data the CHARMED model was fit according to [1].

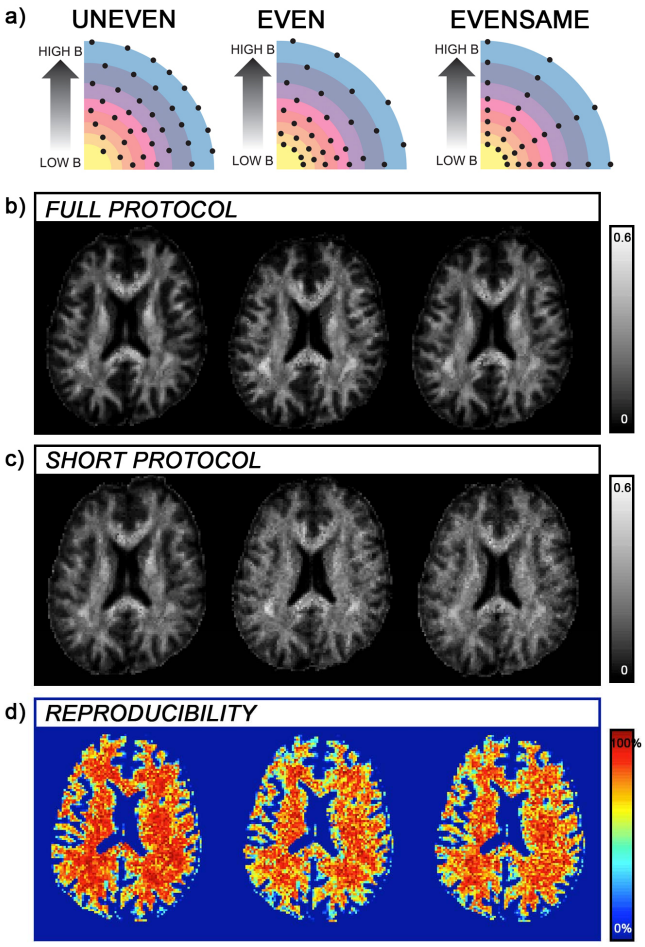

Fig 1: a) 2D illustration of the three schemes tested; b) AD maps for UNEVEN, EVEN and EVENSAME schemes for the full protocol; c) the same for the short protocol; and d) reproducibility of the three schemes

RESULTS AND DISCUSSION: Fig. 1b-c shows *in vivo* for AD maps from the three schemes and shows that the UNEVEN short scheme provides estimates of AD that are closer to those obtained using the full protocol (upper line). Fig 1d also shows that UNEVEN has the highest reproducibility. Similar results are obtained for FO. These experimental results are exactly in line with the Monte Carlo simulations (not shown).
The UNEVEN scheme outperforms the others, as it allows better estimates of both AD and FO with smaller b-values and fewer measurements. For example, for SNR=43 the optimal scheme is the UNEVEN with maximum b-value of 8750 s/mm^2 and 40 measurements, giving an acquisition time of only 12 minutes for whole brain coverage. Both EVEN and EVENSAME need higher b-values (10000 and 11250 s/mm^2, respectively) and longer acquisitions (49 and 50 measurements respectively, corresponding to 14.7 and 15 minutes).

CONCLUSION: The optimal gradient arrangement for multi-shells diffusion acquisitions is a scheme with maximum b-value of 8750 s/mm^2 and 40 unique gradient orientations, in which the number of gradient orientations in each shell increases with the increasing b-value. This experimental setup allows estimates of both hindered and restricted diffusion rates and volume fractions for the whole brain in only 12 minutes.

REFERENCES: [1] Assaf and Basser MRM 52:965 (2004) [2] Zhang et al. Neuroimage 16, 1000 (2012) [3] Jbabdi et al. MRM 2012 (in press) [4] Stanisz et al. MRM 37303:111 (1997) [5] Alexander D. MRM 60, 439 (2008) [6] De Santis et al. proc. ISMRM 2011