Optimisation of single-shell HARDI for neonatal imaging

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PURPOSE: A number of methods have been proposed in recent years to overcome the well-known limitations of the diffusion tensor model in crossing fibre regions. These methods are typically based on the high angular resolution diffusion imaging (HARDI) protocol. Although the HARDI approach is now being applied to neonatal

imaging and it has yet to be optimised for use in this cohort. The neonatal brain differs substantially from the adult case, with a much higher free water content leading to higher ADC values. To date, acquisitions have been optimised based on the settings recommended for diffusion tensor imaging, namely $b \approx 1.1/D$ [1], with most neonatal sequences using *b*-values in the region of 700-800 s/mm². However, these settings are unlikely to be optimal for more advanced HARDI methods, which typically work best with higher *b*-values. In recent work, HARDI parameters were optimised for the adult case using a data-driven framework, independent of any particular reconstruction algorithm, by characterising the angular frequency components of the signal [2]. In this study, we apply this framework to investigate the optimal parameters for neonatal HARDI.

METHODS: The framework proposed in [2] uses spherical harmonic basis functions to estimate the amount of signal within each harmonic band, by averaging the signal from single-fibre voxels after re-orientation of the estimated fibre direction. This procedure boosts statistical power since (i) the highest angular frequency content in the DW signal is found in single fibre voxels, (ii) it allows the analysis to focus on the axially symmetric terms only, and (iii) it allows averaging across voxels. Once the effect sizes per harmonic band have been estimated, they can be used to predict the power to detect them for an arbitrary acquisition sequence, guiding the selection of the appropriate *b*-value and number of DW directions required.

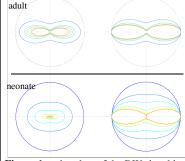


Figure 1: polar plots of the DW signal in the plane of the fibres (fibre axis is updown). Each line corresponds to a different *b*-value (outer circle indicates *b*=0 signal) Top: results from adult data (as shown in [2]). Bottom: neonatal data. Left: raw DW signal. Right: the same DW signal normalised to the same peak amplitude.

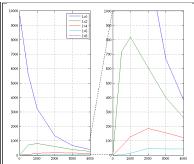


Figure 2: plots of the SH coefficients of the DW signal as a function of *b*-value. While the main DC (*I*=0, in blue) decreases sharply, the other components increase with b-value and peaks at different point. The I=4&6 terms (red & cyan) both peak at $b=2000 \text{ s/mm}^2$. No higher order terms are detectible.

<u>Data acquisition & processing:</u> HARDI data were collected from 5 neonates scanned at term-equivalent age over multiple *b*-values: 0, 500, 1000, 2000, 3000 & 4000 s/mm² (50 DW directions per b \neq 0 shell), on a Philips 3T Achieva system, with 2×2×3 mm³ voxels. The parents gave written consent prior to scanning. The data were corrected for motion and eddy-currents using FSL5's EDDY routine [3]. The DW signal intensities for each shell were then fitted to the even-degree spherical harmonic series using a Rician-bias corrected procedure (similar tp [4]). The fibre directions were then estimating from the *b* = 2000 s/mm² shell using constrained spherical deconvolution [5] followed by peak extraction. Subsequent analysis was restricted to the 200 voxels with highest ratio of first peak amplitude to second peak amplitude, which we assumed to contain single fibre populations (similar to [6]). The angular frequency terms of the signal were then estimated as outlined above, by reorientation of the dominant peak orientation (as estimated in the previous step) to the *z*-axis, and averaging the axially symmetric (m=0) terms of the SH fit of the DW signal over all 200 voxels in the processing mask.

RESULTS: Figure 1 shows polar plots of the raw and max-normalised DW signal in the neonatal data as a function of *b*-value, compared to the adult case. The signal can be seen to drop much more rapidly with *b*-value than in adults, as expected. However, as shown in Figure 2, the angular frequency components tend to increase with *b*-value, and peak at different points in the curve. The l = 2 term reaches maximum value around b = 1000 s/mm², while the l = 4 & 6 terms both reach maximum around b = 2000 s/mm². No l = 8 terms could be detected in these data.

The power analysis (figure 3) demonstrates clearly that the *l*=6 term, while present, is simply not detectible in practice on a voxel-wise level, regardless of *b*-value or SNR within the feasible range. On the other hand, optimal power to detect the *l* = 4 term occurs at $b \approx 2000$ s/mm².

DISCUSSION: This analysis demonstrates the need to specifically optimise HARDI protocols for use in studies of neonates, given the marked differences compared to the adult case. The analysis suggests that the maximum harmonic order detectible in practice is l = 4, although l = 6 terms are present. This contrasts with the adult case where terms up to l = 8 can potentially be detected.

These results suggest that neonatal HARDI protocols should use at least 15 uniformly distributed directions (the minimum necessary to characterise a full $l_{max} = 4$ expansion), and preferably much more than that to ensure adequate overall SNR. To ensure optimal sensitivity to the l = 4 terms, a *b*-value ≈ 2000 s/mm² should be used. ACKNOWLEDGMENTS: MRC, GSTT BRC, and the ERC-funded dHCP project.

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