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Accurate estimation of a multiple fascicle model is enabled by manipulation of gradient strength in a two-shell HARDI to achieve low TE.

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Introduction. There is a growing interest in parametric models to represent the diffusion-weighted signal [1-3] and to extend the common diffusion tensor imaging (DTI) model to better capture and characterize properties of the brain white matter (WM). Among them, a multi-fascicle model (MFM) which represents the signal contribution from each fascicle with a tensor and the freely diffusing water with an isotropic tensor enables characterization of multiple WM fascicles. Additionally, this enables characterization of the CSF contamination due to partial volume effect [4] and characterization of pathologies such as edema, stroke or inflammation. Identification of the parameters of such MFM, however, requires imaging of multiple non-zero b-values [5]. We investigate and evaluate a novel Cube and Sphere (CUSP) acquisition scheme based on a two-shell HARDI in which each diffusion gradient is constrained to lie in a cube of constant TE defined by the inner shell. In contrast to a multi-shell HARDI (MS-HARDI), CUSP achieves a low TE and maintains high SNR for each DW image. We show that CUSP enables accurate estimation of a MFM, is not dependent on fascicle orientation and leads to a lower estimation uncertainty than a MS-HARDI. CUSP will enable accurate WM diffusion imaging.

Material and Methods. Modification of the b-value in a diffusion weighted experiment can be achieved by modification of the gradient pulse duration δ, of the time separation between the pulses Δ or of the gradient strength $||g||$. In practice, multiple separate single-shell HARDI may be used, which amounts to utilize $||g||=1$ and different δ and Δ for each shell. However, this leads to different eddy current distortion patterns between the images, making their alignment challenging. In a MS-HARDI, δ and Δ are fixed to achieve the largest b-value when $||g||=1$ and multiple shells in q-space are described with gradients with norm $||g||\leq 1$. This leads to a long Δ and long TE for each image, leading to an exponentially attenuated SNR for *all the shells* due to T2 relaxation. Here we propose to fix δ and Δ and to image with $||g||>1$. The only constraint for g is to have unit norm components, i.e. $|g_x|\leq 1$, $|g_y|\leq 1$, $|g_z|\leq 1$, which describes a 3-D cube in q-space corresponding to a cube of constant TE [5]. We propose a Cube and Sphere (CUSP) acquisition based on the projection of a MS-HARDI on the cube of constant TE. We first consider an inner shell of N_{inner} gradients that uniformly samples q-space with $b_{nominal}$ chosen to provide the optimal SNR for imaging the white matter. We then consider a second shell HARDI at $3b_{nominal}$ with N_{outer} gradients maximally separated with respect to the inner shell using the electrostatic repulsion algorithm of [6]. Because $b=b_{nominal}||g||^2$, this shell passes exactly through the corners of the cube of constant TE and any other gradients cannot be imaged without increasing TE. Instead, we propose to project them onto the faces of the cube of constant TE, by reducing the gradient strength until the cube surface is reached (see Fig.1, red gradients). This provides *maximally separated diffusion encoding directions* and *multiple non-zero* b-values up to $3b_{nominal}$ *while* keeping TE constant. We sought to compare CUSP and MS-HARDI to determine the angular sensitivity and precision of parameters estimates. We fixed the number of encoding gradients and carried out simulations and bootstrap evaluation with in vivo acquisitions.

Experimental design. We considered a CUSP65 acquisition (5b=0/N_{inner}=30 at $b_{nominal}$=1000/N_{outer}=30/b_{max}=3000) and its corresponding non-projected MS-HARDI (5b=0/N_{inner}=30 at b=1000/N_{outer}=30 at $b_{nominal}$=3000) with same gradient directions. In vivo imaging was performed on a healthy volunteer on a Siemens 3T Trio scanner with a 32 channel head coil and parameters as follows: 68 slices, FOV=240mm, matrix=128x128. The minimum TE for CUSP and MS-HARDI was respectively 78ms and 108ms. We achieved simulations of the diffusion signal for both CUSP (TE=78ms/SNR=20dB) and MS-HARDI (TE=108ms/SNR=16dB) for N_f=2 tensors crossing at 75 degrees in various orientations to compare the angular dependency. Additionally, we compared the estimation uncertainty with CUSP and MS-HARDI with in vivo acquisitions via bootstrap.

Results. Fig.2 illustrates the MFM estimation from in vivo CUSP. Fig.3 shows the mean and variance of the FA of one fascicle (Fig.2a-b, ground truth: 0.9) and of the fraction of free water (Fig.2c-d, g. truth: 0.15) among 500 simulations of the diffusion signal, and Fig.4 the bootstrap results.

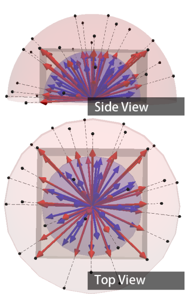

Fig.1 The Cube and Sphere (CUSP) acquisition constructed as a *projected* multi-shell HARDI.

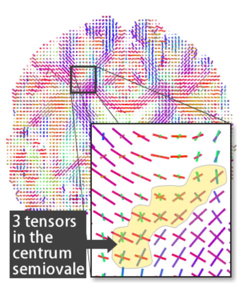

Fig.2. MFM estimation results with in vivo CUSP acquisition and f-test based model selection. The estimated MFM from CUSP matches the known anatomy.

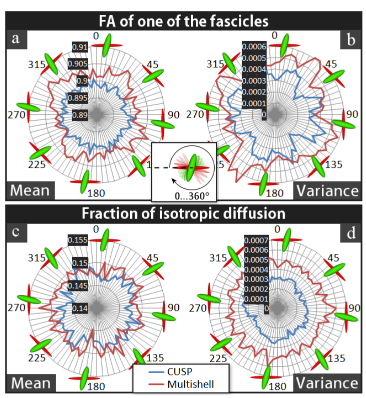

Fig.3. Numerical simulations. The signal arising from two crossing tensors in various orientations was simulated and MFM parameters estimated. CUSP accurately estimates the parameters, does not introduce any significant angular preference, and achieves a lower variance than MS-HARDI

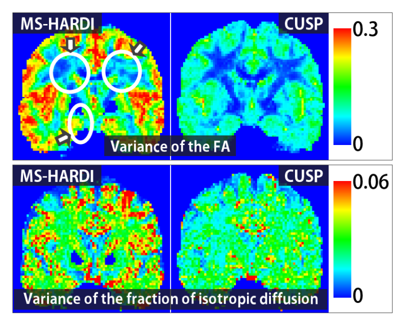

Fig.4. Bootstrap evaluation with in vivo data, with N_f=3 fascicles at each voxel *without any model selection*. CUSP achieves a lower estimation uncertainty, both in the grey and the white matter.

Conclusion. We proposed a novel gradient encoding scheme to image multiple non-zero b-values based on the projection of a MS-HARDI on the cube of constant TE of the inner shell. CUSP *achieves a low TE* and images *a large number of different b-values* up to $3b_{nominal}$ with high SNR and *maximally separated directions*. The typical TE gain compared to a MS-HARDI is ≈30ms which corresponds to *a signal gain factor of 1.5 for each DW image* and therefore a two-fold reduction in imaging time for a same SNR. Our results shows that, despite CUSP not having as much uniform spherical coverage as a MS-HARDI, it *does not introduce any angular sensitivity* to fascicle orientation and provides a *lower estimation uncertainty*. The SNR gain of each DWI has a greater impact while the projection of the diffusion gradients is sufficient to enable accurate estimation of each tensor. Importantly, the projected outer-shell can be incorporated as a separate scan in an imaging protocol containing already a conventional single-shell HARDI, facilitating straightforward incorporation of CUSP in existing studies. CUSP enables accurate DWI in clinical practice and research.

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