High-spatial and high-angular resolution diffusion imaging with a fragmented acquisition scheme

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Introduction: HARDI methods have become increasingly popular for fiber tracking and/or to extract quantitative diffusion measures. However, they require a substantially larger number of diffusion-weighted images (DWIs) than in DTI [1, 2], leading to prohibitively long scan times. Even for the most cooperative subjects, scan times are limited to 30-60min, meaning that for HARDI we are still heavily dependent on single-shot EPI acquisition. This limits the effective resolution to a 2×2×2mm isotropic voxel size or larger. Multi-shot pulse sequences, including DW-SSFP and 3D EPI, can offer submillimeter voxel resolution but are impractical, due to the even longer scan times [3-7]. Excessively long scan times put impossible demands on the volunteers, which decreases their comfort and increases the likelihood of motion. Since the neuroscience community is nevertheless eager to get to higher resolution data, we propose a fragmented imaging setup. In this study, we developed an imaging protocol and procedure to acquire the whole high spatial and high-angular resolution dataset over different scan sessions.

Materials and methods: Without proper consideration, different scan sessions will result in different scan orientations, and thus different levels of distortions, which limit reproducibility and proper data fusion. • *Head holder:* For accurate repositioning of our volunteer over different sessions, a custom-made 'head holder' was created based on the geometry of the head coil (determined via CT) used for this study and an anatomical MR scan of the subject's head, fitting tightly into the coil and exactly around the subject's head. This also allowed near-perfect immobilization of the subject in the head coil. This design, shown in **Fig. 1**, was manufactured using a 3D printer. A Nova Medical 32-channel head coil with a noncircular cross-section was used, so that the insertable head holder fits into the coil in only one unique way. • *Acquisition protocol:* High-spatial resolution HARDI was performed with a variant of a multi-slab 3D EPI sequence [4,5]. Each 3D EPI slab z-encode was acquired after a separate excitation, (non-linearly) phase-corrected using a navigator, and stacked to form a 3D k-space. Data was acquired on a 3T GE 750 MR using 30 slabs of 7mm thickness, read out with FOV_{SLAB} = 232×232×8mm and $matrix_{SLAB}$ = 232×232×8 for 1mm true isotropic resolution and full-brain coverage, TR/TE = 7s/72ms, T_{ACQ} per volume 56s, GRAPPA acceleration of 4, and 0.7 partial Fourier factor. Single-refocused diffusion preparation was used with a b-value of 1000s/mm^2. Images with positive and negative EPI phase-encoding blips ('blip up' and 'blip down') were acquired for each b=0 image and diffusion direction, to correct for eddy-current induced geometric distortions using the Jacobian-weighted RPGM [8,9]. To correct for differences in inter-session overall image intensities – caused by different receiver gain settings – a global scaling approach was used, so that the average intensity of the b=0 scan in each session was set to 100, and correcting all DWIs from that session with the same factor. • *Reproducibility analysis:* To demonstrate the reproducibility of diffusion acquisitions between different scan sessions, DWI data was acquired in ten sessions, each consisting of two b=0 and ten b=1000 DWIs. In two sessions, a 3D T1W SPGR scan was also acquired to get an accurate measure of the anatomical intersession alignment. The localizers from all sessions are registered to each other to determine the "most representative" image, and that session's b=0 scan is used as a reference, with each b=0 scan being registered to this reference by the transformation matrix TB0_i. DWIs from each session are registered to their b=0 scan by transformation matrix TDWI_i and combined with TB0_i for a single interpolation step to the reference b=0 scan, with b-matrix correction [10].

***Fig. 1**: Head holder in the coil and around subject's head.*

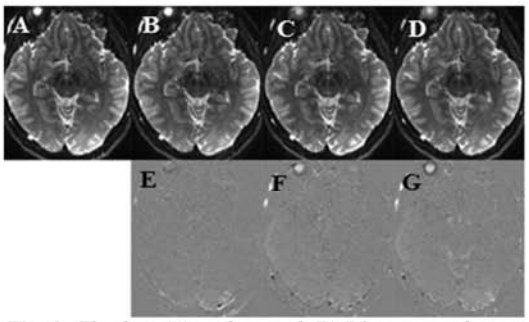

***Fig. 2:** The first (A) and second (B) B0 images of session 1; and the first (C) and second (D) B0 of session 2. Difference images are shown as well, to illustrate proper realignment and scaling: E is the difference image between A and B (E=A–B); F=A–C; and G=A–D. E, F, and G show there is no difference between intra-session and inter-session B0-images.*

***Table 1**: Transformation parameters of intersession re-alignment*

	T1 registration	Mean ± std. dev. of DWI sessions
Tx (mm)	1.96	-0.51±0.82
Ty (mm)	0.59	-0.40±0.65
Tz (mm)	3.69	-1.90±4.61
Rx (deg)	0.33	-0.16±0.76
Ry (deg)	0.71	0.85±0.64
Rz (deg)	0.24	0.65±0.59

Results: Transformation parameters of both the T1W scan and localizer registration are shown in **Table 1**. Mean and standard deviation of the rotations are smaller than 1 degree. Distortion corrected, affine-registered and scaled b=0 images from different session are shown in **Fig. 2.**

Discussion: Combining DWI data from different sessions into one large dataset is possible if proper care is taken to ensure accurate subject realignment. Because of the head holder, rotations are well within one degree, and in-plane translations (Tx and Ty) are on the order of a millimeter. Through-plane translations are bigger, likely caused by inaccuracies in repositioning the patient table. Unlike thin slice 2D EPI, which gives a poor slice profile, through-plane shifts in 3D EPI are much less of a problem. Geometric distortions of EPI are in the phase-encode direction, so different head orientations with respect to this axis leads to distorted images that could not be merged. Thus, for our axial acquisition, rotation around the z-axis is detrimental. It is therefore crucial that the coil inset secures the head far enough forward to restrict motion around this axis. The use of the Jacobian-weighted RPGM method ensures that any residual misalignment and thereby induced different distortions are corrected to ensure image correspondence. With modern 3D printers such head holder can be produced within 24 hours. Data combination from different session has previously only been used, not validated, in [11]. Our work aimed to 1) validate that data combination is feasible, and 2) present a method to ensure accurate data fusion for high-quality high-spatial and high-angular resolution data.

Conclusion: A fragmented acquisition scheme can be used to acquire high-resolution HARDI data over several sessions, facilitating the combination of high spatial resolution and high angular resolution diffusion weighted imaging for neuroscience research. While this is not suitable for use in clinical studies, the approach allows one to obtain data *in vivo* that would be otherwise only be possible in cadaver studies.

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