## HARDI and fiber tractography at 1 mm isotropic resolution

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Introduction: Two major challenges in diffusion-weighted MRI (DWI) are how to improve 1) spatial resolution and 2) angular resolution. Advances in DWI pulse sequences, such as PROPELLER, RS-EPI, multi-slab 3D EPI, 3D DW-SSFP, can be used to acquire images with less geometric distortions and/or spatial resolutions up to ~1.25mm isotropic [1-5], and have led to increased diagnostic confidence, e.g., in pediatric brain imaging [6]. Conversely, high-angular resolution diffusion imaging (HARDI) approaches can be used to better describe the directional variability of diffusion in each voxel, which allows one to better resolve complex fiber architecture

[7,8] and in turn improves tractography [9]. However, research so far has focused on improving either spatial or angular resolution. In this work, we aim to bridge the two. Specifically, we compare a unique dataset that offers both high spatial *and* high angular resolution vs. subsamples of this dataset that have either a high spatial *or* high angular resolution. The overarching aim of this study was to determine which of these two factors, if any, provides the largest gain and when (if at all) there are diminishing returns.





**Materials and Methods:** • *Data acquisition:* An improved variant of the recently proposed 3D multi-slab EPI method [4,5] was used to acquire high-resolution isotropic DWI data. Thirty 7mm slabs were excited and then each slab was subpartioned by 8  $k_z$  phase-encode steps, each of which was acquired in a separate excitation, and non-linear phase correction was applied before combining the  $k_z$  encodes. Imaging was performed on a 3T GE 750 unit

with a Nova Medical 32ch head coil. Sequence parameters were:  $FOV_{SLAB}=232\times232\times8mm$ , matrix<sub>SLAB</sub>=232×232×8 for  $FOV_{TOTAL}=232\times232\times150mm$  yielding 1mm true isotropic resolution; 0.7 partial Fourier factor and GRAPPA acceleration of 4. Single-refocused diffusion preparation was used with a b-value of 1000s/mm<sup>2</sup>. • *HARDI acquisition:* Because of the 3D nature of the sequence, the total acquisition time per DW direction volume is  $T_{ACQ}=TR\timesNk_z=56s$ . The 60 DW directions in this work, each acquired with top-down *and* bottom-up diffusion gradient direction [10], were therefore separated over several sessions, with 2 b=0 images and 20 diffusion directions for a total session time of 20.5min. To ensure optimal repositioning per scan session, and thus proper data fusion, a coil-inset was created that fit fully around the subject's head and exactly in the head coil. A detailed description of this positioning approach has been described elsewhere. • *Test sets:* The full 1mm isotropic dataset with 60 directions (dubbed 60\_1mm) was reconstructed into optimal subsets of 30 (30\_1mm) and 15 (15\_1mm) of the acquired directions. In addition, these datasets were also resampled to 2mm isotropic resolution (60\_2mm, 30\_2mm, and 15\_2mm). All datasets will become available for download at

neuroquant.stanford.edu/data/HiRes-HARDI • Analysis: For each dataset, tractography was Fig. 3 performed using DTI and constrained-spherical deconvolution (CSD [7]) with the maximum order of spherical harmonics (L<sub>MAX</sub>) depending on the number of directions (Lmax=8 for 60; 4 for 30) in *ExploreDTI* [11]. To quantify overlap mismatch between fiber tractography results, the Dice similarity coefficient was used [12]. From all reconstructed fiber pathways within a bundle, a binary mask was created of all voxels intersected by those pathways. As the tracts are continuous space-curves, this tract-mask can be created at the same 1mm resolution for the original 1mm isotropic data and the subsampled 2mm isotropic data. From these 1mm isotropic tract-masks, the Dice overlap is calculated for all reconstructed subsets.

**Results:** Fig. 1 shows the 60\_1mm "ground truth" data. Fig. 2 shows tracts from the reconstructed arcuate fasciculus (AF), based on different subsets. Fig. 3 shows the Dice overlap of all 10 subsets with each other for the posterior limb of the internal capsule (PLIC), where the top half of the matrix is the left PLIC, and the bottom half the right PLIC. The ten subsets are ordered top-to-bottom (as shown), and left-to-right. Fig. 4 shows the Dice overlap for the AF. An example of the overlap and mismatch between tractography results of the right PLIC can be seen in Fig. 5, where the white volume rendering indicates overlap between fiber bundles reconstructed with the 60\_1mm and 60\_2mm datasets; blue indicates voxels only found in the PLIC based on the 60\_1mm dataset; red those voxels of the PLIC only found in the 60\_2mm dataset.

**Discussion:** Comparison of tractography from datasets with different spatial and angular resolutions, as well as different diffusion models, are visually similar but show inconsistent quantitative overlap values between different reconstructed datasets. For both bundles investigated, 15 directions seems to be insufficient to properly reconstruct the bundles, as seen in **Fig. 2**, bottom row, and the two top rows in **Figs. 3** and **4**, where a marked difference in overlap can be seen between the subsets of 15 and 30 directions. For 30 and 60 directions, for both spatial resolutions, the Dice overlap values are quite similar, in the range of 0.4-0.6. The fact that all overlap values are relatively low is well illustrated in **Fig. 5**, where the overlap and mismatch between the right PLIC is shown for high-angular resolution and different spatial resolutions (60\_1mm and 60\_2mm). Although there is gross anatomical correspondence, visualized as the white volume indicating overlap, throughout the entire PLIC there are regions of subtle mismatch.

**Conclusion:** We have shown that high-spatial, high-angular resolution diffusion imaging is possible, for both obtaining top-quality tensor maps (Fig. 1) as well as fiber tractography. Correspondence between different spatial resolutions and angular resolutions is relatively low, but consistent across subset of 30 directions or higher.

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