Diffusion Tensor Imaging of Human Brains In-vivo at 3 Tesla with Very High Spatial Resolution: 0.85mm x 0.85mm x 0.85 mm

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<u>**Target Audience:**</u> Researchers and clinicians who are interested in high-resolution DTI

<u>**Purpose:**</u>
Progress in MRI-based connectivity network mapping for translational neuroimaging is currently limited by the spatial resolution that can be achieved with conventional DTI protocols. Although it has been clearly demonstrated in a post-mortem human brain study that DTI can resolve many small white-matter fibers with very high spatial-resolution ($0.73mm^3$) [1], it is extremely challenging to achieve this spatial-resolution for in vivo human DTI. The recent progress in 3D multi-slab EPI sequences makes it possible to acquire human DTI data with $1.3mm^3$ isotropic voxel size [2]. However, the in vivo human brain DTI at sub-millimeter isotropic resolution, to our knowledge, has not yet been routinely achieved yet. Here we report that, through integrating the 3D multi-slab EPI acquisition and the multiplexed sensitivity encoding (MUSE) post-processing algorithm [3], we are able to acquire high-quality and high-SNR human brain DTI data in vivo at high spatial resolution: $0.85mm^3$. At this spatial-resolution, the structural connectivity networks of human brains can be mapped much more accurately and completely.

<u>**Methods:**</u>
A 3D multi-shot interleaved spin-echo EPI sequence, equipped with a parallel navigational echo, was used to acquire the DTI data. The shot-to-shot phase inconsistencies (in both ky and kz segments) were measured from navigator echoes, and this information was then used to minimize the interleaved EPI aliasing artifact through the recently developed MUSE algorithm [3], comprising five steps: First, each 3D k-space interleave and its associated 2D navigator were Fourier transformed along the ky and kx direction (i.e., into x-y-kz space); Second, images free from in-plane aliasing artifacts were reconstructed from each of the navigator segments using the conventional SENSE algorithm [4]; Third, the phase information obtained from step 2 was spatially smoothed; Fourth, the smoothed phase information obtained from step 3, and the known coil sensitivity profiles were incorporated into a mathematical framework that jointly solved the unknown complex signals of in-plane overlapping from all EPI segments in the x-y-kz plane, producing a final set of data with higher SNR and free from aliasing artifacts. Fifth, the corrected x-y-kz-space data were Fourier transformed along the kz direction to produce a 3D image data set.

The 3D DTI data were acquired on a 3.0T MRI scanner (GE MR750, Waukesha, WI) using an 8-channel coil, and the 4-shot phase-encoded interleaved EPI parameters included: effective TEs = 59ms (image) / 115ms (navigator), TR = 3000 ms, partial-Fourier (PF) factors along the ky direction = 60% (image) and 67% (navigator), slab thickness = 10mm, z-FOV = 12mm, 11 axial slabs with 3.4mm gap, in-plane FOV = 21.8cm, matrix size = 256*256*12 per slab, voxel size = $0.85*0.85*0.85$ mm^3, 15 DTI encoding directions with b=800 s/mm^2, total acquisition time = 40 min. The colored fractional anisotropy (cFA) maps were calculated using the FSL program.

<u>**Results:**</u>
The cFA maps calculated from images acquired from 6 selected slices are shown in Figure 1. The comparison between the cFA maps calculated from routine standard resolution DTI image ($2.0*2.0*2.0$ mm^3) and high resolution DTI image ($0.85*0.85*0.85$ mm^3) obtained with the developed 3D-MUSE algorithm are shown in Figures 2a and 2b, respectively. The white arrows (in Figure 2) indicate a side-by-side comparison between the two cFA maps, showing that the cFA map calculated from high resolution DTI data can resolve small white-matter fibers much better.

<u>**Discussion & Conclusion:**</u>
The integration of 3D multi-shot interleaved EPI acquisition and the 3D-MUSE post-processing algorithm can reliably enable in vivo human brain DTI at very high spatial resolution ($0.85*0.85*0.85$ mm^3). Although the original 2D version of the MUSE algorithm is capable of measuring the phase variations between shots of 2D interleaved EPI without relying on navigator echoes, navigator-less phase estimation cannot be achieved in 3D interleaved EPI for non-zero kz planes. For this reason, we used the navigator echo (with?) zero kz-encoding to measure shot-to-shot phase inconsistencies among EPI segments.

A major advantage of the 3D-MUSE reconstruction algorithm is that the noise amplification in conventional parallel image reconstruction procedures can be largely avoided. As a result, the produced 3D DWI data (even at $0.85mm^3$ isotropic voxel size) have higher SNR than that obtained with alternative reconstruction procedures. The comparison of cFA maps obtained with different resolutions (Figure 2) clearly demonstrates the advantage of achieving high spatial-resolution for structural connectivity mapping, and we expect the developed tool should play an important role for advancing neuroscience research in the future. We plan to further improve the slice excitation profiles, and implement multi-slab acquisition with negative gap, enabling whole-brain DTI at this resolution. In conclusion, the 3D-MUSE algorithm can address shot-to-shot phase variations in 3D multi-shot interleaved EPI acquisitions and thus enable high-resolution and high-quality in vivo DTI data.

<u>**References:**</u> [1] Miller KL, et al., Diffusion imaging of whole, post-mortem human brains on a clinical MRI scanner, Neuroimage;57(1-4):167–181, 2011. [2] Mathias E, et al., Diffusion-Weighted 3D multislab echo planar imaging for high signal-to-noise ratio efficiency and isotropic image resolution, MRM, 2013. [3] Chen NK, et al., A robust multi-shot scan strategy for high-resolution diffusion weighted MRI enabled by multiplexed sensitivity-encoding (MUSE). Neuroimage;72:41-47, 2013. [4] Pruessmann KP, et al., SENSE: sensitivity encoding for fast MRI. MRM;42:952-962, 1999.
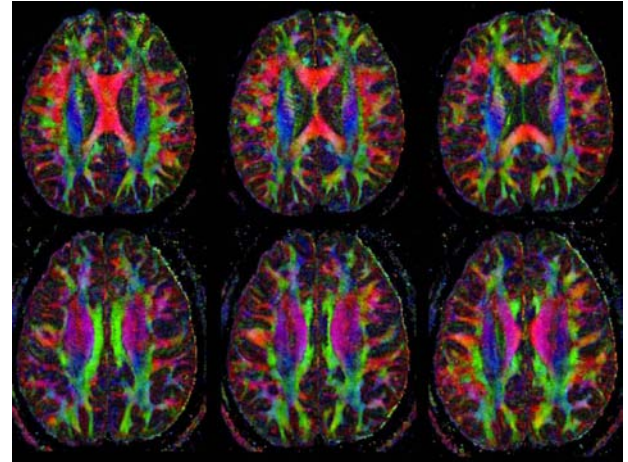
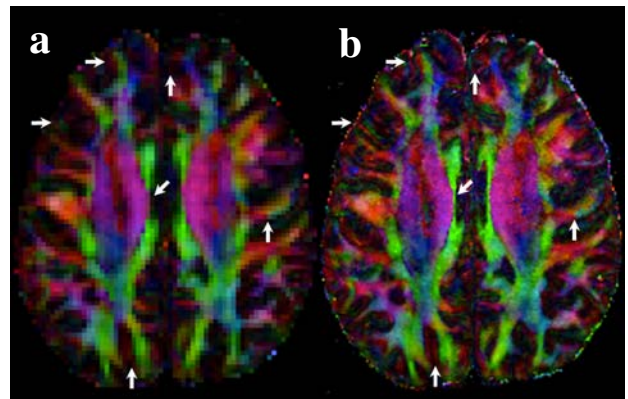**Fig 1** The cFA maps calculated from images of 6 selected slices.

Fig.2 The comparison between the cFA maps calculated from a) routine standard resolution DTI image ($2.0*2.0*2.0$ mm^3) and b) high resolution DTI image acquired and reconstructed from the developed 3D-MUSE algorithm.