SLIce Dithered Enhanced Resolution Simultaneous MultiSlice (SLIDER-SMS) for high resolution (700 um) diffusion imaging of the human brain

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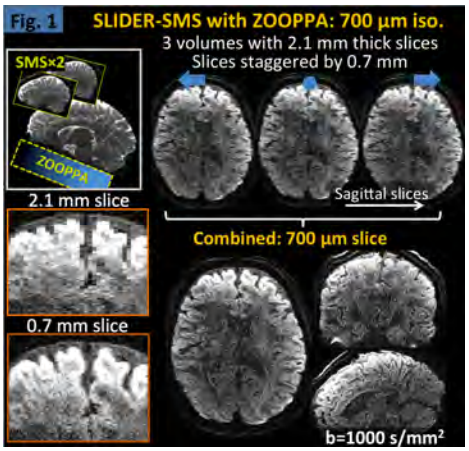
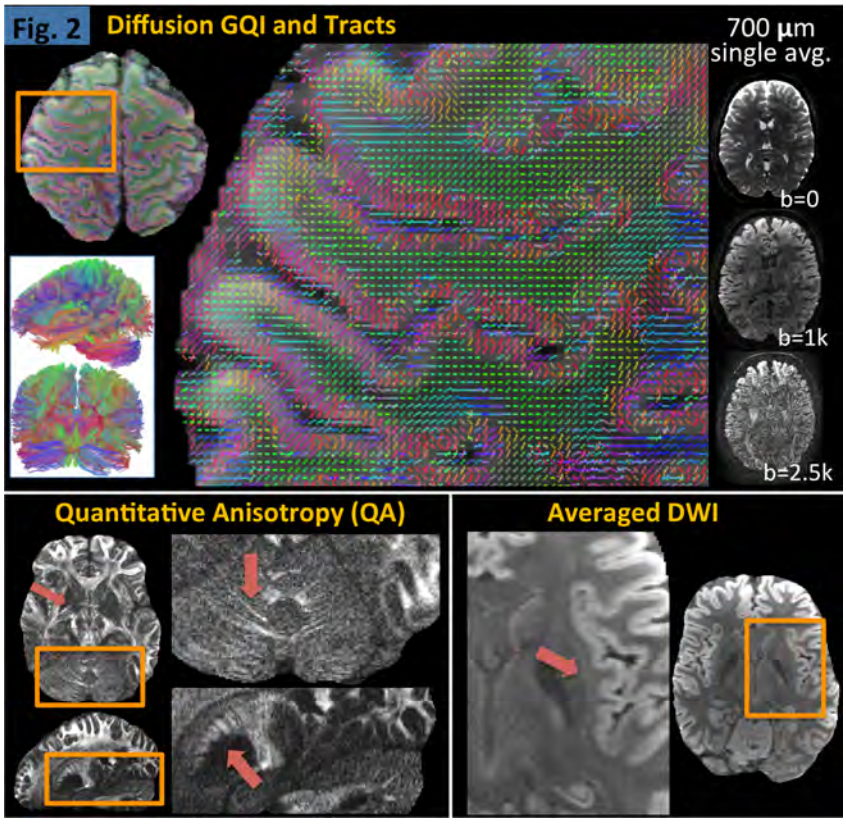
Target audience: Neuroimaging scientists and clinicians interested in diffusion imaging and advanced acquisition/reconstruction.

Purpose: Sub-millimeter isotropic resolution *in vivo* diffusion imaging (DI) is extremely challenging due a number of issues including: the difficulty of maintaining thin slice profiles in SE sequences, geometric distortion, long readout window with increased T_2 blurring and signal loss from long TE, long scan time, and low SNR particularly at high b-values. A large number of acquisition techniques have been developed to mitigate some of these issues, but have not enabled sub-millimeter isotropic whole brain DI, particularly in a reasonable time frame and with b>1000 s/mm^2. Zoomed imaging methods such as ZOOPPA (1) and multi-shot acquisition such as rs-EPI (2) and MUSE (3) reduce distortion and shorten the readout window, but limits brain coverage and cause long scan time, respectively. Recently, Simultaneous MultiSlice (SMS) imaging with blipped-CAIPI (4) and Hadamard encoding (5) have been shown to reduce scan time and improve SNR efficiency of DI. In particular, SMS imaging has gained significant popularity, with combination of SMS with ZOOPPA (6), rs-EPI (7) and MUSE (8) being proposed. Another area of development is in super-resolution techniques, where sub-voxel spatial shift in the slice direction has been shown to increase resolution in anatomical MRI, while application of voxel shifts in the in-plane direction of Fourier encoded images has proven to not be useful (9). Recently, super-resolution technique has been applied to DI using orthogonal anisotropic acquisitions, with careful correction for geometric distortion in each spatial acquisition direction (10). Similar to SMS and Hadamard encoding, super-resolution provides desirable gain in SNR efficiency since signal from a larger volume is being excited and acquired during each acquisition. In this work, we propose a new acquisition strategy, which modifies and synergistically combines a number of aforementioned acquisition techniques to allow high quality sub millimeter (700μm) whole brain DI at b>1000 s/mm^2 in a reasonable time frame. Specifically, we propose i) SLIDER-SMS (SLIce Dithered Enhanced Resolution Simultaneous MultiSlice), which combines SMS with super resolution via sub-voxel spatial shift in the slice direction to allow further improvement in SNR efficiency and fast acquisition, and ii) SLIDER-SMS is combined with ZOOPPA to reduce distortion and the long readout window. We demonstrate that SLIDER-SMS with ZOOPPA can be used to acquire high quality DI that enables visualization of fine scale structures in both gray and white matter and at the gray-white matter boundaries.



Methods: *Theory* Fig. 1 *top*) illustrates SLIDER-SMS with ZOOPPA for the 700μm isotropic acquisition case that will be used in this work. Here, ZOOPPA is performed with outer volume suppression applied to the neck area with phase encoding in the head-foot direction to provide low distortion while retaining whole-brain imaging capabilities. The sagittal EPI used a MB acceleration of 2, with 3x-SLIDER encoding shown in Fig. 1, where three imaging volumes at 2.1 mm slice thicknesses are acquired with relative center positions of 0mm, 0.7mm and -0.7mm. As in (9), an inverse matrix approach is used to combine these volumes to generate 0.7 mm slice data. Fig. 1 *bottom*) zooms into this reconstruction and compared it to image from one of the 2.1 mm volumes. Also, shown is the resulting *single-direction* 700um DI at b =1000s/mm^2, where MB-2 and 3x-SLIDER provides a large √6 SNR benefit of volumetric encoding when compared to conventional DI.

Acquisition Data were acquired using SLIDER-SMS with ZOOPPA in a healthy volunteer on the 3T CONNECTOM system (Siemens Healthcare, Germany) using a custom-built 64-channel RF head array. Imaging parameters were: 700 μm iso; FOV = 222×128×155.4 mm; R_{zoom}×R_{grappa} = 3.5 (1.74×2); MB-2; Partial Fourier = 6/8; TE = 82ms, TR_{eff}=17.1s (TR *per* dithered volume = 5.1s); effective echo spacing = 0.29ms, 64 diffusion directions at both b = 1000 and 2500 s/mm^2 with an interspersed b0 image every 15 volumes, total scan time ~40 min. FLEET-ACS acquisition was employed to provide robust GRAPPA and slice-GRAPPA training data (11,12). The resulting diffusion data were analyzed via DSI Studio using Generalized Q-space Imaging (GQI) model (13).



Results: Fig. 2 *top*) shows the fiber and tractography results, where the fiber results in the zoomed region (orange box) contain multiple voxels across the cortical depth at this resolution, with fibers appearing perpendicular as they enter into the cortex. *Top right*) shows 700 μm single average DWIs at b = 0, 1000, and 2500 s/mm^2 with good SNR. *Bottom left*) shows Quantitative Anisotropy (13) results, where in the Axial image the anterior commissure is observed (red arrow). In the zoomed Axial image, fine scale cerebellar white matter tracts are observed with the arrow indicating a particularly thin tract (with a single voxel diameter) running oblique to the slice direction (L-R) of SLIDER-SMS. This points to the ability of SLIDER-SMS in achieving high slice resolution. Further, the zoomed Sagittal image of the Striatum also clearly depict the cell-bridge connecting between the Caudate and Putamen. *Bottom right*) shows the averaged DWI, where fine scale gray matter structures such as the Claustrum (arrow) can be seen.

Conclusion: In this work, we proposed SLIDER-SMS with ZOOPPA and demonstrated its ability in providing high quality sub-millimeter DI at high b-values in a reasonable time frame. Such acquisition allows depiction of fine scale structures and opens up exciting possibilities in analyzing diffusion tracts at the gray-white matter boundary as well as within the cortex.

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