High-resolution zebrafish white matter fibertracks

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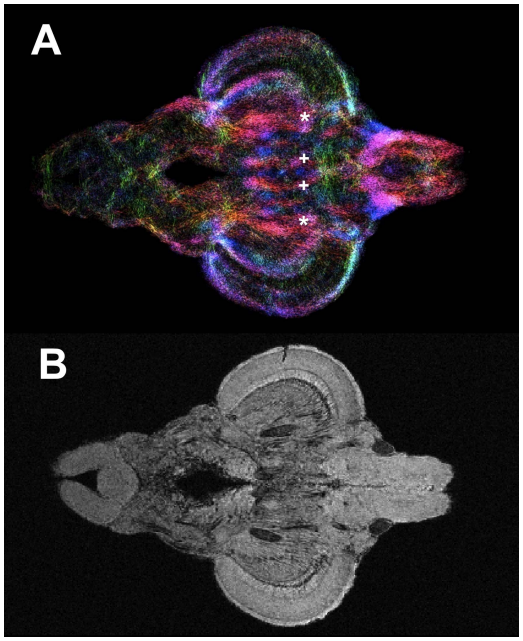
Introduction: High angular resolution diffusion imaging (HARDI) has been used extensively to study the brain white matter architecture. However, the spatial resolution of 3D HARDI data acquisition, for example of a mouse brain, is still limited at ~100-micron[1]. This limitation is primarily due to a lengthy acquisition time, high diffusion-gradient requirement and signal-to-noise ratio. In contrast, a conventional 3D gradient echo of the same sample can produce a higher resolution image, typically at ~30 micron 3D isotropic resolution, at a much shorter period. Recently, track-density imaging (TDI) reconstruction has been proposed as a way to increase the spatial resolution of reconstructed diffusion images beyond the actual resolution of MRI acquisition[2].

Previously, Ullmann *et al*., 2010 completed an anatomical brain map segmentation of a wildtype adult zebrafish using a 3D gradient-echo MRI data acquired at 10-micron isotropic resolution[3]. As the next step, we extend the study to look into finer definitions of the white matter tracks. The adult zebrafish brain has a relatively small size (4×2×1mm), whose volume is approximately 64 times smaller than an adult mouse brain. Therefore, high-resolution diffusion images are absolutely essential to get a meaningful interpretation of its neurological structures. This requirement is difficult to meet solely from the acquired data due to the limitations of MRI hardware. In this study, we used TDI to reconstruct fibertrack maps into a resolution 10 times higher than the raw HARDI data.

Method: After anaesthesia, the dorsal cranium of an adult zebrafish was removed and the brain was incubated for 12h in 4% paraformaldehyde and 0.5% Magnevist. Subsequently, the brain sample was set in fomblin for imaging using a 5 mm solenoid coil. MRI was performed using 16.4T Bruker vertical wide-bore NMR spectrometer equipped with Micro2.5 gradient. Anatomical images were acquired using 3D-Gradient echo (TR/TE = 8.3/50 ms, FA=30^o), 16 averages at 10-micron isotropic resolution (17h). HARDI data was acquired using 3D diffusion spin-echo sequence TR/TE=450/22 ms, 4 averages, matrix = 144×54×54, 48-micron isotropic resolution (47 h), with uniformly distributed 30 diffusion gradient directions at B=5000 s/mm^2, two B=0 with diffusion times δ/Δ = 2.5/14ms.

Fibertracks were reconstructed using the programs DiffusionToolkit/TrackVis (Q-Ball/FACT)[4] and MRTrix (constrained spherical deconvolution (CSD)/probabilistic fibertracking). Q-Ball/FACT fibertracks were calculated from single seeding points of each voxel and propagated with a 35^o angle threshold. CSD model for multiple fiber orientations was calculated using the maximum harmonic order l_{max}=6. A whole brain CSD probabilistic tractography was used to calculate 2 million tracks with the minimum track length is ≥ 2 voxel size. TDI maps were then generated by calculating the total number of tracks in a 10 or 5-micron isotropic grids[2].



Results: A 3D-T_1/T_2* weighted gradient echo image produced good contrast for delineating zebrafish brain structures, where the white matter tracks appear more hypointense compared to the grey matter regions. The TDI map reconstructed 5-micron grid resolution revealed more structural information not easily visible in the 10-micron gradient echo image. For example the medial and lateral medial longitudinal fascicles are more clearly visible in TDI (Figure 1). The fibertracks resulting from Q-ball/FACT calculation produced more definite and conservative profile, and were used for segmentation of the major white matter fibertracks.

Figure 1: (A) Horizontal TDI map with directional colour scheme of zebrafish brain reconstructed at 5-micron resolution. (B) A corresponding plane of the 3D Gradient echo image at 10-micron isotropic resolution. The medial and lateral medial longitudinal fascicle are marked by (+) and (*) respectively.

References:

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