Localized in vivo high resolution HARDI reveals complex microstructure in the mouse brain

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Purpose: Advanced diffusion MRI techniques, e.g., diffusion tensor imaging (DTI) and high angular resolution diffusion imaging (HARDI) [1], provide unique tissue contrasts and microstructural information, and allow the noninvasive study of neuronal microstructure and connectivity. However, the lengthy acquisition required for these techniques often limits their widespread application in vivo, especially for research in rodent models, which require high spatial resolution to resolve small structures or lesions. We combined fast imaging sequence and selective excitation of the structures of interest to achieve fast HARDI of the mouse brain in vivo. The high resolution HARDI data revealed the local circuitry of the live mouse brain in unprecedented detail.

Methods: Five 3-month old C57BL/6J mice were studied. Experiments were performed on a Bruker horizontal 11.7T system. Based on the theory of a linear class of large tip angle (LCLTA) [2] pulses, 90° pulses of 2.5 ms duration were designed to selectively excite desired regions in the axial plane using a 72mm quadrature volume transmitter coil. The designed pulses were combined with a modified 3D diffusion weighted gradient spin echo (DW-GRASE) sequence. The images were acquired using a 10 mm planar surface receiver coil placed near the selected region. A conventional slice-selective refocusing pulse was used to restrict the imaging slab along the *z*-axis. Imaging parameters were: TE/TR = 33/500ms, NEX=2, 60 directions, b = 3000 s/mm^2, 6 x 4 x 4 mm^3 field of excitation (FOE) and 0.1 mm isotropic resolution for the hippocampus (plus part of the cortex) and 8 x 6 x 5 mm^3 FOE and 0.125 mm isotropic resolution for the cerebellum. It took less than 2 minutes to acquire one diffusion-weighted image and approximately 2 hours for the entire dataset. The intensity of the diffusion images were corrected based on reference scans acquired from an oil phantom. Diffusion MRI data were analyzed using MRtrix [3].

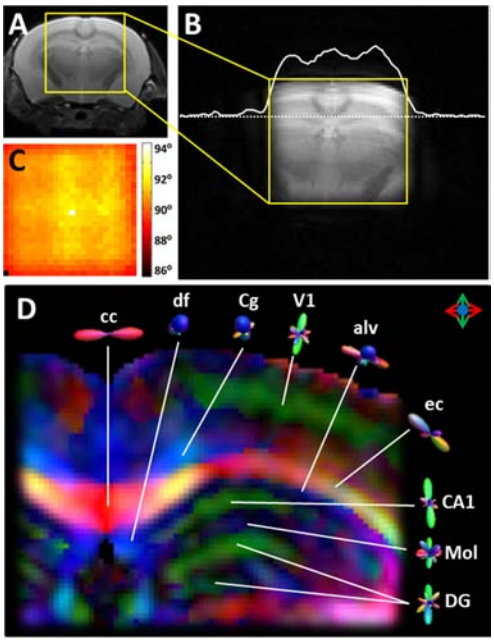

Fig. 1 A-C): Illustration of the efficiency of localization for one rectangular FOE. The overlaid profile in B) shows the image intensity along the dashed line. C) The uniformity of the excitation measured using the double flip-angle method. D): Local high resolution in vivo HARDI of the mouse cortex and hippocampus with the 3D FODs shown for indicated voxels.

Results: For circular or rectangular FOEs, the designed RF pulses provided uniform excitation within the intended region (90º ± 2.2º, Fig. 1C) and excellent outer-volume suppression (< 6%, Fig. 1B). Fig. 1D illustrates a FOE that included the cerebral cortex and dorsal hippocampus acquired at 0.1 mm isotropic resolution. Small white matter structures, e.g., the dorsal fornix (df), could be resolved at this resolution, as well as complex axonal organization, e.g., the crossing fibers in the alveus (alv) of hippocampus, and the well-organized fibers in the dentate gyrus (DG) and CA1. In the mouse cerebellum, the HARDI generated fiber orientation density (FOD) map revealed three groups of crossing fibers (Fig. 2B): the parallel fibers (red), Purkinje fibers (blue), and afferent mossy or climbing fibers (green), crossing each other in an orthogonal arrangement. The FOD-based fiber tracking results further showed clusters of the Purkinje fibers along the medial-lateral directions (Fig. 1C), which may correspond to the Purkinje cell clusters in the cerebellum.

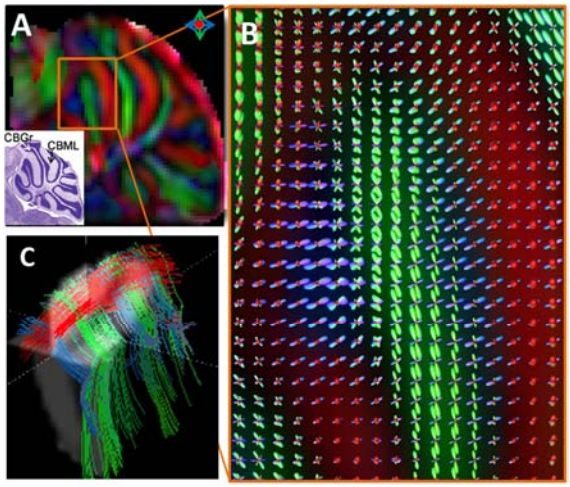

Fig. 2 Local high resolution in vivo HARDI of the mouse cerebellum: A) A direction-encoded colormap showing the cerebellar granule layer and cerebellar molecular layer. B) FOD map of a sagittal section in a cerebellar lobe, and C) the reconstructed fiber tracts showing three groups of fibers in the cerebellar cortex.

Discussion and conclusion: We used reduced field of view MRI (4) to improve imaging resolution and speed. High resolution (up to 0.1 mm isotropic) diffusion MR imaging in the mouse brain could be achieved in a rapid fashion. At this resolution, small structures in the mouse brain could be resolved and complex axonal organization visualized. While imaging with whole brain coverage is ideal for many studies, localized high resolution imaging is useful for studies that focus on a particular brain region, e.g., in mouse models of stroke or tumor. Given that conventional Cartesian imaging uses rectangular field of view, simple rectangular or circular FOE is sufficient for general applications. For more advanced studies, complex excitation patterns such as demonstrated recently by Ullmann et al [4] using parallel transmission technique may be needed.

References: 1. MRM 2002 48(4): 577-82. 2. JMR 1989 82(3): 571-87; 3. Neuroimage 2007 35(4): 1495-72. 4: JMRI 2009 29(4): 987-03. 5: MRM 2012 doi: 10.1002/mrm.24381. **Acknowledgement:** P41EB015909, R21NS059529, R01NS070909, R21NS065306