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Axon Diameter Inferences in the Corpus Callosum and Fornix of the Mouse Brain from Images with Low SNR

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It is thought that the diameters of axons change due to disease. Until recently measurements of axon diameters (AD) could only be done invasively. AD can now be inferred non-invasively using a magnetic resonance imaging temporal diffusion spectroscopy (TDS) technique that requires many images to be collected with a range of diffusion-times or frequencies. Collecting many images to average together for a higher signal-to-noise ratio (SNR) becomes too time-consuming. Thus, low SNR (5-6) images of mouse brain were analyzed to infer axon sizes.

TDS methods require many measurements at different gradient strengths and frequencies making data collection time consuming and difficult to obtain high SNR in a reasonable amount of time. This work uses oscillating gradient TDS to study the corpus callosum (CC), fornix and optic tract (OT) of the mouse brain under the condition of low SNR to determine if reasonable results can be obtained with low SNR.

A 15.5 week-old female mouse (Kras/p53 on a C57BL/6 background) was perfused with formalin. Brain (in skull) was soaked in a formalin solution for 24 hours then transferred into a Phosphate-buffered saline (PBS) solution for 24 hours then transferred into another PBS solution for 24 hours prior to imaging to filter out any remaining formalin. All experiments were approved by both Universities'Animal Care Committees.

The sample was imaged using a 7 T Bruker Avance III NMR system with Paravision 5.0 with a BGA6 gradient set with a maximum gradient strength gmax of 430357 Hz/cm, and a 3.5 cm diameter bird cage RF coil. Each 20 ms apodised cosine gradient pulse ranged from n=1-20, in steps of 1. Two different gradient strengths were used for each frequency and gradient pulses were separated by 24.52 ms.

TDS was able to infer ADs of 4.8±1.2μm in the CC and 2.4±0.6μm in the fornix using low SNR images. The models used to infer ADs assume the diffusion gradient direction to be perpendicular to the axons. The gradient direction was approximately parallel to the axons in the OT and we suspect this explains why we were unable to infer ADs in the OT. The gradient frequency range successfully targeted ADs ˜2-4 μm in the fornix and CC. The low SNR did not seem to have an effect on the ability of the method to infer ADs. This study is the first step toward showing the feasibility of using OGSE TDS to infer ADs in situations of low SNR.

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