Pushing the limits of ex-vivo diffusion MRI and tractography of the human brain

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TARGETED AUDIENCE

Clinical Researchers, Physicists, Neurologists

PURPOSE

While DWI-based tractography is a powerful non-invasive method to reconstruct and visualize white matter fiber tracts, its in-vivo resolution is limited by the maximum examination time that is appropriate for human subjects. Ex-vivo DWI can overcome this limitation and therefore achieves significantly higher spatial and angular resolution in reconstructed fiber pathways. The aim of this study was to explore the limits of spatial and angular resolution in long acquisition and high b-value ex-vivo diffusion weighted imaging and tractography of the human brain.

METHODS

With increasing spatial resolution, SNR was expected to be the limiting factor. To ensure the highest possible SNR and allow very high resolutions, a 60 channel coil array with optimized geometry for ex-vivo human brain slabs with thickness between 2 and 5 cm was designed and constructed.[1] As tissue fixation significantly reduces tissue T_1 and T_2 relaxation times[2], a segmented phase-navigated 3D diffusion weighted EPI sequence was used to provide short echo times and sufficiently high SNR values. Images were acquired on a 3T Siemens Magnetom Connectom MRI system with AS302 gradients (300 mT/m maximum gradient strength, 200 mT/m/ms maximum slew rate) to further shorten diffusion gradient durations and TE while maintaining high b-values. SNR and diffusion contrast as well as the quality of selected fiber reconstructions were evaluated and compared to an in-vivo reference data set from the Human Connectome Project (HCP).[3]

RESULTS

For the tissue sample used in this study, the minimum field of view yielded a maximum isotropic resolution of 350 µm with a matrix size of 322x430x128. Although SNR at this resolution was lower than in vivo, especially in the center of the sample, it was still sufficient to reconstruct the diffusion orientation distribution functions (ODF). The total acquisition time for sampling 120 diffusion directions was 20 hours. Compared to the standard in-vivo protocol of the Human Connectome Project at 1.5 mm resolution, ODF density could be increased by a factor of 78.

An exemplary tract reconstruction at the intersection of the corpus callosum with the corticospinal tract shows the significantly higher level of detail in the ex-vivo data set (see Fig. 1).

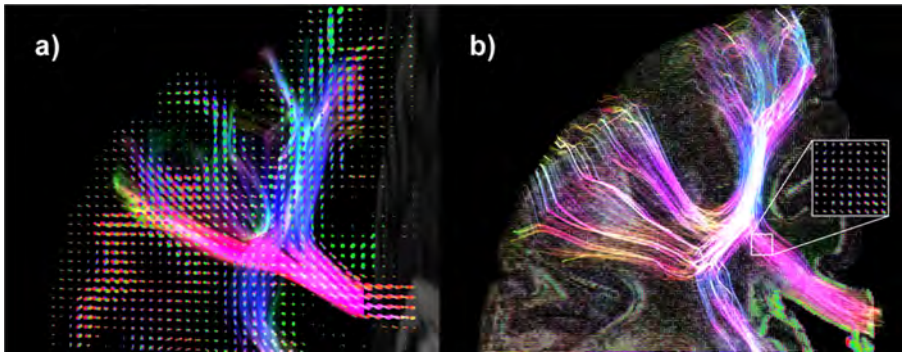

Figure 1: ODF visualization and exemplary fiber tract reconstructions in the crossing area of the corticospinal tract and corpus callosum. **a)** HCP in-vivo reference (full brain, 1.5 mm isotropic resolution, 128 directions, b=5.000 s/mm^2, acquisition time: 20 minutes) **b)** Formalin-fixed brain tissue sample (coronal slab of left hemisphere 8x14x4 cm, 350 µm isotropic resolution, 120 directions, b=30.000 s/mm^2, acquisition time: 20 hours, TE/TR=79/400 ms)

DISCUSSION

The high density of diffusion ODFs is beneficial for the reconstruction and qualitative analysis of small fiber structures. Furthermore, statistical analysis of local indices such as fractional anisotropy along reconstructed tracts or within volumes of interest may also benefit from the additional information. However, the overall diffusion contrast in the ex-vivo acquisition is significantly reduced by the tissue fixation as water content and mobility are reduced. This leads to lower FA values and less variation in the shape of the reconstructed ODFs. Therefore, angular resolution, i.e. the number of resolvable diffusion directions per voxel is limited, even for a high number of sampled diffusion directions and very high b-values of 30.000 s/mm^2.

CONCLUSION

Increasing SNR by using an optimized coil geometry in combination with a fast image acquisition sequence (short TE) lowers the limit for spatial resolution in ex-vivo DWI. The very high spatial resolution of 350 µm gives insight into small-scale and complex fiber architectures. However, the need for tissue fixation imposes a limitation on the achievable diffusion contrast by reducing image SNR, relaxation times and water mobility. Application of this method to unfixed fresh brain specimen may allow even higher resolutions with stronger diffusion contrast to resolve higher-order fiber crossings. This will be the subject of future studies.

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