

# Resolving White Matter Structures of Human Hippocampus in vivo with High Resolution DTI at 3 T

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## Introduction

The human hippocampus is an important region for memory formation and vulnerable to numerous neurological disorders, such as temporal lobe epilepsy, Alzheimer's disease, mild cognitive impairment and schizophrenia. The hippocampus cross-section has a well-defined laminar structure. The connections within the hippocampus generally follow this laminar format, and, as a rule, are unidirectional. Diffusion tensor imaging (DTI) is a good candidate for probing the underlying neural architecture and monitor pathological changes in the hippocampal pathways [1]. However, because of the small size of the human hippocampus (of the order of  $50 \times 8 \times 8 \text{ mm}^3$ ), high spatial resolution DTI measurements have been mostly conducted *ex vivo* at high magnetic fields [2]. *In vivo* DTI measurements of the hippocampus have been also complicated by the sensitivity to susceptibility artifacts because of the proximity of the hippocampus to the surface of the temporal lobe. High resolution *in vivo* DTI measurements have been attempted by using a reduced-FOV approach in single-shot imaging [3] or by implementing multi-shot techniques with navigators [4]. To our knowledge, previous high resolution hippocampus DTI measurements were acquired at 1.5 T and with a limited number of diffusion encoding directions. We describe the application of a multi-shot technique combined with reduced-FOV imaging [5] to increase the spatial and angular resolution of *in vivo* hippocampus DTI at 3 T.

## Materials and Methods

**Acquisition technique:** Self-navigated variable density spiral encoding was implemented for oversampling the central *k*-space region in order to correct for motion-induced phase errors among interleaves. Spatially-selective RF pulses were applied on four outer volume regions to create a square with a reduced field of view of  $\text{FOV}/r$ , corresponding to a FOV reduction factor  $r$  and the *k*-space trajectory were designed to satisfy Nyquist over the reduced-FOV. The required number of interleaves and the total acquisition time was therefore reduced, without an increase in the readout time of each interleaf [5]. A reduction in SNR accompanied the reduction in FOV, but the shorter acquisition time for each DW image allowed for using higher number of diffusion encoding directions.

**In vivo measurements:** The interleaved variable density spiral diffusion-weighted spin-echo sequence was implemented on a head-only Siemens Allegra 3 T system. Spatially-selective RF pulses were applied to create a square reduced-FOV= 4 cm for imaging 4 coronal slices perpendicular to the main axis of the right hippocampus of a healthy human volunteer in accordance with the institutional review board (Figure 1). The imaging parameters were: TE=58 ms, TR=2 R-R intervals, 22 interleaves, matrix size=400 for full-FOV=24 cm and slice thickness=5 mm. The voxel size was  $0.6 \times 0.6 \times 5.0 \text{ mm}^3$  and the gradient readout duration was equal to 8.5 ms. Thirty diffusion directions were applied to obtain the diffusion tensor with diffusion-weighting parameters:  $\delta=22 \text{ ms}$ ,  $\Delta=32 \text{ ms}$  and  $g=30 \text{ mT/m}$ , corresponding to  $b=770 \text{ s/mm}^2$ . Peripheral gating was used with a zero trigger delay to reduce the sensitivity of the acquisition to tissue motion caused by blood and CSF pulsation. The acquisition was repeated 2 times resulting in a total scan time of 45 mins for a subject with an R-R interval of 1 s. The acquired diffusion-weighted data were fitted to the diffusion tensor model.

## Results and Discussion

The diffusion trace-weighted images (Figure 1) enable delineation of the multiple laminar layers of the hippocampus. The fractional anisotropy maps show elevated FA values in the regions surrounding the hippocampus because of the surrounding white matter tracts (i.e. the angular bundle running along the anterior-posterior direction). Increased FA values are also observed within the superior part of the hippocampus originating from the white matter bundle of alveus and fimbria, running along the anterior-posterior direction. The present DTI results are in agreement with the results of Porter [5] and show the ability to perform high spatial resolution DTI at 3 T with voxel volume below  $2 \text{ mm}^3$  and immune to magnetic susceptibility effects. The total scan time is relatively long, but the proposed acquisition scheme employs short readout gradients for spatial encoding with voxel volume of  $0.6 \times 0.6 \times 5 = 1.8 \text{ mm}^3$ , which is the lowest achieved to our knowledge in hippocampus *in vivo* DTI (voxel volume was  $4.1 \text{ mm}^3$  in [4]). The employed acquisition strategy also enables high angular resolution diffusion encoding.

The proposed acquisition scheme constitutes a potential alternative for high resolution imaging of the human hippocampus, as recently achieved with  $T_1$ ,  $T_2$  and  $T_2^*$  contrast at 7 T [6, 7]. High spatial and angular resolution DTI can provide gross or localized anatomical information based on the diffusion trace-weighted maps or the color-coded FA maps, but it is also able monitor changes in the diffusion properties of the tissue, which can be used in evaluating patients with seizures, epilepsy or Alzheimer's disease.

## Conclusion

The present study provides the highest spatial resolution of *in vivo* hippocampus DTI at 3 T enabling the depiction of the white matter structures of alveus and fimbria for coronal slice orientation.

## References

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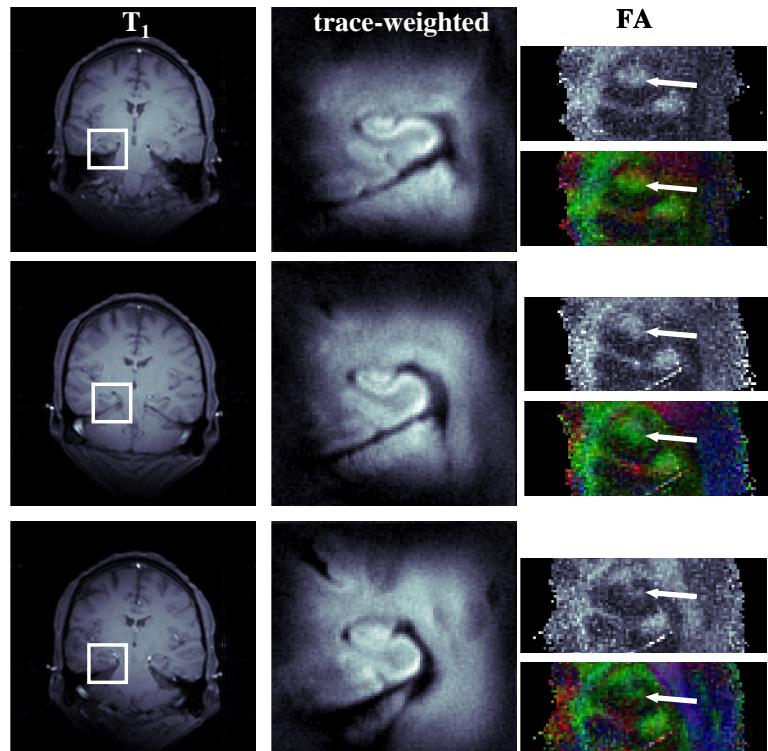


Figure 1: Three coronal slices through the hippocampus of a healthy volunteer, representing full-FOV  $T_1$ -weighted images, and trace-weighted, fractional anisotropy (FA) and color-coded FA maps for the high resolution DTI acquisition of a reduced-FOV centered on the right hippocampus (red corresponds to L/R, green to A/P and blue to S/I). The white box on the  $T_1$ -weighted images shows the position of the reduced-FOV. Regions of elevated FA are observed within the hippocampus region (indicated by the white arrows) for both slices with fibers running in the anterior-posterior direction, corresponding to the white matter structures of alveus and fimbria.