# MR-microscopy of human hippocampi: Multiparametric characterization of hippocampal sclerosis

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## Purpose

According to guidelines of the International League against Epilepsia (ILAE), the neuropathologic differentiation of hippocampal sclerosis is based on the quantification of cell loss in subfields (CA1-CA4) of the hippocampus [1]. In this initial study, we investigate whether the detection and subfield-specific evaluation of the underlying tissue changes is also possible using multiparametric MRI in high resolution at 7T.

## Materials and Methods

MR sequence evaluation was performed on the basis of a resected non-sclerotic (ILAE no-HS) and a sclerotic (ILAE Type 1) hippocampus using a preclinical 7T-MRI scanner (ClinScan 70/30, Bruker). Morphologic images were acquired using a T1-weighted gradient echo sequence (repetition time (TR)/echo time (TE): 2000/25 ms, averages (av): 2, resolution (res): 43x43x300 µm, acquisition time (TA): 37 h) and a T2-weighted turbo spin echo sequence (TR/TE: 8520/95 ms, av: 4, res: 43x43x300 µm, TA: 54 h). Voxel based maps of T1-, T2- and T2*-relaxation times were calculated for each hippocampus. Diffusion tensor imaging (DTI) was performed with six b-values (b=0, 200, 400, 600, 800, 1000) in 265 directions (TR/TE: 8000/50 ms, av: 3, res: 300 µm isotropic, TA: 8.5 h). CA1, CA2, CA3 and CA4 were delineated on T2-weighted images according to [2]. In each subfield, T1-, T2-, T2*-relaxation times, apparent diffusion coefficient (ADC) and fractional anisotropy (FA) were determined. Based on DTI data, fiber tracts were reconstructed for the non-sclerotic hippocampus using syngo software (Siemens). After imaging, hippocampi were passed on to histological examination for being matched with MRI data.

## Results

On morphologic images, a narrowing of the pyramid cell sector CA1 and a subtotal to total loss of efferent fibers for the sclerotic as compared to the non-sclerotic hippocampus are discernible (Figure 1). The dentate gyrus is broadened (histologically corresponding to a granule cell dispersion) and focally not definable (granule cell rarefication). The ADC is increased by 90, 117, 111 and 78 % in CA1, CA2, CA3 and CA4 as compared to the non-sclerotic hippocampus. Further parameters vary only moderately between sclerotic and non-sclerotic hippocampi (T1: 19, 20, 19, 9 % in CA1, CA2, CA3 und CA4, respectively; T2: 4, 3, 12, 18 %; T2*: 3, 31, 14, 13 %; FA: 1, 6, 1, 1 %). Tractography based on DTI data of the non-sclerotic hippocampus is shown in Figure 2.

## Conclusions

Distinct morphologic differences between sclerotic and non-sclerotic hippocampi are clearly visible on T1- and T2-weighted high-resolution images. With respect to multiparametric imaging, ADC is most promising for differentiation of sclerotic and non-sclerotic subfields. In conclusion, MR-microscopy at 7T supplements neuropathologic evaluation of hippocampal sclerosis. Furthermore, time-adapted imaging protocols might be translated for patient application on ultra high field systems.

## References

[1] Blümcke I., et al, A new clinico-pathological classification system for mesial temporal lobe sclerosis. *Acta Neuropathol* (2007) 113:235-244.
[2] Mueller S.G., et al, Measurement of hippocampal subfields and age-related changes with high-resolution MRI at 4T. *Neurobiology of aging* (2007) 28:719-726.

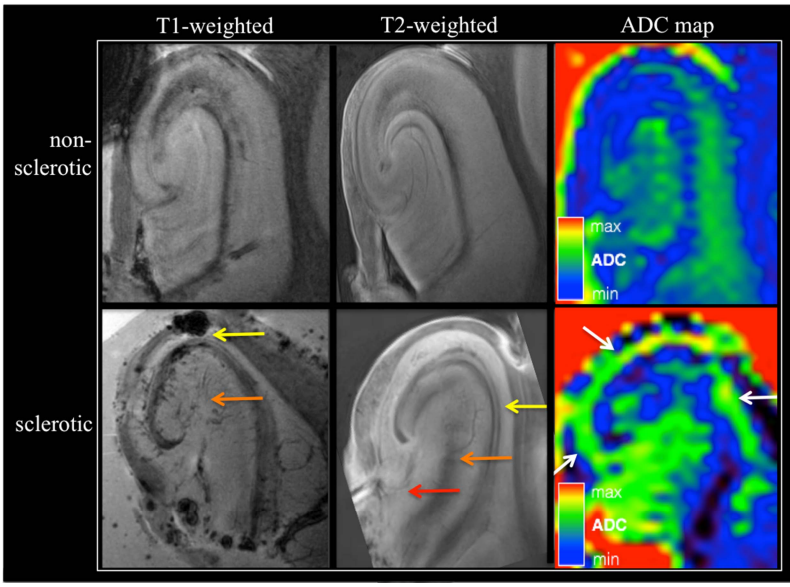


**Figure 1:** Ex vivo MR-microscopy of a non-sclerotic (first row) and a sclerotic hippocampus (second row). T1-weighted (first column), T2-weighted (second column) morphology and color-coded ADC map (third column). A narrowing of the pyramid cell sector CA1 (yellow arrows) and a broadening of the dentate gyrus (histologically corresponding to a granule cell dispersion, orange arrows) are visible. Red arrow indicates a subtotal to total loss of efferent fibers for the sclerotic as compared to the non-sclerotic hippocampus. The ADC is increased for the sclerotic hippocampus in all subfields (white arrows).

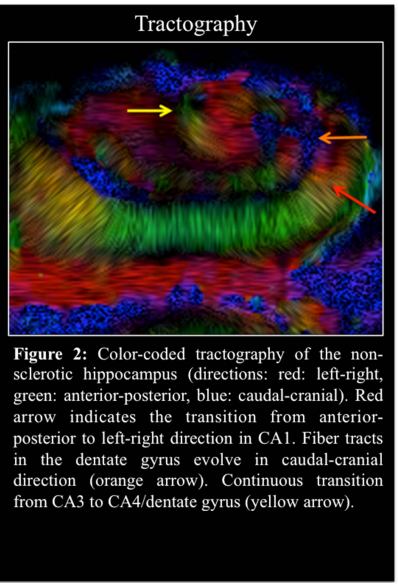


**Figure 2:** Color-coded tractography of the non-sclerotic hippocampus (directions: red: left-right, green: anterior-posterior, blue: caudal-cranial). Red arrow indicates the transition from anterior-posterior to left-right direction in CA1. Fiber tracts in the dentate gyrus evolve in caudal-cranial direction (orange arrow). Continuous transition from CA3 to CA4/dentate gyrus (yellow arrow).