Visualisation and Quantitative Assessment of the NAWM in MS Patients by using Q-space Analysis of the Slow Diffusion Component at 3T

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Introduction: Diffusion weighted MRI (DWI) is sensitive to changes of structural and functional status of brain parenchyma. It has been suggested, that the slow diffusion might predominantly represent intra-axonal/intra-cellular water diffusion. Imaging of the slow diffusion components is interesting for theoretical considerations and challenging for technical reasons. In previous studies at 1.5 T, a very high sensitivity of Q-space imaging to detect and visualise subtle tissue changes in the normal appearing white matter (NAWM) was noted. We optimised the imaging approach using the increased SNR of a 3 T system to study the NAWM. We therefore developed and implemented sequences and analysis strategies along the lines suggested by Assaf, Cohen et al. One part of the analysis focused on the visual analysis of the normal appearing white matter, a strategy usually not helpful with other imaging modalities.

Methods: We examined 16 MS patients (6 women and 10 men; mean age = 37 years (22-51); mean disease duration = 8.8 years; mean EDSS = 4 (0-6.5)) with various disease courses (CIS, RRMS, SPMS, PPMS) and 10 normal controls (NC) (5 women and 5 men; mean age 32.7 years (26-46)) on a 3 T Siemens ALLEGRA system. The standardized brain MRI protocol included transverse 5mm T2w-TSE, FLAIR and DWI including high *b*-value measurements for q-space analysis. DWI: 6 directions, 16 *b*-values in each direction, *b*-value range: *b*= 0 to 9021 s/mm^2 by linearly increasing the diffusion gradient amplitude, **δ/Δ** = 43/48 ms; TE/TR = 125/1450 ms, 128x128 matrix, voxel size = 1.875x1.875x5 mm^3. This sequence provided 8 axial slices centered at the level of the corpus callosum. Acquisition time for the whole DWI data set was 14 minutes. The NAWM was analysed on probability of zero displacement (PZD) maps (the peak intensity of the displacement distribution probability function). The maps display the information using a color scaling scheme. Lesions were marked on FLAIR images and after coregistration with the DWI data, lesion areas were excluded from quantitative analysis. Grey and white matter were segmented and the NAWM was analysed. Furthermore images were visually analysed by comparison to normal control data.

Results: *Normal controls:* PZD maps provided strong contrast between grey and white matter emphasising the relatively low diffusion in normal white matter. Warm colors indicate a high probability for zero displacement, cold colors describe areas with higher water proton mobility, e. g. in the sulcal or ventricular CSF. *MS patients:* All macroscopically visible lesions and areas of questionable hyperintensity on T2-weighted MRI were strongly contrasted and displayed on PZD maps (Fig. 1). Regardless of the clinical characteristics NAWM changes were noted in all but 3 patients with mild signal change. Furthermore it is visually apparent, that large parts of relatively normal appearing white matter have lost slow diffusion components (as represented by increase of cold colors). This is also apparent on average PZD plots (Fig. 2). Further histogramm analysis comparing controls and patients clearly demonstrated the loss of slow diffusion pixels in the white matter of MS patients. Mean values of PZD in controls were significantly higher than in MS patients.

Discussion/Conclusion: In this study on a 3T system we used an adapted protocol for clinical use of PZD maps. It is demonstrated again, that PZD maps are highly sensitive to detect reductions of the slow diffusion component in the NAWM of patients with different MS types. The data appears suitable for a visual analysis as demonstrated in conjunction with a conventional contrast image. None of the clinical characteristics were predictive of the NAWM changes, which indicates the additional information and the tendency to under- or overestimate pathological changes in MS patients. This study demonstrates the need for more methods to identify NAWM changes in an accessible way.

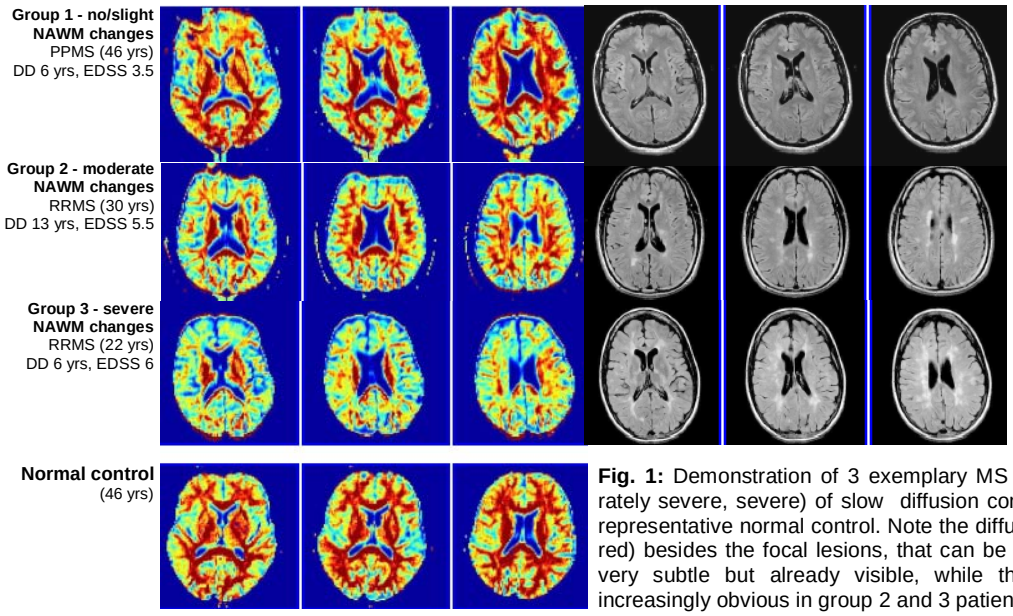
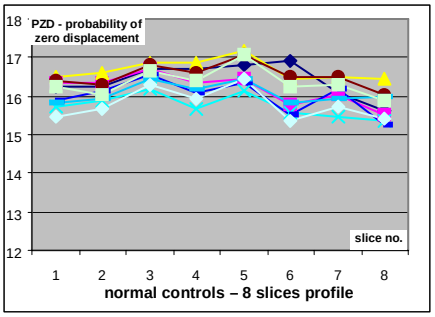


Fig. 1: Demonstration of 3 exemplary MS patients with different degrees (mild moderately severe, severe) of slow diffusion component reduction in direct comparison to a representative normal control. Note the diffuse reduction of the warm colors (red, brown-red) besides the focal lesions, that can be seen as well. In the first group (mild) this is very subtle but already visible, while the reduction and loss of warm colors is increasingly obvious in group 2 and 3 patients.



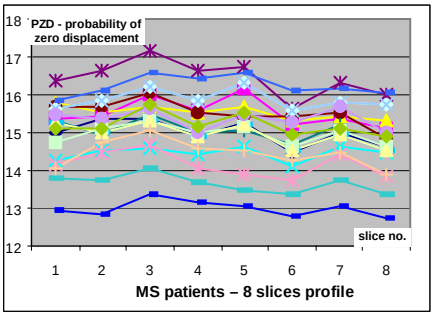


Fig. 2: Values of average probability of zero displacement (PZD) in normal control data and patient data.