Relationships between Brain Water Content and Diffusion Tensor Imaging Parameters (Apparent Diffusion Coefficient, Fractional Anisotropy) in Multiple Sclerosis

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Purpose For a better understanding of the diffusion tensor imaging (DTI) properties of multiple patients relative to controls, their brain tissue water contents were quantified and correlated to the apparent diffusion coefficient and fractional anisotropy.

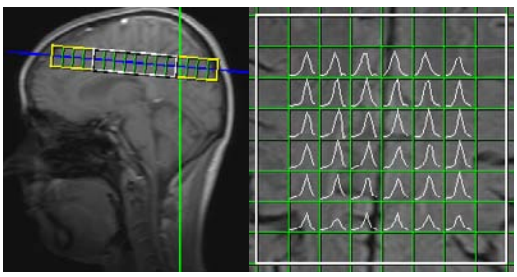
Introduction Considering that brain tissue water signal has practically become the gold standard in quantitative magnetic resonance spectroscopy, meaning that ‘absolute concentrations’ of choline, creatine and N-acetyl aspartate are generally derived from the water signals obtained in measurement repeated without water suppression (making use of assumed brain tissue water contents), it is striking how scarcely documented brain tissue water contents are themselves. It has been reviewed that changes in tissue content can have an important effect of global measures of brain volume (1). Changes as much as 30-40 ml were observed after dialysis of patients with renal failure. In MS acute lesions are associated with breakdown of the blood-brain barrier, inflammation and vasogenic oedema. Visible swelling is sometimes seen on MRI in these lesions of the brain, spinal cord and optical nerves. The extent and volume of gadolinium enhancing lesions in the brain may therefore affect overall brain volume, and is a variable to consider when assessing and interpreting tissue volume changes. This is especially relevant in therapeutic trials or natural history studies, where therapies are known to have an anti-oedema or anti-inflammatory effect. The potential of subtle variations in the blood-brain barrier and brain water content to affect volume measures is therefore not excluded (1). Presented here is the first study in which the results of DTI in MS patients relative to controls are compared with their brain tissue water contents.

Methods 15 patients (mean age 45 ± 8 years) with definate MS according to McDonald’s criteria and with expended disability status scale ratings of 6 or lower, were examined by MRI and ^{1}H MRS at 1.5 Tesla using the standard head coil of a Magnetom Sonata system (Siemens AG, Erlangen, Germany). The MRI protocol included a diffusion-weighted spin-echo echo-planar imaging (SE-EPI) sequence in order to reduce motion artefacts. DTI: Diffusion weighted images were obtained in 12 independent directions with a b value of 0 to 1000 s/mm^2 and 4 mm slice thickness without gap oriented parallel to the CSI volume of interest in order to facilitate the determination of DTI parameters for the voxels defined by MRS (2). MRS determination of water contents: PRESS 2D-CSI measurements (TR/TE 1500/135 ms) were performed without water suppression. A T2 weighted MRI series was used as guidance for defining a CSI volume of interest of 8x8 cm^2 (64 spectra) within a 16x16 cm^2 FOV (256 phase encode steps) located cranial to the ventricles, a transverse 2 cm thickness slice in that part of the brain where the white matter (WM) is most abundant, for MRS. At 1 acquisition per phase encode step the CSI measurements took 7 min.

Results The water contents and DTI parameters in the inner 6x6=36 CSI voxels of the total of 8x8=64 voxels of 2 cm^2 each were compared. The spectral map of water is shown in Fig.1. Water content was increased in patients compared with controls (gray matter (GM): 244±21 vs 194±10 a.u.; WM: 245±32 vs 190±11 a.u.), FA decreased (GM: 0.226±0.038 vs 0.270±0.020; WM: 0.337±0.044 vs 0.402±0.011), and ADC increased (GM: 1134±203 vs 899±28 {x10^{-6}mm^2/sec}; WM: 901±138 vs 751±17 {x10^{-6}mm^2/sec}). Correlations of water content with FA and ADC in WM were strong ($r = -0.68$, $P < 0.02$; $r = 0.75$; $P < 0.01$, respectively), those in GM were weaker ($r = -0.50$, $P < 0.05$; $r = 0.45$, $P < 0.1$, respectively). Likewise, FA and ADC were more strongly correlated in WM ($r = -0.88$; $P < 0.00001$) than in GM ($r = -0.69$, $P < 0.01$). Fig.2, left part, shows that the slopes of ADC against water content are very similar in GM and WM while having different intercepts, and that the control values exactly match the lower left positions obtained by extrapolation of slopes of the patients data. The same applies to the inverse correlation plots of FA against water content (Fig.2, middle). Furthermore, FA and ADC are more strongly correlated to each other in WM than in GM (Fig.2, right part).

Discussion We have shown that the DTI parameters ADC and FA, while important indicators of neuron structure and of a loss of structure in patients suffering from MS, an inflammatory demyelinating disease, relate to alterations in brain water content. The observed increases in WM (+26%) as well as GM brain tissue water content with MS (+29%) are much larger than has been reported before (2.2-5.6%)(3-5). Those studies are questionable, however: in view of our data incorrectly assuming unaltered GM water content (3), performed post mortem (4) and on tissue samples (5). Further analyses of our data indicated that water relaxation time changes and/or increased CSF contents in MS patients compared to controls contributed not significantly to our observations. We suggest potential clinical benefits from the monitoring of water content in both normal appearing brain tissue and white matter lesions during any therapy known to have anti-oedema or anti-inflammatory effects.

References 1. McDonald WI, Compston A, Edan G, Goodkin D, Hartung H-P, Lublin FD, McFarland HF, Paty DW, Polman CH, Reingold SC, Sandberg-Wollheim M, Sibley W, Thompson A, Van Den Noort S, Weinshenker BY, Wolinsky JS (2001) Recommended diagnostic criteria for multiple sclerosis: Guidelines from the international panel on the diagnosis of multiple sclerosis. Ann Neurol 50:121-127. 2. Irwan R, Sijens PE, Potze JH, Oudkerk M. Correlation of MR spectroscopy and diffusion tensor imaging. Magn Reson Imaging 23:851-858. 3. Laule C, Vavasour IM, Moore GRW, Oger J, Li DKB, Paty DW, MacKay AL (2004) Water content and myelin water fraction in multiple sclerosis; a T1 relaxation study. J Neurol 251:284-293. 4. Tourtellotte W, Parker J (1968) Some spaces and barriers in postmortem multiple sclerosis. Progr Brain Res 29:493-525. 5. Sappey-Marinier D (1990) High-resolution NMR spectroscopy of cerebral white matter in multiple sclerosis. Magn Reson Med 15: 229-239.



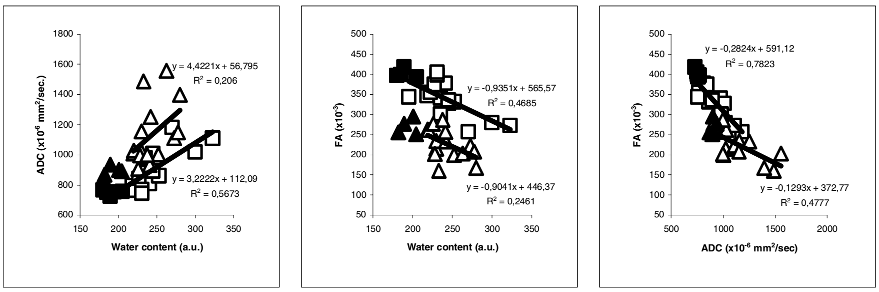


Fig.1. Chemical shift imaging showing the water map of the 6x6x2 cm^3 plane quantified in MRS and DTI.

Fig.2. Plots of ADC vs water content, FA vs water content and FA vs ADC in WM (blocks) and GM (triangles) of MS patients (open symbols) and controls (closed symbols)