Development and Evaluation of a Quantitative Brain Atlas @1.5T and its Application to MS

V. Ermer[1], H. Neeb[2], and N. J. Shah[1,3]

[1]Institute of Neurosciences and Biophysics, Research Centre Juelich, Juelich, Germany, [2]RheinAhrCampus Remagen, University of Applied Sciences Koblenz, Remagen, Germany, [3]Faculty of Medicine, Department of Neurology, RWTH Aachen University, JARA, Aachen, Germany

Introduction:

The work presented here is based on the combination of quantitative MR imaging and human brain mapping. Since many diseases are related to pathological changes of the water content, a quantitative measurement can provide significant information about the physiological hydration status at any given time. This work therefore reports on the development of the first quantitative brain atlas for tissue water content. Although the use of standard brain atlases is well established in the MR community, none of the commonly utilised standard brains or atlases, such as MNI305 or ICBM152 [1-4], provide quantitative information. The quantitative information allows for a definition of normal values and the corresponding confidence ranges for the water content in each voxel of a healthy human brain. In order to allow for a comparison of the water content distribution between healthy and diseased brains, quantitative data sets from 35 healthy volunteers were averaged to create an atlas of the absolute brain water content. Several approaches for atlas formation were extensively investigated and validated. Using a one-sample t-test, water content maps of multiple sclerosis (MS) patients were compared to the newly obtained water content atlas.

Methods:

A fast and reliable method for the quantitative measurement of absolute water content in the brain was used and sequence protocols were optimised with respect to the precision and accuracy of the individual measurements [7]. Water content, T_1 and T_2^* were simultaneously mapped based on an acquired series of spoiled gradient echo images with different T_2^*-weighting (QUTE) [5,6]. Following extensive simulations, measurement parameters were optimised as follows: FA=40°, TR=60ms, TE=4.8ms, echo-spacing =3.74ms, 14 time points, 100 slices. To correct for signal saturation effects, two further QUTE measurements were acquired [7], thereby extending the work in the aforementioned reference. According to Mihara et al. [8], the acquisition of two spoiled gradient echo images with different TRs and/or different flip angles allows one to accurately determine T_1. As the relative error in the T_1 measurement is proportional to the number of slices and increases with increasing flip angle [7], two separate QUTE data sets were acquired with a flip angle of 100°, each with 50 slices and a gap between slices of 100%. Data sets were acquired in an interleaved manner to provide full brain coverage. To allow for an accurate quantification of the water content, several factors, such as B_1 inhomogeneities and receiver coil inhomogeneities, which influence the measured signal intensity, were corrected [7]. The sequence protocol for patient measurements was slightly modified in order to reduce the acquisition time, in concordance with the protocol given in [7]. Additionally, a 3D anatomical data set for every volunteer was acquired. To develop the quantitative water content atlas, seven different approaches were investigated. In the first approach (ICBM_Standard), water content maps were first coregistered to the anatomical 3D data set using normalised mutual information as the objective function to be minimised by an affine geometrical transformation (SPM5 [Wellcome Department of Cognitive Neurology, www.fil.ion.ucl.ac.uk]). Then, the 3D data set was normalised to the ICBM standard space based on the MNI305 template [3,4]. Applying the resulting transformation matrix to the coregistered quantitative maps, 35 normalised water content maps were created. The maps were then averaged for each voxel individually to create the quantitative water content brain atlas (called ICBM_standard). For the second approach, instead of using the standard MNI template, the water content map of a randomly chosen subject from the acquired data pool was used as a template to which the other 34 water content maps were directly normalised without using the anatomical 3D datasets (performed for two volunteers and therefore termed Subject No. 3 and Subject No. 8). Further, during the normalisation process, quantitative water content data were smoothed with a) a 4mm Gaussian filter and b) an 8mm Gaussian filter to investigate the influences of the normalisation process with different kernel sizes for smoothing. For the last approach, a randomly chosen order of all 35 subjects was determined. The 3D data set of the first subject was then normalised to the ICBM standard template. The corresponding transformation matrix was applied to the quantitative maps coregistered to the anatomical 3D data set. Then, the second subject was normalised to the normalised water content map of the first subject. From the resulting two data sets, an initial water content atlas based on two subjects was calculated. In the next step, the water content map of the third subject was normalised to this preliminary atlas consisting of two subjects resulting in the generation of a new 3-subject atlas. This procedure was repeated for all subjects until the final atlas consisted of all 35 volunteers. Two randomly chosen orders were defined to create two different iterative atlases (Iterative 1 and 2).

Results:

The average water content of all 35 volunteers investigated was determined to be 70.97% in WM and 81.00% in GM, respectively. The standard error, as defined by standard deviation divided by the square root of the number of subjects, was calculated as a function of the number of subjects contributing to the atlas. The corresponding curves, as presented by Figure 1, provide information about: (1) the approach which results in the lowest standard error; and (2) if the curve converges to a specific value. All seven approaches investigated converge to a standard error of approximately 2% after all 35 subjects were included. The standard error of the approaches using two separate subjects as starting template for the atlas development initially differ by approximately 1%. In contrast, the different kernel sizes employed during the spatial normalisation do not show any significant difference. Both iterative atlases show a similar error evolution, but Iterative 1 initially shows a standard error of approximately 1% higher than Iterative 2. Figure 2 represents one slice of the final water content atlas of (a) the ICBM_Standard approach and (b) the Iterative 1 approach. In Figure 3, the calculated t-map of a one-sample t-test between the ICBM_Standard atlas and the water content map of an MS patient overlaid on the normalised 3D data set of the specific subject is presented.

Figure 1: Standard error evolution of all seven atlases plotted as a function of the number of subjects.
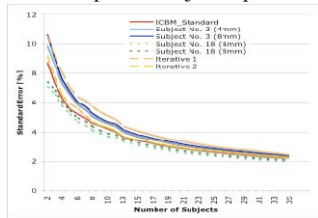

Figure 2: One slice of the quantitative water content brain atlas for (a) the Iterative 1 and (b) the ICBM_Standard approach.
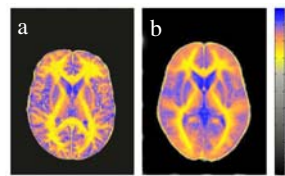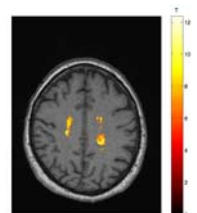

Figure 3: T-maps of an MS patient, overlaid on the 3D data sets after matching the patient data to the water content atlas.

Discussion:

Using the ICBM_standard approach provides a very stable and reliable result, representing the average water content of a healthy population and a certain intersubject anatomical variability based on MNI coordinates. In contrast, the iterative generation of the atlas using a randomly chosen order of subjects, shows a large influence of the precise order in which subjects are used. However, it provides the highest anatomical accuracy of all approaches and the final standard error converges also to 2 %. In particular, for applications where small local differences in the water content need to be investigated, such as the detection of GM lesions in MS patients, this atlas might provide a better reference basis. On the contrary, for the detection of WM lesions, e.g., the standard water content atlas in ICBM standard space might be superior as it provides a direct access to the exact coordinates of the lesions and therefore the possible physiological effects. As shown in Fig. 3, clearly defined WM lesions with t-values ranging between four and twelve were clearly visible in the difference between the water content maps of an MS patient and the ICBM_standard atlas, demonstrating the possibility to investigate MS lesions based on their absolute water content.

References: [1] Talairach et al. 1988, Thieme Medical Publishers, New York, NY [2] Mazziotta et al. NeuroImage 1995, 2:89-101, [3] Evans et al. 1992, Journal Soc. Neurosci. Abstr. 18:408, [4] Evans et al. 1993, Proc. IEEE-Nuclear Science Symposium and Medical Imaging Conference, 1813-1817, [5] Neeb et al. NeuroImage 2006, 29(3):910-22, [6] Neeb et al. NeuroImage 2006, 31(3):1156-68, [7] Neeb et al. NeuroImage 2008, 42(3):1094-109, [8] Mihara et al. Journal Of Applied Physics 2005, 97