Development and application of a quantitative water content brain atlas

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Introduction:

Quantitative MRI of the brain has gained much in importance in the last few years [1]. Especially for widespread diseases, such as multiple sclerosis (MS) which is one of the most frequent neurological diseases amongst young people, quantitative imaging can provide earlier diagnosis and accurate stage monitoring of the disease and therefore can lead to more precise therapy treatment. It has been previously reported that the water content of MS lesions in white matter (WM) is approximately 8% higher compared to that of healthy WM [1]. Therefore, a fast and reliable method for quantitatively measuring the absolute water content of the brain has been previously developed in-house [2,3]. In order to have the possibility of earlier diagnosis, viz to compare the water content of healthy brain to that of the diseased brain, several quantitative data sets of healthy volunteers have been averaged to create an atlas of the absolute brain water content. This task requires the optimisation of sequence protocols to achieve the highest precision and accuracy of the measurements. The use of standard brain atlases is well established in the MR community, but none of the commonly utilised standard brains or atlases, such as MNI305 or ICBM152 [4-7] provides quantitative information. The presented work shows first results of the newly developed quantitative brain atlas and a comparison to an MS patient data set is also shown.

Methods:

As recently published [2,3], a series of spoiled gradient echo images with different T_2*-weighting (QUTE) was acquired. 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 three further QUTE measurements were acquired [4]. 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. To compensate for inaccuracies resulting from the different relaxation times (T_1) of WM/GM and CSF, two different T_1 maps were acquired using a flip angle of 70° for high T_1 values (CSF) and a flip angle of 100° for lower T_1 values (GM/WM). Due to the fact that the relative error in the T_1 measurement is proportional to the number of slices and increases with increasing flip angle, 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. Additionally, to correct for B_1 inhomogeneities the effective flip angle was determined by measuring two EPI images with different nominal flip angles (30° and 90°) [9]. Receiver coil inhomogeneities can then be calculated by acquiring a third EPI image (FA=90°) using the body coil for transmission and reception and relating this measurement to the corresponding EPI data set acquired with the head coil for signal reception [1]. By placing a reference probe filled with 100% H_2O in the FOV, the measured signal intensity (proportional to the proton density) can be related to the signal intensity of the reference probe and therefore becomes a quantitative measure. Temperature differences between brain tissue and the reference probe need to be corrected because the spin density depends on temperature [10]. During the whole measurement, temperature was monitored by placing a temperature sensor in the reference probe. To provide a more precise normalisation a standard 3D data set for each volunteer was acquired. All experiments were performed on a 1.5T Scanner (1.5T AVANTO, Siemens Medical Systems GmbH, Erlangen, Germany). The sequence protocols for patient measurements were slightly modified to reduce the acquisition time.

The final water maps of seven volunteers were transformed to the same stereotactic space by normalising the 3D data to the ICBM space template provided by SPM5 and transferring the resulting transformation matrix to the water maps. The resulting warped water maps were averaged to create the new standard water map. Conditions such as hypertension and diabetes were used as exclusion criteria during volunteer recruitment. Along with the creation of a water template, a customised 3D template for the presented group was produced simultaneously. The 3D data set of an MS patient was normalised to the customised 3D template and the transformation matrix was transferred to the measured water map of that patient. For verification of the obtained results, a FLAIR (Fluid-Attenuated Inversion Recovery) measurement was performed in addition. In clinical daily routine the FLAIR sequence is the gold standard for detecting white matter lesions.

Results

Simulations have shown that water maps with a precision of > 97% can be acquired. The optimised water mapping protocol provides high-resolution water maps ($1x1x1.5mm^3$) with full brain coverage within 30 minutes. Figure 1 presents the water content of one single slice acquired with the optimised sequence protocol. The water content in WM is approx. 70% and in GM approx. 80 %. In Figure 2, the first standard water map template, averaged over the water content of seven volunteers, is shown. It is representative of a young and healthy population with an average age of 26.71 $\pm$ 5.8 years. From Figure 3, which shows the FLAIR acquisition of an MS patient, one can easily recognise a large white matter lesion in the brain (denoted by the red circle). In the corresponding water map of that patient the same slice is presented (Fig. 4) and the lesion shows a water content of approx. 82%. By matching this water map to the water map template a difference image was calculated (Figure 5). The large differences in the region of the ventricles are due to the fact that the brain of the MS patient is in an acute inflamed stage and therefore the size of the ventricles might be reduced by an overall swelling of the brain. An independent comparison of the absolute water content in WM in the template and the MS brain shows an increase of 5% in the brain of the MS patient.

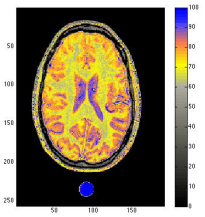

Figure 1: Water map of a healthy volunteer

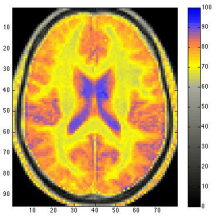

Figure 2: Water map template

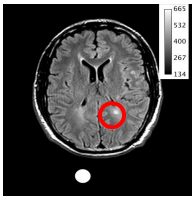

Figure 3: FLAIR (MS patient)

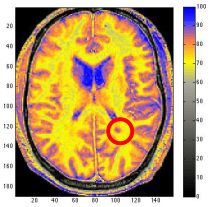

Figure 4: Water map of an MS patient

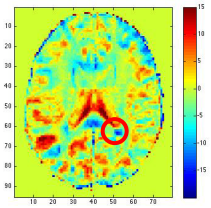

Figure 5: Difference image of the water template and the water map of the MS patient

Discussion:

The first water content atlas of the human brain is presented. A comparison between the atlas and an MS patient data set shows clear differences in the white matter water content and lesions can be clearly identified. These preliminary results provide a good basis for future work. Data acquisition is straightforward and the number of volunteers who contribute to the template data will increase quickly. Previous studies have shown that the water content changes with age and therefore several age-specific templates need to be created [2]. Especially for the early diagnosis of neurological diseases related with a change in the water content of the brain, this work could lead to a highly automated and accurate diagnostic tool.

References:

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