Fully Automated Detection of Quantitative Water Content Changes: Application to the Study of Age-and Gender Related Cerebral H2O Patterns

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INTRODUCTION

Many pathological conditions are accompanied by a local or global increase in water content. Diseases of the brain with a high prevalence, such as stoke and tumours, are often associated with oedema of varying extent. A new method which enables the fast and precise measurement of quantitative water content based on T_2^* and T_1 mapping has recently been published [1]. Even through quantitative water content maps can be acquired in clinically relevant measurement times using this approach, manual image analysis is still necessary which generally mitigates against full use of the gathered quantitative information. Therefore, a more objective approach relying on automated image processing without user-interaction is highly desirable to extract all relevant information contained in the quantitative water maps. We present a method based on quantitative T_1-based image segmentation of white matter and cortical grey matter combined with the determination of parameters that are sensitive to changes in both absolute water content and the local cerebral distribution thereof. To demonstrate its power, the method was applied to study cerebral water content and water distribution changes with age and gender in a cohort of 32 normal, healthy volunteers. The results obtained with this approach define normal ranges as well as baseline variations in healthy subjects and therefore form a basis for any future study involving brain pathologies. In addition, the method is ideally suited for the use in both clinical studies and diagnostic routine as it enables the fast processing of relevant information under the constraint that no user interaction is required.

METHODS

Quantitative water content determination was based on the fast and precise measurement of T_2^* and T_1 relaxation curves using the QUTE-EPI and TAPIR sequences [2][3][4]. The T_2^* relaxation curve was extrapolated to an echo time TE=0 to extract the parameter M_0 (tissue). An absolute measure of water content is obtained by placing a reference probe containing doped water within the FOV thereby relating the parameter M_0 (tissue) to M_0 (reference). Corrections for temperature differences between tissue and reference probe, T_1 saturation as determined by TAPIR, receiver coil imperfections, inversion-pulse inefficiency and local flip angle miscalibrations were included. Incorporating all correction factors, the spatial water content in the human brain can be determined in approximately 21 minutes with a precision of >98% including statistical and systematic errors [1].

In order to extract information from the acquired water maps in an automated manner, white and cortical grey matter were segmented based on quantitative T_1 information acquired with TAPIR. Voxels with T_1 in a range of [450ms - 650ms] where considered to be white matter while grey matter was segmented by constraining the longitudinal relaxation time to [1000ms - 1150ms]. The resulting distribution was plotted as a histogram and fitted with a Gaussian function to extract mean μ and width σ of the water content distribution for the respective tissue types. The mean water content difference between adjacent voxels in the vertical (σ_y) and horizontal (σ_x) directions were determined by plotting this difference for all voxels as a histogram. The values for σ_x and σ_y are given by the Gaussian width of the resulting distribution. To determine spatial and local changes in the water distribution, a horizontal (vertical) spatial correlation coefficient $r_{S,x}$ ($r_{S,y}$) was determined as follows: for each voxel, the water content was plotted against its direct right (bottom) neighbour resulting in a 2-dimensional scatter plot. The Pearson correlation coefficient for this distribution was defined as spatial correlation coefficient $r_{S,x}$ as this quantity represents the degree of similarity between neighbouring voxels. The whole procedure was then repeated N times in by increasing the distance between voxels to calculate the correlation between each voxel and its second, third, …, N^{th} neighbour voxel resulting in the measurement of spatial correlation $r_S(d)$ as a function of voxel spacing d. Using this relation, a horizontal (vertical) spatial correlation distance $d_{S,x}$ ($d_{S,y}$) was defined as the distance d_S, where $r_S(d_S)$ equals half the corresponding value r_S between neighbouring points. Finally, the segmented water maps were automatically divided into 4 parts and the mean water content was calculated for the upper right (μ_{UR}), upper left (μ_{UL}), lower right (μ_{LR}) and lower left (μ_{LL}). Based on these mean values, a forward-backward asymmetry was determined as $\delta_{FB}=(\mu_{UR}+\mu_{UL})/(\mu_{LR}+\mu_{LL})$ and a left-right asymmetry as $\delta_{LR}=(\mu_{UR}+\mu_{LR})/(\mu_{UL}+\mu_{LL})$.

Water content mapping was performed in 18 healthy male and 14 healthy female and the parameters described were automatically determined for white and cortical grey matter resulting in 19 partly dependent measurement values for each individual subject. To check the relevance of the two independent predictor variables age and gender for the explanation of the observed data structure, principal component analysis was performed based on the resulting dataset.

RESULTS AND DISCUSSION

Fig. 1(a) shows the white and grey matter water content as a function of age. A significant negative correlation is observed for cortical grey matter in both males and females ($p<0.05$). Furthermore, the concentration of water in the female brain is approximately one percent higher than in the male cortex. White matter water content is not significantly correlated with age for males and females. Fig 1(b) shows the correlation between age and the 2nd principal component which is a linear combination of σ_x and σ_y for both grey and white matter with negative component loadings. This implies that the spatial homogeneity of cerebral water content increases between the second and 4th decade of life, being maximal in the fifth decade before decreasing again. The effect is not statistically significant between male and female as shown in Fig 1(b). Fig 1(c) demonstrates the usefulness of the spatial correlation distance d_S as an important measure for the determination of age and gender specific baseline changes in human grey and white matter water content. The spatial correlation distance d_S as a surrogate marker for the spatial organisation of water in grey matter decreases significantly with increasing age. Results for the forward-backward and left-right asymmetry are shown in Fig 1(d). A clear left-right asymmetry is observed for both white and cortical grey matter while only grey matter shows a forward-backward asymmetry which decreases significantly with increasing age (data not shown). No statistically difference between male and female is observed.

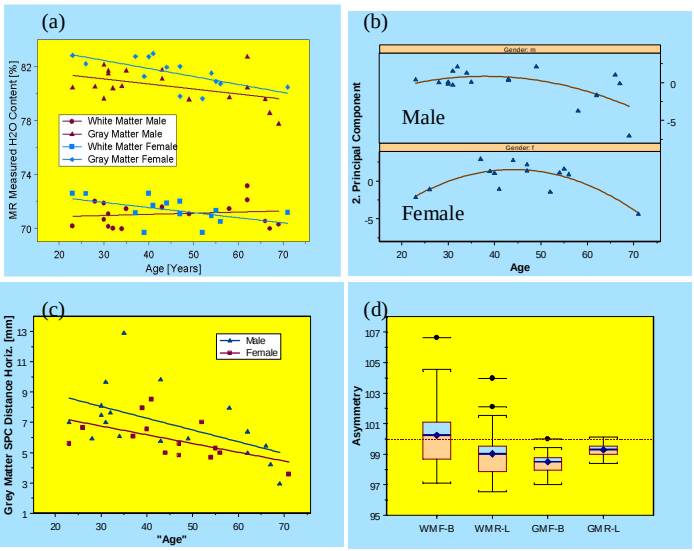

Fig 1: (a) White and cortical grey matter water content as a function of age and gender. (b) Age dependence of the first principal component for male (top) and female (bottom). (c) Horizontal spatial correlation distance for male (blue points) and female (red points) as a function of age and (d) Box-Whisker plots showing the forward-backward and left-right asymmetry for grey and white matter.

The results demonstrate the usefulness of the presented approach in describing the absolute cerebral water content and spatial changes thereof depending on external factors. Significant age and gender specific changes in H_2O content and H_2O distribution were demonstrated which forms the baseline for any further studies involving brain pathologies. The method is easy to use, fully automated without user interaction, and is therefore ideally suited for routine application in clinical studies and diagnosis based on absolute cerebral water content.

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