A 7min protocol for quantitative, whole-brain, accurate water mapping at 3T for neurological applications

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Introduction: Water concentration is highly regulated in the healthy human brain and changes only slightly with age and sex in normal volunteers. It is affected by different pathologies such as alcoholism, haemodialysis, stroke, tumour, hepatic encephalopathy and multiple sclerosis (see [1] for a review). These changes are highly significant and thus an important parameter to be determined in the study of the disease; however, they are still only in the low percentage range. Any useful method for water content measurement must cope with this challenge of very high accuracy. A remarkable correlation between water content measured by non-NMR methods and the longitudinal relaxation time, T_1, in biological tissue was noticed early on [2] and has been used by several groups to derive surrogate water content values based on T_1. However, this is only an inferred quantity and changes in NMR relaxation times represent a composite of both water content and water structuring in the tissue under study [3]. Despite full acknowledgement of this issue by most groups, true water measurements by MRI remain rare [4-9]. This is, to a large extent due to the long measurement time of the existing methods if whole brain coverage is required and the rather sophisticated data processing. Furthermore, the translation of clinical applications from 1.5T to 3T has made the task of many quantitative methods more difficult. Effects of the considerable B_1 and B_0 inhomogeneities must be accounted for and corrected. We have developed and tested a method for accurate water content measurement with whole-brain coverage in only 7 minutes [10]. The method uses a standard sequence – multiple-echo gradient echo with long TR - and involves few postprocessing steps which are easy to implement.

Materials and methods: Ten healthy male volunteers (mean age 26 yrs) were scanned on a 3T scanner (Siemens Tim Trio) equipped with a 40mT/m gradient coil. Written informed consent was obtained before scanning in accordance with the requirements of the local ethics committee. A body coil was used for RF transmission and a 12 elements phased-array coil for signal reception. A 2D GRE was acquired with parameters: TR=10s, FOV=200x162mm^2; slice thickness 1.5mm, 1mm gap; matrix size=192x117; 57 slices; phase resolution 75%; 32 echoes; BW=280Hz/px; TE_1=3.87ms; ΔTE=4.08ms; iPAT=2. Phantom results were obtained on a "revolver" phantom with 9 tubes, each containing different, known mixtures of H2O/D2O. Data processing and analysis were performed with in-house MATLAB scripts (The Mathworks, Natick, MA, USA) and SPM8 (http://www.fil.ion.ucl.ac.uk/spm). M0 is related to percent tissue water content by comparison with the signal from CSF, considered to consist of 100% water, after correcting for T2*, transmit B1+ and receive B1- effects. This can be expressed schematically as: $H2O[\%]=M(90^o)\cdot f_{T2*}(T2^*)\cdot f_{B1+}(B1+)\cdot f_{B1-}(B1-)\cdot f_{ref}(\text{reference; } 90)$, where $f_i(\ldots)$ are the different corrections detailed in [1,6-9]. The most important feature of the equation describing our novel implementation of water mapping is the fact that all corrections are multiplicative. This leads to a substantial simplification of the postprocessing and, most importantly, a reduction in the measurement time. The acquired data were fitted with an exponential function in order to estimate T2* on a voxel-by-voxel basis and the image intensity from the first echo was corrected. The remaining transmit and receive inhomogeneities were treated as a bias field correction [11] and evaluated using the probabilistic framework for segmentation provided by SPM (http://www.fil.ion.ucl.ac.uk/spm).

Results and Discussion: The mapping method was validated by phantom results. A very good correlation (R=0.95) between the measured and known water content of the tubes was found. Fig. 1 a, b and c shows the *in vivo* results: water maps for a representative slice and 4 volunteers (Fig. 1a), distribution of percentage water values (Fig. 1b) and the average histogram over the 10 volunteers (Fig. 1c). The centroids of the percent water content distributions are 69.1+-1.2 for WM and 80.5 ± 1.1 for GM (SD calculated for 10 volunteers). The widths of the distributions, in percent water content, are 2.0 ± 0.2 for WM and 2.5 ± 0.2 for GM. The very narrow distributions are representative of both the highly regulated water content and of the accuracy of the heuristic SPM-based correction. The same approach for the correction of RF inhomogeneity in quantitative imaging has been recently used by Weiskopf et al [12] for T1 mapping with a 3D variable flip angle method. We mention here that the SPM-based bias field correction was found [10] to perform significantly better than the usual corrections [1] regarding the homogeneity of the obtained water maps at 3T. The reason was determined to be an inaccuracy in the broadly-used translation of the principle of reciprocity into equating the transmit and receive sensitivities of a T/R coil. Whereas the deviations from this approximation are small at 1.5T, they become very important at 3T. The water mapping methods as published at 1.5T are therefore not applicable at higher fields. The centroid values obtained after SPM filtering are very close to values obtained previously at 1.5T (70.9±1.1% and 81.2±1.2% [7]). Small variations in the measured water content with field strength can be expected if several water pools are present in the brain. Indeed, we only start sampling the water signal at the first TE and pools of water with short relaxation are only partly detected. Some changes in the distribution of T2* values in the brain with field strength can affect to some extent the amount of visible water.

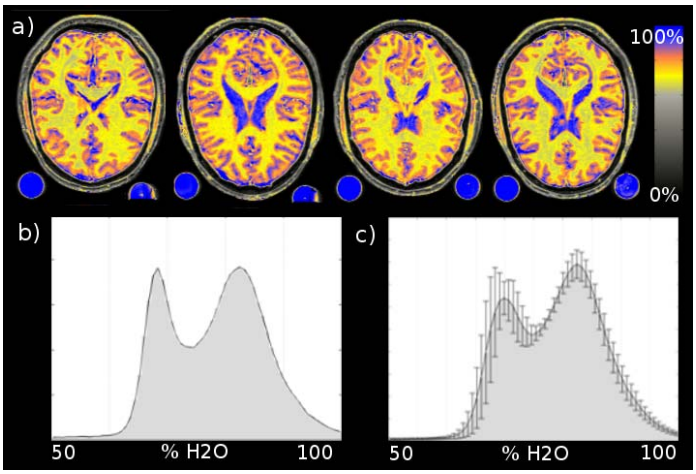

Fig.1: *Water maps from 4 volunteers (a), histogram of the whole brain water distribution (b) and a mean water content histogram from 10 volunteers.*

Conclusions: Advances in scanner technology and image reconstruction have brought an otherwise largely conceptual "gold standard" for water mapping (very long TR proton density weighted imaging) into the realm of clinical possibility. The method proposed here is based on a TR=10s GRE measurement (7:21 minutes for 1x1mm^2 in-plane resolution and whole brain coverage) and uses simple postprocessing steps and normalisation to CSF (as 100% water) to produce quantitative water maps. Bias field correction (e.g. with SPM) is widely used in the neuroimaging community and constitutes the main postprocessing step in our method. A simple exponential fit of the signal decay with echo time is the other ingredient. It is anticipated that this easy to use, high-quality water mapping method will open the road to routine, widespread quantitative MR imaging of water content.

References: [1] Shah et al., Methods Mol Biol. 2011;711:29-64; [2] Bottomley et al., Med Phys 4 (1984): 425; [3] Mathur De Vre, Br. J. Radiol. 57 (1984): 1145-1148; [4] Lin et al., Magn Reson Med, 38: 303–310 (1997); [5] Tofts, John Wiley & Sons, 2003; ; [6] Neeb et al., NeuroImage, 29(3):910-22 (2006); [7] Neeb et al., NeuroImage, 31(3):1156-68 (2006); [8] Shah et al., NeuroImage, 41(3):706-17 (2008); [9] Neeb 2008; [10] Oros-Peusquens et al., NeuroImage, in revision; [11] Ashburner and Friston, NeuroImage, 26, 839-851 (2005); [12] Weiskopf et al., NeuroImage 54: 2116–2124 (2011)