## A new 3D method for water and relaxation time mapping: comparison to the 2D "gold standard"

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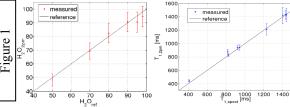
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## Introduction

Water concentration is highly regulated in the healthy brain. Several pathologies - stroke, tumour, hepatic encephalopathy, to name a few - were shown to lead to either local or global disturbances in the water distribution and content [1,2]. The highly accurate water mapping methods developed in our group [2,3] were based on 2D acquisitions. However, several applications, such as quantitative VBM and quantitative imaging on small animals, require whole brain coverage with isotropic and high resolution. Here, we have developed a new 3D method for water content and relaxation time mapping in which the magnetisation density and longitudinal relaxation time are determined from a two-point fit to measured data sets including several corrections. The method is based on 3D multiple-echo gradient echo (meGRE) acquisitions, which also allow for accurate determination of the transversal relaxation time  $T_2^*$ . We have applied this method at 3T to healthy volunteers. Multiple-echo GRE is the method of choice at very high fields due to its low SAR values and at any field it offers a very efficient read-out-time/TR ratio. Since the inhomogeneity of the RF field and the accuracy of its mapping are found to have a large effect on the precision of the method, already at 3T, we have compared the results of the new method to those obtained with a 2D method which combines aspects which can be largely considered to be a "gold standard": B<sub>1</sub> mapping with the double-angle method and M<sub>0</sub> mapping from proton density images acquired at TR>5T<sub>1</sub> for the brain tissue. The accuracy of T<sub>1</sub> mapping has been investigated by comparison to results obtained with a fast, accurate, multi-slice Look-Locker sequence, TAPIR [4,5].

## **Materials and Methods**

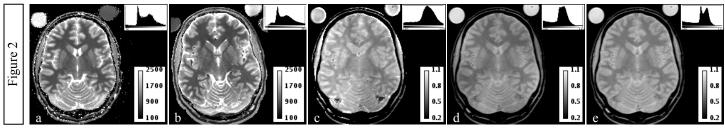
The basic ingredients of the 3D protocol are: a) two 3D multiple-echo spoiled gradient echo scans with TR=50ms and 12 echoes, b)  $B_1^+$  mapping using AFI [6] and c)  $B_1^-$  (receiver coil) calibration using GRE scans with short TR. Two reference probes filled with MnSO4-doped water with  $T_1$  values close to those of WM and GM and water content of 100 and 90% were included in the FOV. The temperature of one probe was continuously monitored during the measurements. The signal equation on which the fit of  $T_1$  and  $M_0$  is based is that of spoiled GRE, as described for example by [7]. Details of the general corrections required for accurate



water mapping are given in [2,3]. The flip angles of the two TR=50ms acquisitions were determined based on Monte Carlo simulations such that the accuracy and precision of both  $M_0$  and  $T_1$  mapping were maximised. The optimal flip angles are 7 and 40deg and both the precision and accuracy of the method can be expected to be higher than 10% for  $T_1$  and better than 5% for  $M_0$ . They both increase with increasing SNR. Results were obtained from five healthy volunteers (mean age 26y, from 24 to 27) scanned on a 3T TIM-Trio Siemens scanner equipped with a gradient system capable of 40mT/m, body coil (BC) transmit and 12 elements phased-array (PA) receive coil. Other parameters of the experimental 3D meGRE protocol were: FOV=200x162.5x128mm³, matrix size=192x156x128, 12 echoes,  $T_2$ =2.33ms,  $T_3$ =3.89ms; b) for AFI: TR=90ms, alpha=60deg, n=5, FOV=same as meGRE, matrix size=192x156x64; for  $T_3$  (receiver coil) calibration TR=7ms, alpha=10deg, FOV=same as meGRE, matrix size=208x256x128, 6avg(BC/PA) and 8avg(BC/BC). Slab selective pulses have been used throughout (and mapped with AFI). For the 2D acquisition, 2 sets of 57 slices of 2mm thickness with 1 mm gap were acquired, with TR=10000ms and flip angles of 90 and 30deg. The signal intensity is thus purely  $M_0$ - and  $T_3$ - weighted, with no influence from  $T_1$  effects (except a small factor for CSF) and no expected effects from possibly imperfect spoiling. The latter is a cause of concern for quantitative imaging using acquisitions with short TR [8]. An additional advantage of the very-long-TR data is that all the corrections to  $T_3$ - multiplicative and can be eliminated by proper intensity inhomogeneity correction algorithms without being actually measured.

## **Results and Discussion**

Phantom results obtained with the 3D method are compared in Fig.1 to spectroscopic results for a range of T<sub>1</sub> and M<sub>0</sub> values relevant for the *in vivo* case. The agreement is within 5%. Representative M<sub>0</sub> (Fig. 2c) and T<sub>1</sub> (Fig. 2b) maps acquired with the 3D method from a healthy volunteer are compared to the M<sub>0</sub> map obtained with the 2D method for a similar slice (Fig. 2d) and a T<sub>1</sub> map obtained with TAPIR (Fig. 2a) on the same volunteer. The agreement is seen to be very good, and extends to comparison of the mean values and standard deviations of the centroids for  $M_0$ ,  $T_2^*$  and  $T_1$  for GM and WM for all five volunteers. The agreement with the 2D method is within 2% for M<sub>0</sub> and T<sub>2</sub>\* and within 5% for T<sub>1</sub> comparison with TAPIR. We stress the fact that the 2D and 3D methods use very different B<sub>1</sub> mapping (3D AFI versus 2D double-angle method) and that the 2-point T<sub>1</sub> mapping of the 3D method differs radically from the extensive multi-time-point acquisition of the inversion recovery of TAPIR. Agreement is, of course, expected for methods which are truly quantitative, but is seldom met in a survey of the literature regarding, for example T<sub>1</sub> values. The centroid values obtained for five volunteers are 70(3)% (WM) and 82% (GM) for H<sub>2</sub>O content, 880(20)ms WM and 1502(60)ms GM for T<sub>1</sub> and 51(3)ms for the whole brain T<sub>2</sub>\* and agree well with values previously published by our group. One unexpected aspect was the rather broad distribution of M<sub>0</sub> values shown by the 3D method, and also by the 2D "gold standard" method, as illustrated in the whole-brain histograms (Fig. 2). Correction of the image inhomogeneity of the 90deg scan with TR=10s was performed using a SPM8 routine [8]. The resulting histogram of grey-scale values over the whole brain displays much better separated peaks corresponding to the white and grey matter (Fig. 2e). Unfortunately, the correction factor at the position of the probes was inaccurate. A more accurate inhomogeneity correction and/or more adequate probe geometry and extension would give one the possibility of doing water mapping with one scan. In conclusion, accurate water and relaxation time mapping with a meGRE-based 3D method is feasible at 3T. However, although the centroid values of the H2O distributions from 5 volunteers compare well to those obtained in our group at 1.5T, the broadening of the distributions is noticeable. Comparison to the distributions following inhomogeneity filtering alone indicates that higher accuracy of B1 mapping is required in order to describe the water distributions as accurately as at lower fields.



**References:** [1] Shah et al., NeuroImage 41:706-717(2008); [2] Neeb et al., NeuroImage, 31(3):1156-1168(2006); [3] Neeb et al., NeuroImage, 42(3):1094-1109(2008); [4] Shah et al., NeuroImage 14(5):1175-1185(2001); [5] Steinhoff et al., MRM, 46(1):131-140(2001); [6] Yarnykh, MRM, 57(1):192-200(2007); [7] Helms, MRM, 59(3):667-672(2008); [8] Preibisch and Deichmann, MRM 61(1):125-135(2009); [8] Ashburner and Friston, NeuroImage 26:839-851(2005)