IN VIVO MYELIN WATER IMAGING USING 3D MULTI-GRADIENT-ECHO PULSE SEQUENCES

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Introduction. Quantitative imaging of the myelin water fraction (MWF) is able to show demyelinating processes and therefore provides insight into the pathology of white matter (WM) diseases such as multiple sclerosis. So far, mapping of the MWF most often was performed using single-slice multi-echo spin-echo sequences (1). Lately, a different approach, using multi-gradient-echo pulse sequences, was introduced by one study measuring formalin-fixed brains (2) and has been adapted to in vivo measurements by different groups since then (3,4). In this work, we present a solution for 3D in vivo myelin water imaging with whole brain coverage by applying multi-gradient-echo pulse sequences and using a non-negative least squares (NNLS) algorithm to analyze the T_2^* decay.

Methods. Experiments were performed on a 1.5T system on three healthy volunteers based on a 96 x 128 x 80 matrix with 2 mm isotropic resolution. To minimize B_0 inhomogeneities, a careful second order manual shim was conducted first, which resulted in frequency variations of less than 15 Hz within the shimmed volume. The multi-gradient-echo sequence had alternating readout gradient polarities and consisted of 96 different echo times with a first echo time of 1.43 ms and an echo spacing of 0.98 ms. Moreover, TR was 96.3 ms, the flip angle was chosen to be 32° and the pixel bandwidth was 1565 Hz/pixel. Additionally, an MPRAGE sequence was applied for anatomical reference. Total scan time was 16 min. The signal amplitudes y_k of the T_2^* decay were assumed to be of multi-exponential behavior (Eq. [1]), where t_i are the measured echo times, T_{2k}^* are the logarithmically spaced T_2^* relaxation times and s_k is the relative amplitude for each corresponding T_2^* relaxation time. The expression from Eq. [2] was then minimized using an NNLS algorithm and applying the energy constraint given in Eq. [3], finally resulting in regularized smooth T_2^* distributions (5). The MWF was defined as the sum of all amplitudes s_k with T_2^* times < 25 ms relative to the total sum of all amplitudes of the T_2^* distribution.

$$y_k = \sum_{k=1}^{M} s_k \exp\left(-t_i / T_{2k}^*\right), \quad i = 1, 2, \ldots N \qquad [1]$$

$$\chi^2 + \mu \sum_{k=1}^{M} s_k^2, \quad \mu \geq 0 \qquad [2]$$

$$1.02\chi_{\min}^2 \leq \chi^2 \leq 1.025\chi_{\min}^2 \qquad [3]$$

Results & Discussion. Fig. 1 illustrates a fit example of one ROI from a healthy subject. Excellent correspondence between measured data points and fitted signal is observed yielding residuals < 2 %. The corresponding regularized T_2^* distribution depicts two isolated smooth peaks, the first one belonging to the myelin water pool, whereas the second peak can be assigned to the intra- and extracellular water present in brain tissue. Pixelwise fit results of one volunteer are presented in Fig. 2. Averaged MWF results over all WM pixels and corresponding standard deviations are: 6.1 ± 2.8 % for the axial view, 5.8 ± 2.7 % for the sagittal view and 6.7 ± 3.2 % for the coronal view. The results for the myelin water fraction correspond well with literature values (5 < MWF < 25 %) and agree as well with the results from (2). Moreover, due to the overall low MWF pixelwise results, the applied fit procedure is mainly conducted in WM pixels, whereas MWF = 0 % is observed in gray matter pixels. However, one might detect partial volume effects in the MWF maps having consequent lower MWF values than surrounding pure WM pixels.

Conclusion. We present a new solution to in vivo imaging of the myelin water fraction based on 3D T_2^* mapping. Applying multi-gradient-echo pulse sequences has the advantages of a short first echo time and short echo spacing. Furthermore, the technique introduced in this work offers not only whole brain coverage, but also clinically feasible acquisition times (12.5 min. for the multi-gradient-echo pulse protocol, which can be further shortened by parallel imaging techniques) and might therefore provide a real alternative to conventional MWF imaging using multi-echo spin-echo sequences.

References. 1. MacKay et al., *MRM* **31** (1994) 2. Du et al., *MRM* **58** (2007) 3. Hwang et al., *JMRI* **30** (2009) 4. Lenz et al., *Proc ISMRM* **1507** (2009) 5. Whittall et al., *JMR* **84** (1989)

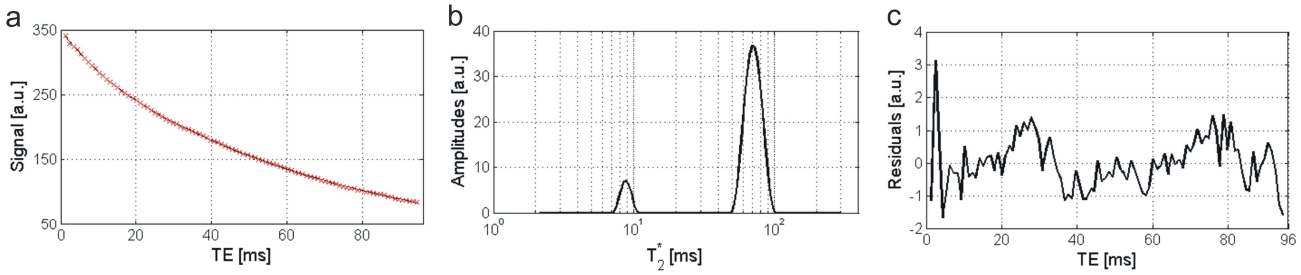

Fig.1: *Introductory fit example of one ROI from a healthy subject (location illustrated in Fig. 2a).* ***a:*** *Acquired T_2^* decay curve (red crosses) and fitted signal using NNLS algorithm (black line).* ***b:*** *Corresponding regularized T_2^* distribution.* ***b:*** *ROI fit residuals.*

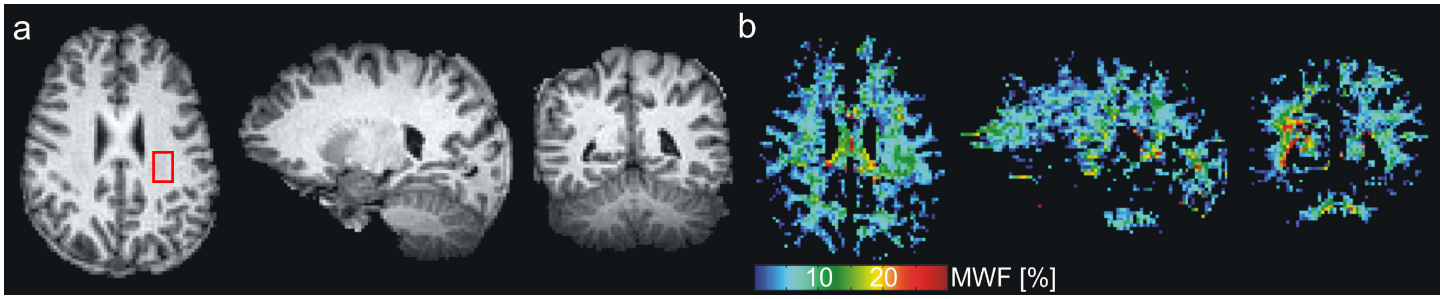

Fig.2: ***a:*** *Axial, sagittal and coronal MPRAGE images from one healthy subject.* ***b:*** *Corresponding pixelwise sample images showing 2 mm isotropic MWF parameter fit results.*