A novel approach for fast MWF quantification

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Target audience: Myelination is an important and crucial stage in the development of the brain white matter. However, there is still no gold-standard for its evaluation *in vivo*. A novel MRI index, named ***Myelin Water Fraction (MWF)***, is a promising candidate as it shows better correlation with the amount of myelin than conventional MRI indices[1-2]. MWF is defined as the fraction of water trapped by the myelin sheaths and can be derived from the multicomponent analysis of the relaxation signals. Nevertheless, there is still no agreement about how MWF should be measured. Existing strategies require long acquisition and/or post-processing times[3-4], limiting their practical applications especially in pediatric patients. Thus, finding new ways for fast and robust quantification of the MWF is an important challenge for both scientists and clinicians.

Purpose: The goal of our work is to design a novel strategy for MWF quantification with reasonable acquisition and post-processing times, and little *a priori* assumptions on the T1 and T2 values of the individual components.

Methods: *Model*: A 3-component model (myelin-related water, intra/extra-cellular water,cerebro-spinal fluid CSF) that links f_i (component fractions), $T1_i$ and $T2_i$ (relaxation times associated with each component), S_{T1} (T1 relaxation signal measured for N_{TI} inversion times TI_m) and S_{T2} (T2 relaxation signal measured for N_{TE} echo times TE_k) was adapted from Lancaster et al.[5] Since fitting this non-linear model with a limited number of measurements is an ill-posed problem, we implemented the following 2-step approach. First, for each component the most appropriate (i.e. that provide the best fit of the model over the whole brain volume) $T1_i$ and $T2_i$ values were computed using "calibration" data acquired in adults with a large number of measurements. Second, MWF maps were computed from data with a reduced number of measurements (e.g. from infants) by fixing these $T1_i$ and $T2_i$ values, and thus, reducing the task to solving a set of linear equations.

$$\begin{cases} \sum_i^3 f_i = 1,\ f_i \in [0,1]; \\ S_{T1}(TI_m) = S_0\left(1 - 2exp\left(-TI_m/T1\right)\right), m = 1..N_{TI}; \\ 1/T1 = \sum_i^3 f_i/T1_i; \\ S_{T2}(TE_k) = S_0 \sum^3 f_i exp\left(-TE_k/T2_i\right), k = 1..N_{TE}; \end{cases}$$

Subjects and Data Acquisition: T1 and T2 relaxation signals were acquired on a 3T MRI system using EPI single-shot inversion recovery and spin-echo sequences with a 1.8mm or 2mm isotropic resolution. Adult data (3 subjects) had a large number (N=30-60) of TIs (sampled between 100 – 3100ms) and TEs (sampled between 30 - 350ms). Our strategy was tested on the data from 17 healthy infants (age 3-21 weeks) with 8 TIs (TI=250->1500ms each step 250ms + TI=2000, 2500ms) and 8 TEs (TE=50->260ms each step 30ms). *Model Fitting*: Fitting the model with adults' data was done using an original combination of a region contraction approach and a non-negative least-square (NNLS) algorithm (**Fig.1**). The initial $T1_i$ and $T2_i$ search intervals were fixed based on the literature evidence[5-6]. The resulting $T1_i$ and $T2_i$ values were the weighted (with inversed model fitting errors) averages from 3 adults. In infants model fitting was done with a standard NNLS algorithm.

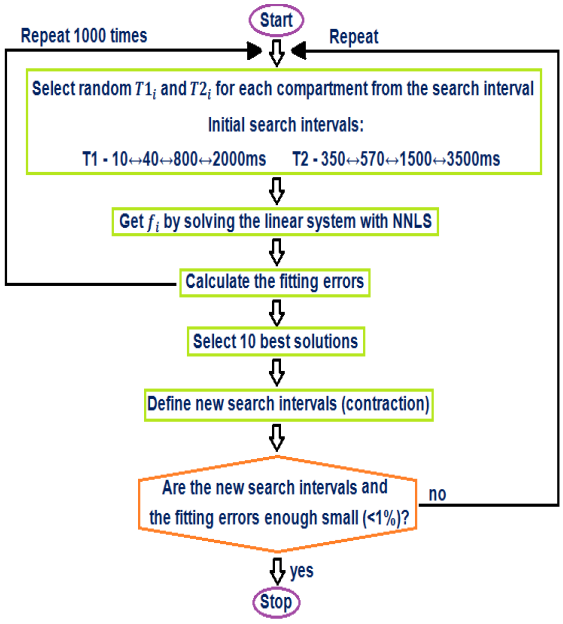

Fig.1: Fitting algorythm

Results and Discussion: First, fitting the model with the adults' data resulted in the following T1 (357±21ms, 1483±17ms, 3441±36ms) and T2 values (18±5ms, 52±6ms, 858±47ms) for the myelin-related water, intra/extra-cellular water and CSF components respectively. Second, fixing these values and reducing the number of data points in the adult dataset (same TEs and TIs as in infants) did not significantly change (0.8±0.1%) the MWF maps over the brain volume; neither were they changed with the voxel size. In infants MWF maps showed progressive myelination of the white matter with age (**Fig.2**).

Conclusions: The suggested approach allows fast MWF mapping in datasets with a limited number of measurements, for instance in infants within 5 min acquisition time. The generated MWF maps are able to reveal maturational changes across early development and are in qualitative agreement with the maps from other studies[7-8]. Quantitative comparison remains difficult because MWF quantification is very sensitive to acquisition and fitting parameters[9].

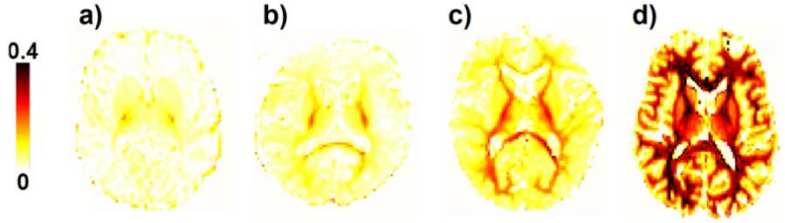

Fig.2: MWF maps for infants at 6 (a), 19 (b) and 34 (c) weeks, and an adult (d).

References: 1. Madler et al. (Brain, 2008); 2. Vavasour et al. (J MagnReson Imaging, 2011); 3. Mackay et al. (MagnReson Med, 1994); 4. Deoni et al. (MagnReson Med, 2012); 5. Lancaster et al. (J MagnReson Imaging, 2003); 6. Guo et al. (MagnReson Med, 2012); 7. Deoni et al. (Journal of Neuroscience, 2011); 8. Deoni et al. (NeuroImage, 2012); 9. Levesque et al. (J MagnReson Imaging, 2010).