Rapid whole-brain myelin water mapping using multi-component gradient echo sampling of spin echoes (mcGESSE)

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Introduction: Multi-component T2 imaging has been used to investigate the pathophysiology of white matter in various disorders such as multiple sclerosis (1). The metric of interest is principally the myelin water fraction (MWF) which is the proportion of the T2 signal arising from water trapped within layers of the myelin sheath surrounding myelinated axons. The most established method used to obtain the MWF involves the acquisition of 32 or more spin echoes to sample the T2 signal decay. The inability to perform a multi-slice acquisition and the high specific absorption rate of this method are drawbacks that have motivated the development of alternative acquisition schemes to obtain the MWF. In earlier work (2), we proposed a new acquisition scheme which consists of symmetrically sampling, using gradient echoes, the rephasing and subsequent dephasing parts of multiple spin echoes, termed multi-component gradient echo sampling of spin echoes (mcGESSE). Based on simulations, we demonstrated the potential of this acquisition strategy and simple model to evaluate the MWF. The purpose of the study was to implement mcGESSE in-vivo on our Siemens Verio 3T scanner and establish a protocol with whole brain coverage within a clinically relevant scan time.

Methods: The approach is based on the work of Yablonskiy and Haacke (3) which takes advantage of the refocusing nature of the 180° refocusing pulse to disregard the irreversible component of the transverse relaxation (T2′) The signal is sampled at equal intervals using gradient echoes placed symmetrically about a spin echo while it rephases and subsequently dephases. Extending the approach to a two component model with a bi-exponential signal decay, a ratio of the signal before and after the spin echo can be obtained which depends on $T2_{short}$, $T2_{long}$ and the MWF (Eq. 1). In separate acquisitions, with spin echoes times of 19 and 52 ms, decay curves were sampled with 8 and 28 gradient echoes respectively, spaced 1.5ms apart. The repetition time was set at 2500 ms, which allowed the interleaving of up to 42 slices with a thickness of 2.5 mm. The field of view was set at 220 mm x 185 mm with a 192 x 162 matrix, giving a 1.1 mm x 1.1 mm in-plane resolution. Total acquisition time was 16.5 minutes. All subjects were imaged twice within an hour to assess reproducibility, leaving the scanner room in between scans. Imaging data were processed off-line and fitted to Eq. 1 using a randomly seeded, iteratively reweighted, least squares algorithm implemented in Matlab. The normalization and segmentation routines available within the SPM8 software package were used to normalize the MWF maps to standard space and obtain tissue probability maps. ROIs were constructed in standard space using PickAtlas and the LONI WMPM atlas, intersected with the white and/or grey matter probability maps of each subject as appropriate. The inter-scan reproducibility of MWF calculations for each subject was assessed with a two-sample t-test of the MWF distributions. Healthy volunteers (5 males, 1 female) aged 23 to 56 were recruited under our institution's sequence development ethics approval and all participants provided written consent.

$$\frac{S(TE-n\Delta t)}{S(TE+n\Delta t} = \frac{MWF\cdot exp(\frac{n\Delta t-TE}{T2_{short}})+(1-MWF)\cdot exp(\frac{n\Delta t-TE}{T2_{long}})}{MWF\cdot exp(\frac{-n\Delta t-TE}{T2_{short}})+(1-MWF)\cdot exp(\frac{-n\Delta t-TE}{T2_{long}})} \quad [1]$$

Results: MWF maps, as shown in native space in figure 1a, were influenced by regions of severe magnetic field susceptibility as well as in deep iron rich grey matter structures. Normalization and segmentation of images (figure 1b) allowed for the automated calculation of MWF distributions (figure 1c) while avoiding spurious values such as those caused by partial volume effects. Mean MWF values based on the scans of 6 participants are shown in figure 1d for both gray and white matter structures. Only a single ROI, cerebral gray matter, within one subject was significantly different between scans. This significant difference vanished if the distributions were normalized to unity, pointing to a difference in image normalization and/or segmentation.

Discussion: The implementation of mcGESSE in-vivo was investigated at 3T with an eye to future clinical studies utilizing this approach. To this end, mcGESSE provides large coverage with a reasonable scan time which could further be reduced with a shorter repetition time. Further, the automated nature of MWF calculations in selected ROIs used in this study parallel those which are used in many clinical studies. Elevated MWF values in deep gray matter structures are suspected to be a result of elevated iron concentrations and/or the lower SNR of data in those brain regions. Future work will focus on establishing the cause of high MWF values in deep grey matter and assess the influence of the B_0 shim on data quality.

Conclusion: The implementation and reproducibility of a new technique for whole-brain mapping of the MWF was demonstrated based on the gradient echo sampling of spin echoes.

References

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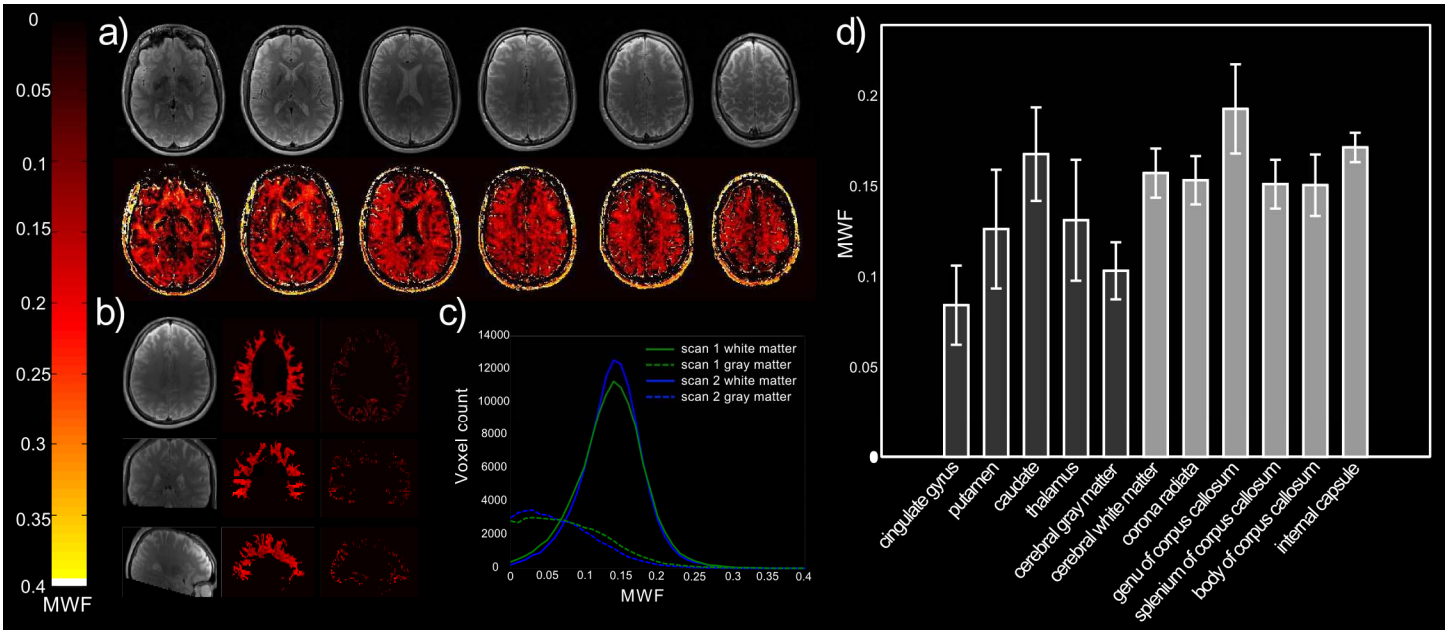

Figure 1. a) A subset of T2-weighted images and respective MWF. **b)** In standard space for the same participant, a normalized T2-weighted image and corresponding MWF maps of the cerebral white and gray matter. **c)** The MWF distributions of both cerebral white and gray matter, along with the distributions calculated from this participant's second scan. **d)** Group mean MWF values and standard deviations based on the first scan of all 6 subjects.