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Rapid whole cerebrum myelin water imaging using a 3D GRASE sequence

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ABSTRACT

Myelin water imaging, a magnetic resonance imaging technique capable of resolving the fraction of water molecules which are located between the layers of myelin, is a valuable tool for investigating both normal and pathological brain structure in vivo. There is a strong need for pulse sequences which improve the quality and applicability of myelin water imaging in a clinical setting. In this study, we validated the use of a fast multi echo T_2 relaxation sequence for myelin water imaging. Using a multiple combined gradient and spin echo (GRASE) technique, we attain whole cerebrum myelin water images in under 15 minutes. Region of interest analysis indicates that this fast GRASE imaging sequence produces results which are in good agreement with pure spin echo measurements ($R^2 = 0.95$, $p < 0.0001$). This drastic improvement in speed and brain coverage compared to current spin echo standards will allow increased inclusion of myelin water imaging in neurological research protocols and opens up the possibility of applications in a clinical setting.

Introduction

Myelin water imaging (MWI) is an increasingly active field of magnetic resonance imaging (MRI) research. The ability to generate maps of the myelin water fraction (MWF) from a human brain in vivo enables clinicians and researchers alike to directly examine the myelination state of white matter in the central nervous system (CNS). As myelin is of great importance in the CNS and there are many known diseases which lead to degradation of the myelin sheath which surrounds white matter neurons (Barkovich, 2000), most notably multiple sclerosis (MS), MWI is a valuable tool in the investigation of the patho-physiological causes and possible treatments of white matter diseases.

The majority of MWF maps are created via multicomponent T_2 analysis. That is, decay curves from multi echo spin echo images exhibiting T_2 contrast are decomposed into discrete T_2 components to create a T_2 distribution (MacKay et al., 1994; Whittall et al., 1997) whereby no a priori assumptions are made about the number of contributing components. A short T_2 component (corresponding to water within the myelin sheath) may then be identified and its magnitude normalized to the total water signal, yielding a value for the MWF between zero and one. Post mortem MRI-pathology correlation studies in both CNS tissue (Kozlowski et al., 2008; Laule et al., 2006, 2008) and animal peripheral nerve (Webb et al., 2003) have demonstrated a good quantitative relationship between the MR-derived MWF and histological staining for myelin.

Spatially resolved data required for multi-component T_2 analysis are usually acquired with multi spin echo (MSE) based image sequences (MacKay et al., 1994; Poon and Henkelman, 1992). However, in order to prevent magnetization transfer effects from exciting multiple slices (Vavasour et al., 2000), these images should be acquired in 3D, potentially resulting in long data acquisition times. If MWI is to become a commonplace tool in clinical imaging or research that can be used in conjunction with other MR-imaging modalities that exhibit full brain coverage with isotropic voxel size, e.g. functional MRI, diffusion tensor imaging, magnetization transfer imaging, etc., whole brain data at reasonable spatial resolution must be acquired within clinically feasible scan durations (<15 minutes).

A combined gradient and spin echo sequence known as gradient and spin echo (GRASE) (Feinberg and Oshio, 1991) has previously been used to accelerate clinical MR acquisitions (Fellner et al., 1995, 1997; Melhelm et al., 1998; Patel et al., 1995; Rockwell et al., 1997; Umek et al., 1998). By acquiring multiple gradient echoes per refocusing pulse on either side of the spin echo, an accelerated acquisition

Abbreviations: GRASE, gradient and spin echo; MWI, myelin water imaging; MSE, multi spin echo; MWF, myelin water fraction; CNS, central nervous system; MS, multiple sclerosis.

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trajectory may be realized which exhibits pure T_2 weighting in the k-space centre (spin echo signal) and T_2^* weighting in the k-space periphery (gradient echo signal). Some researchers reported that GRASE was less effective in the detection of small or hypointense lesions (Patel et al., 1995; Umek et al., 1998), and produced images with lower signal to noise ratio (SNR) and less pronounced contrast (Fellner et al., 1995, 1997). However, others found that GRASE showed better detection of lesions, especially those with low signal (Melhelm et al., 1998) or those which exhibited paramagnetic susceptibility characteristics (Rockwell et al., 1997). Although not necessarily in agreement about all factors, all authors point out that in circumstances where rapid scanning is indicated, GRASE is very useful. Rockwell et al. go as far as to say that GRASE is a potential replacement for turbo spin echo in routine MRI of the brain (Rockwell et al., 1997).

A similar gradient and spin echo sequence has also been used to collect data for multiexponential T_2 analysis (Does and Gore, 2000). This sequence demonstrated dramatic decreases in scan time while maintaining good agreement of multiexponential T_2 parameters compared to a conventional spin echo acquisition.

Mädler (Mädler and MacKay, 2007) introduced whole brain MWI based on 3D-GRASE. Due to both hardware and software limitations at that time, scan times required for whole brain coverage were on the order of 20 to 30 minutes. We were able to improve scan efficiency of a similar acquisition to less than 15 minutes. In this study we demonstrate whole cerebrum imaging in a scan time under 15 minutes and also compare myelin water fraction results from the 3D-GRASE sequence with results from the 3D-MSE technique (Mädler and MacKay, 2006).

Material and methods

All MR imaging experiments were performed on a 3.0 T whole body MR scanner (Achieva 3.0T, Philips Medical Systems, Best, The Netherlands) using an eight-channel phased-array head coil for reception and the quadrature body coil for transmission. All examinations were performed with approval from our institution's ethical review board, and all subjects provided signed, informed consent prior to participation.

Comparison of MSE and GRASE

To assess the validity of MWF measurements calculated from data acquired with the GRASE sequence, subjects were scanned with the previously introduced 3D-MSE T_2 sequence (Mädler and MacKay, 2006) followed by the 3D-GRASE sequence with comparable resolution and echo times. Due to time constraints with the 3D-MSE, only 7 slices were acquired for both sequences. The 32 echo 3D-MSE sequence was acquired with the following parameters: TR = 1200 ms, echo times = 10,20,30,…,320 ms, 7 slices, 3D slice oversampling factor = 1.8, slice thickness = 5 mm, in-plane voxel size = 0.9 × 1.9 mm, CLEAR = yes, partial k-space scan factor = 0.7, 256 × 108 matrix, receiver bandwidth = 111 kHz, axial orientation, and acquisition time = 19.8 minutes. Following this, a 32 echo 3D-GRASE sequence based on (Mädler and MacKay, 2007) with an EPI factor of 3 was acquired in an acquisition time of 9.4 minutes. With the exception of partial k-space scanning which was not compatible with our GRASE sequence, identical parameters were used. Inversion prepared turbo gradient echo sequences (repetition time (TR) = 6.5 ms, TE = 3.1 ms, inversion time (TI) = 150, 400, 750, 1500, and 3500 ms) were also acquired to facilitate T_1-mapping and region of interest (ROI) identification (Mädler et al., 2006). Data were collected from 9 healthy volunteers (8 male, 1 female; mean age = 28 years; range = 21–52 years).

Accelerating the GRASE sequence

To increase brain coverage in clinically feasible scan durations, we accelerated the GRASE sequence by reducing TR, using partial 3D undersampling in the slice direction (overcontiguous) and reducing the 3D slice oversampling due to the increased number of acquired slices. Scan parameters were TR = 1000 ms, echo times = 10, 20, 30,…,320 ms, 20 slices acquired at 5 mm slice thickness, 40 slices reconstructed at 2.5 mm slice thickness, slice oversampling factor = 1.3, in-plane voxel size = 1 × 1 mm, SENSE = 2, 232 × 192 matrix, receiver bandwidth = 188 kHz, axial orientation, and acquisition time = 14.4 minutes. T_1 weighted inversion recovery images were acquired in order to identify anatomical ROIs (TR = 8.0 ms, TE = 4.6 ms, TI = 150, 400, 750, 1500, and 3500 ms). Data were acquired from 9 different healthy volunteers (6 male, 3 female; mean age = 33 years; range = 20–63 years).

Data analysis

MWF maps were created from data collected with the 7 slice 3D-MSE sequence as well as the 7 slice 3D-GRASE sequence and the accelerated 3D-GRASE sequence. Multiecho decay curves were analyzed on a voxel-wise basis using multicomponent T_2 analysis with concurrent correction for stimulated echo contamination of decay curves resulting from B_1 inhomogeneity (Prasloski et al., 2012). We used a regularized non-negative least squares (NNLS) algorithm to decompose the decay curve into multiple T_2 components (Whittall and MacKay, 1989) with no a priori assumptions about the number of contributing T_2 components; the stimulated echo correction was applied within NNLS. The input theoretical T_2 decay curves were calculated for non-ideal refocusing pulse flip

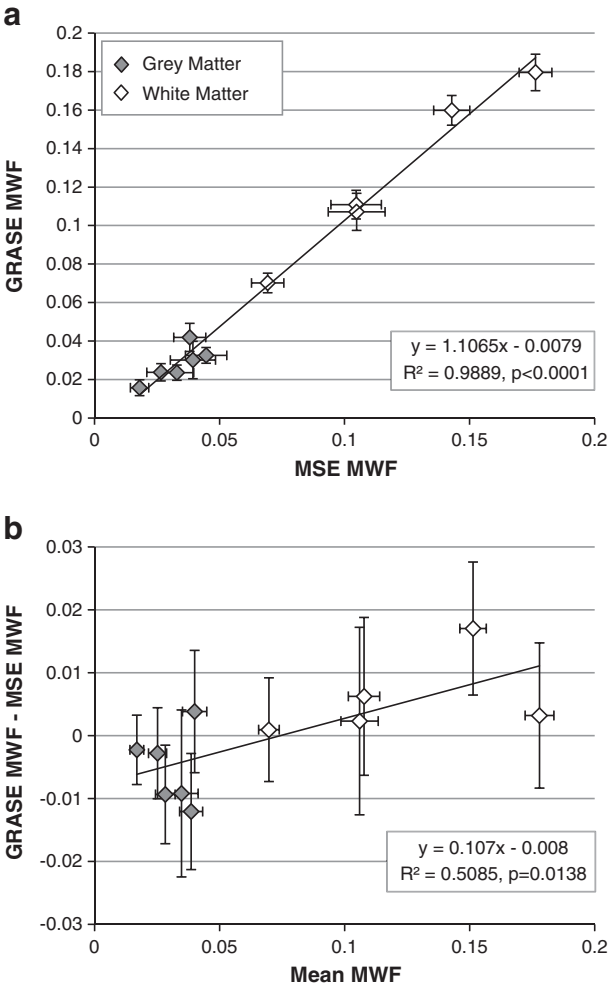

Fig. 1. (a) Correlation plot of mean region of interest MWF values of the 7 slice GRASE and MSE sequences for the same volunteers. Parameters describing the linear fit and correlation are given. (b) Bland Altman plot comparing the difference in MWF as a function of the inter-sequence mean value. Parameters describing the linear fit and correlation are given. In both plots, gray diamonds represent gray matter ROIs while white diamonds represent white matter ROIs. Error bars represent 1 standard error.