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COMPARISON OF MULTI-ECHO GRADIENT AND SPIN ECHO (GRASE) AND FAST SPIN ECHO (FSE) MRI SEQUENCES FOR T1W/T2W RATIO MAPPING

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INTRODUCTION

Myelin plays an important role in normal brain function. However, breakdown of myelin (or demyelination) can occur in diseases such as multiple sclerosis (MS) [1]. Recent advances in MRI methods that enable the estimation of myelin content in the human brain include diffusion tensor imaging [2], magnetization transfer imaging [3], multicomponent T2 relaxation-based myelin water fraction (MWF) imaging [4,5], and the ratio of T1- and T2-weighted MRI images (T1w/T2w) [6]. However, two of the methods (MWF imaging and T1w/T2w ratio) have gained popularity in very recent years. The MWF is derived from the modelling of multicomponent multi-echo T2 relaxation fitting (data acquired with the gradient and spin echo, GRASE sequence) and calculating the short T2 contribution, which is believed to be proportional to the water trapped between myelin sheaths [4,5]. The T1w/T2w ratio mapping is derived by dividing T1-weighted (T1w) by T2-weighted (T2w) images. The major advantage of this method: T1w (acquired with the magnetization prepared rapid acquisition gradient echo MPRAGE sequence) and T2w (acquired with the fast spin echo, FSE sequence) images are commonly used in most clinical exams and scan times are relatively short. However, signal calibration is necessary before computing the T1w/T2w ratio [7]. A recent study documented that T1w/T2w ratio mapping is a very reliable measure and might be suitable for longitudinal studies [8]. The purpose of this study was to compare T1w/T2w ratio mappings obtained using FSE and GRASE sequences for T2w images, and to correlate the T1w/T2w measures with MWF.

METHODS

Ten participants with multiple sclerosis (8 female, age = 57±14 years) were scanned on a 3T Tim Trio MRI system (Siemens Healthcare, Erlangen, Germany) with a 32-channel, receive-only head coil. Approval for the study was obtained from the University of Manitoba Biomedical Research Ethics Board, and all participants gave written informed consent prior to enrollment in the study. The T1-weighted images were acquired using the 3D magnetization prepared gradient-echo (MPRAGE) sequence with a repetition time [TR] = 1900 ms, echo time [TE] = 3.46 ms, inversion time [TI] = 900 ms, flip angle = 9°, matrix size = 512x512, spatial resolution = 1x1x1 mm^3, acquisition time [TA] = 4.26 min. Conventional T2-weighted [T2w] images were extracted from a fast spin echo (FSE) sequence acquired with TR = 4500 ms, TE = 101 ms, turbo factor = 6, matrix size = 192x256, spatial resolution = 1.3x1x1.3 mm^3, TA = 3.45 min. Finally, a series of images with different amounts of T2-weighting were collected using a multi-echo 3D gradient and spin echo (GRASE) sequence [5] with TR = 1500 ms, echo train length [ETL] = 32, first echo = 10 ms, echo spacing = 10 ms, matrix size = 96x128, resolution = 1.75x1.75x5 mm^3, TA = 16.53 min.

Two whole-brain T1w/T2w maps were calculated for each subject using the T1w MPRAGE image and either the T2w FSE image (TE = 101 ms) or the T2w GRASE image with TE = 100 ms. Image analyses were performed

using MRIStudio (Johns Hopkins University, Baltimore, MD, USA), MATLAB (The Mathwork Inc., Natick, MA, USA), SPM12 (Wellcome Trust Centre for Neuroimaging, London, UK), FSL (University of Oxford, Oxford, UK) and SPSS 23.0 (IBM Inc., Armonk, NY, USA). Calibrated T1w/T2w maps (using both T2w FSE and T2w GRASE) were obtained using previously described procedures [7]. In addition, the MWF maps were computed using a regularized non-negative least squares algorithm, while compensating for stimulated echoes due to non-ideal refocusing radiofrequency pulses [5,9]. Each participant's images were then spatially normalised to the ICBM template using a two-stage procedure consisting of a 12-parameter affine transformation, followed by non-linear warping via the Large Deformation Diffeomorphic Metric Mapping (LDDMM) algorithm [10]. For region-of-interest (ROI) analyses, we extracted data from 30 ROIs (i.e., 15 bilateral brain structures) listed in the JHU_MNI_SS ("Eve") atlas [11]. For bilateral ROIs, MRI measures for each subject were averaged across both hemispheres. The concordance between the two methods (i.e., T1w/T2w ratio based on FSE vs. GRASE T2w images) was analyzed using Bland-Altman plots and Passing-Bablok regression, and each method of calculating T1w/T2w ratio was also compared to validated MWF estimates of myelin concentration [12].

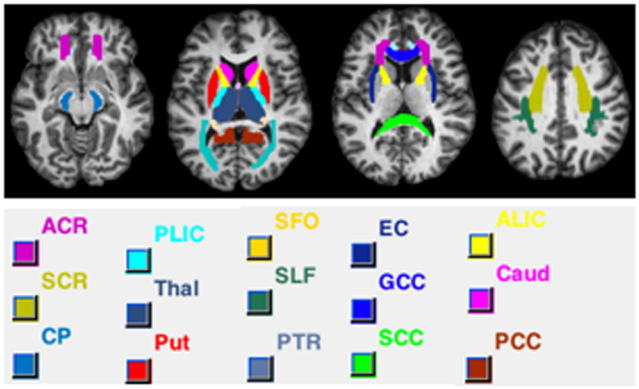

Figure 1: *Regions of interest (ROIs) from the JHU_MNI_SS ('Eve') atlas overlaid on the T1-weighted MPRAGE images of one subject. ACR: Anterior Corona Radiata, SCR: Superior Corona Radiata, CP: Cerebral Peduncle, PLIC: Posterior Limb of Internal Capsule, ALIC: Anterior Limb of Internal Capsule, PTR: Posterior Thalamic Radiation, PCC: Posterior Cingulate Cortex, SFO: Superior Fronto-Occipital Fasciculus, SLF: Superior Longitudinal Fasciculus, EC: External Capsule, GCC: Genu of Corpus Callosum, SCC: Splenium of Corpus Callosum, Caud: Caudate nucleus, Thal: Thalamus, and Put: Putamen.*

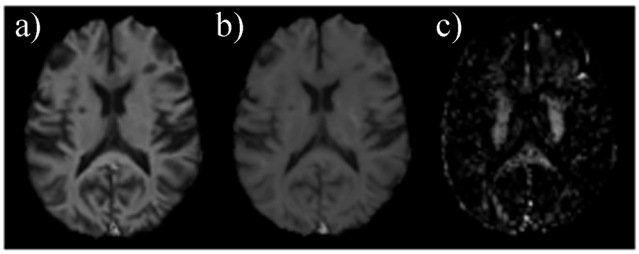

Figure 2: *Example maps of:* ***a)*** *T1w/T2w where T2w image was acquired with a FSE sequence and TE = 100 ms,* ***b)*** *T1w/T2w where T2w image was acquired with a 3D GRASE sequence and TE = 100 ms,* ***c)*** *MWF from the multi-echo GRASE sequence. Note that T1w image used to compute the T1w/T2w maps shown in* ***(a, b)*** *were acquired using the MPRAGE sequence.*

RESULTS AND DISCUSSION

Figure 1 illustrates the location of each ROI from which data were extracted, and representative T1w/T2w and MWF maps from one participant are shown in Figure 2.

Both Figure 2 and Figure 3 show that the T1w/T2w values were slightly underestimated with the GRASE sequence as compared to the FSE sequence. This is almost certainly due to the fact that: 1) the GRASE sequence had a much shorter TR, and 2) that the GRASE sequence used a combination of gradient and spin echoes that were originally optimized for myelin water imaging. Nonetheless, the FSE- and GRASE-based T1w/T2w measurements with comparable TEs (101 ms and 100 ms, respectively) were highly correlated.

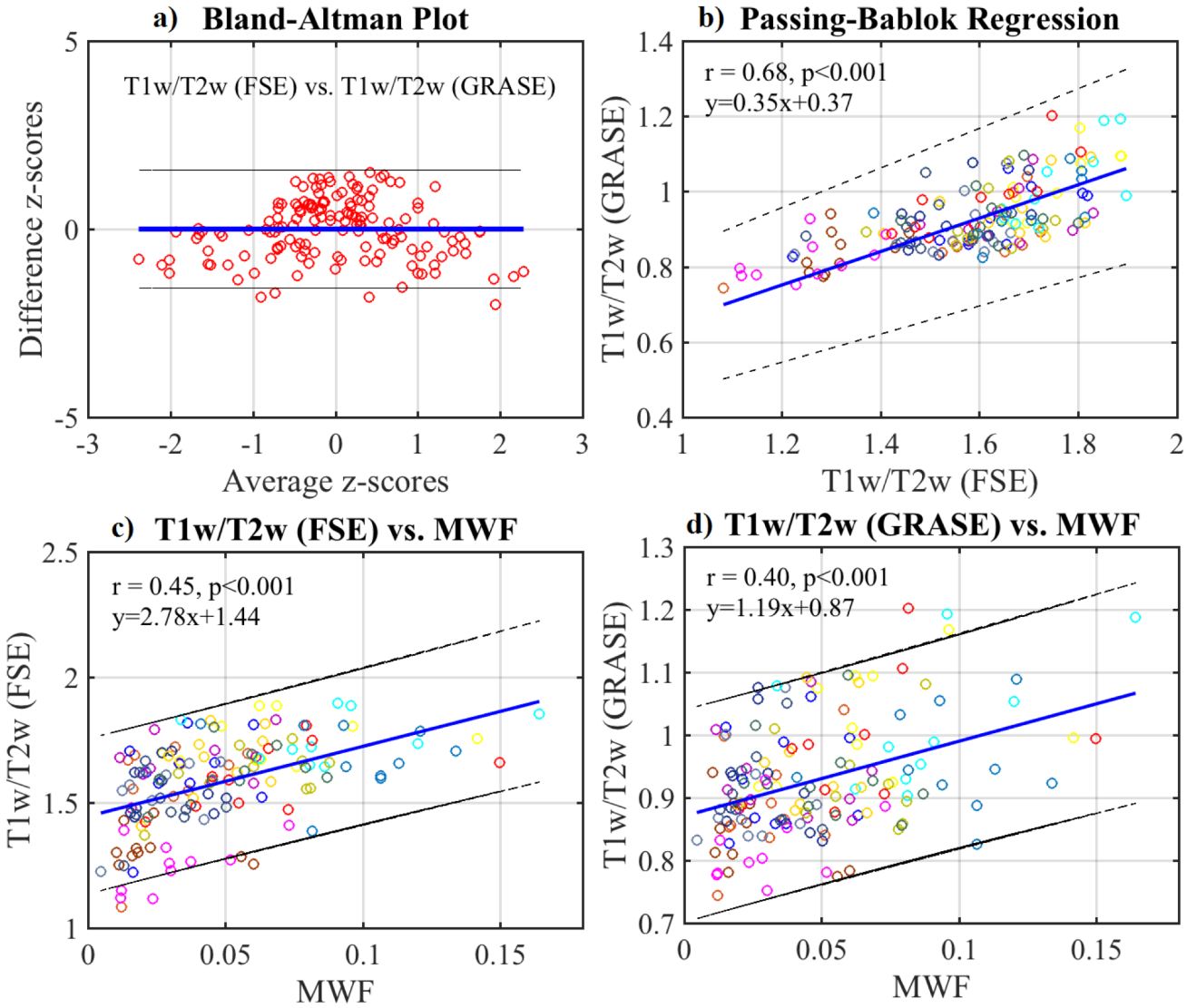

Figure 3: a) *A Bland-Altman plot shows the difference between z-scores of T1w/T2w (FSE) and T1w/T2w (GRASE) against the average z-scores of these measures, with mean absolute difference (solid blue line) and 95% confidence interval of the mean difference (dashed lines).* ***b)*** *Passing-Bablok regression between T1w/T2w (FSE) and T1w/T2w (GRASE).* ***c,d)*** *Linear correlations of T1w/T2w (FSE) vs. MWF and T1w/T2w (GRASE) vs. MWF including 15 brain structures indicated by colors. Very similar correlations were found for both T1w/T2w measures with MWF. Think blue lines are the linear fits and dashed black lines indicate the 95% confidence interval.*

The Bland-Altman plot demonstrated excellent agreement between these two methods (Figure 3a), and the statistically significant (r = 0.68, p<0.001) Passing-Bablok regression across participants and ROIs (Figure 3b) further suggests that images from a multi-echo 3D GRASE sequence can be used for precise (albeit slightly underestimated) T1w/T2w ratio measurements. Moreover, because our data indicate that the relationship (i.e., equation of the regression line) between the GRASE and FSE methods is: T1w/T2w (GRASE) = 0.21+0.44*T1w/T2w (FSE), this offset could even be partially corrected in future studies.

Finally, the MWF values in our MS cohort were consistent with previous work [12], and linear regressions between T1w/T2w (FSE) vs. MWF (Figure 3c; r= 0.45, p<0.001) and T1w/T2w (GRASE) vs. MWF (Figure 3d; r=0.40, p<0.001) were very similar. However, although these correlations were highly significant, the modest correlation coefficients indicate that T1w/T2w ratios – based on either method (FSE or GRASE) – are not a specific proxy for myelin concentration. The T1w/T2w ratio might be sensitive to other microstructural features such as cellular density, axon diameter, or inflammation/swelling, but caution should be exercised in future work involving T1w/T2w measurements to not over-interpret findings in terms of "myelination".

CONCLUSIONS

Our findings indicate that there is significant concordance between T1w/T2w ratio mappings obtained using FSE and GRASE sequences for T2w image acquisition. Therefore, as long as a T1w anatomical image is acquired (as would be the case in practically any MRI study), both T1w/T2w ratio maps (which are a general measure of tissue microstructure) and MWF maps (which are specific to local myelin concentrations) can be obtained using the same GRASE data.

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