Gleaning Multi-Component T1 and T2 Information from Steady-State Imaging Data

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INTRODUCTION: A limitation of the Driven Equilibrium Single Pulse Observation of T_1 and T_2 (DESPOT1 and DESPOT2) methods[1,2] is the inherent assumption of single-component relaxation. In a variety of biological tissues, specifically white and gray matter, the relaxation is more faithfully characterized by the summation of at least two relaxation components (3), a fast-relaxing species ($T_{1,F}$ < 500ms, $T_{2,F}$ < 50ms)[4,5] broadly attributed to a myelin-bound water pool and a slow-relaxing component ($T_{1,S}$ > 900ms, $T_{2,S}$ > 70ms)[4,5], associated with the intra and extra-cellular water pools. Unfortunately, quantification of these components is hindered by impractical acquisition times with low spatial resolution and limited volume coverage. In this work we extend the DESPOT1 and DESPOT2 methods to include multi-component relaxation and demonstrate the ability to perform whole-brain voxel-wise multi-component quantification *in vivo* in a clinically feasible 16 minutes. Results demonstrate the potential of the approach in identifying tissue change associated with neuro-degenerative disorders, particularly those associated with white matter.

METHODS: The spoiled gradient recalled echo (SPGR) and fully-balanced steady-state free precession (bSSFP) signal arising from two separate but exchanging species has been derived previously[6,7] and include 8 free parameters: the component specific T_1 and T_2 values (denoted by $T_{1,F}$, $T_{1,S}$, $T_{2,F}$ and $T_{2,S}$), component volume fractions (f_F and f_S) and the relative exchange rates between them (k_{FS} and k_{SF}, which are the reciprocals of the mean residence times, τ_F and τ_S - the average time a proton is expected to remain in a component before exchanging to the other). Under conditions of chemical equilibrium, $f_F k_{FS} = f_S k_{SF}$ and assuming conservation of mass ($f_F + f_S = 1$), reducing the free parameters to 6. Here, we re-term f_F and τ_F the myelin water fraction and myelin residence time. Applying these expressions, a hybrid genetic algorithm-local search[8] fitting approach[9] can be used to determine the best discrete fit of $T_{1,F}$, $T_{1,S}$, $T_{2,F}$, $T_{2,S}$, myelin water fraction and myelin residence time to multiple flip angle SPGR and bSSFP data.

To demonstrate the method *In vivo,* data were acquired of four healthy volunteers (2 male, 2 female, age: 26-31 years) and two male primary progressive multiple sclerosis (MS) patients (age 32 and 52 with EDSS scores of 2 and 7). Imaging was performed on a 1.5T Siemens Sonata clinical scanner. Sequence parameters for the healthy volunteers were: 22cm^2 x 16cm field of view (*FOV*) with a 256 x 160 x 118 matrix, SPGR: TE/TR = 3.1ms/6.5ms, α=2˚,4˚,6˚,8˚,10˚,12˚,14˚,16˚,18˚ and bandwidth (*BW*)=±22.7kHz, bSSFP: TE/TR = 2.3ms/4.6ms, α=6˚,14˚,22˚,30˚,38˚,46˚,54˚,62˚,70˚ and *BW*=±62.5kHz. Total time was 30 minutes. For the patients, to reduce the scan time to less than 16 minutes a 24cm^2 x 18cm *FOV* with 128 x 128 x 60 matrix was used, SPGR: TE/TR = 3.9ms/8.5ms and *BW*=±16.6kHz, bSSFP: TE/TR = 2.2ms/4.5ms and *BW*=±62.5kHz.

RESULTS: Representative axial slices through the $T_{1,F}$, $T_{1,S}$, $T_{2,F}$, $T_{2,S}$, myelin water fraction and myelin residence time maps are shown in Fig. 1. Mean values obtained from different brain regions are shown in Fig. 2 and closely agree with those reported in literature[3,4,5] (averaged across volunteers, mean values were: $T_{1,F}$ = 390 ms, $T_{1,S}$ = 926 ms, $T_{2,F}$ = 19.1 ms, $T_{2,S}$ = 118 ms and myelin water fraction = 0.295 which compare with literature ranges of: $T_{1,F}$ = 350-460 ms, $T_{1,S}$ ≈ 970 ms, $T_{2,F}$ = 10-55 ms, $T_{2,S}$ = >55 ms and myelin water fraction = 0.17-0.32) The values are also consistent across the healthy subjects. In Fig. 3, we show sagittal and axial slices through the calculated myelin water fraction map of the severely disabled MS patient along with corresponding slices through the a high resolution T_1-*weighted* image. White matter lesions identified in the T_1-*weighted* (arrows) image appear as areas of drastically reduced myelin fraction.

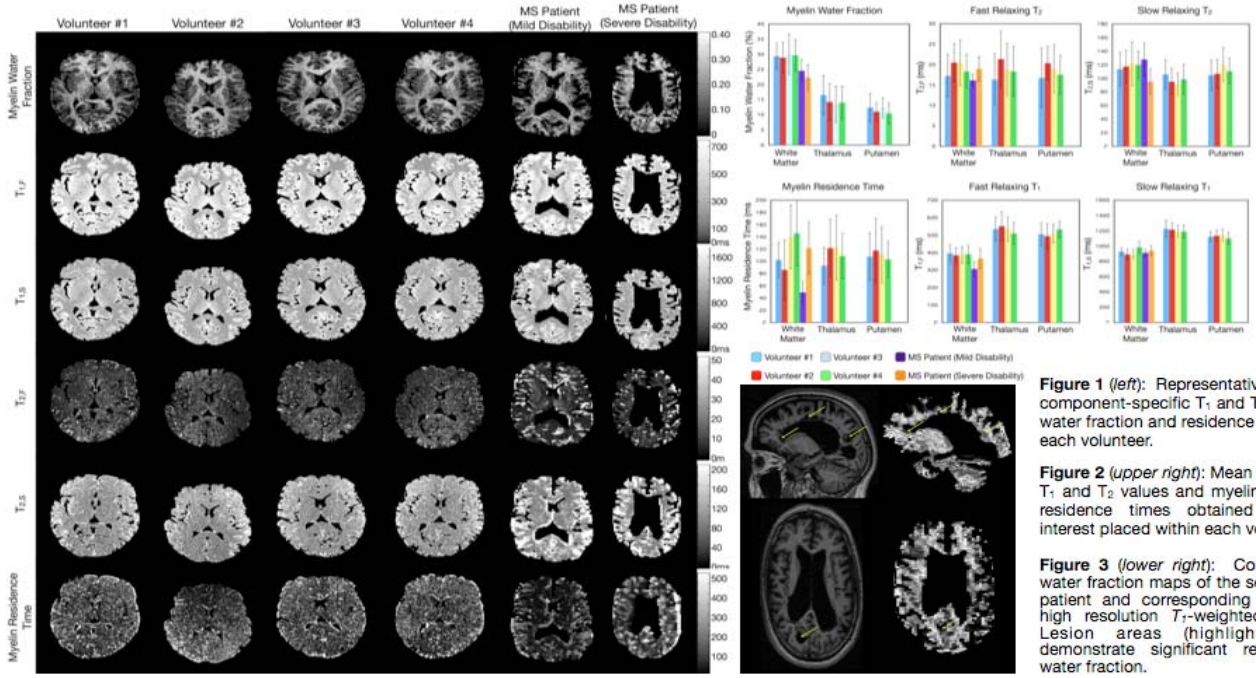

Figure 1 (*left*): Representative slices through the component-specific T_1 and T_2 values and myelin water fraction and residence times calculated for each volunteer.

Figure 2 (*upper right*): Mean component-specific T_1 and T_2 values and myelin water fraction and residence times obtained from regions of interest placed within each volunteer.

Figure 3 (*lower right*): Comparison of myelin water fraction maps of the severely disabled MS patient and corresponding slices through the high resolution T_1-weighted IR-SPGR image. Lesion areas (highlighted by arrows) demonstrate significant reduction in myelin water fraction.

DISCUSSION / CONCLUSIONS: Here we have demonstrated the ability to derive multi-component T_1 and T_2 information from high resolution and whole-brain multiple flip angle SPGR and bSSFP data for the first time. The high inter-subject reproducibility amongst healthy volunteers, close agreement with prior literature values, and observed reductions in myelin water fraction in white matter lesions attest to the method's utility in identifying and assessing tissue change associated with neuro-degenerative disorders, in particular MS. With a scan time of approximately 16 minutes, the method may easily be implemented in a clinical setting.

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