Non-Exponential T_2^* Decay in White Matter

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Introduction

Brain function is critically dependent on intact myelination around axonal fibers. An accurate measurement of myelin content in human brain would be valuable for the study of pathologies underlying myelin loss, in particular multiple sclerosis. A number of methods have been proposed to quantify a potentially distinct myelin bound water pool for this purpose. These methods have been based on T_2 (1), a combination of T_1 and T_2 (2) or MT effects (3), and generally assume the presence of an observable myelin associated water pool with a higher relaxation rate than normal, free water. Recently, a T_2^* based method has been proposed as well (4), using a 3T magnet and a triple exponential model to generate an image of myelin-associated water. The potential advantage of a T_2^* method is that the acquisition with a multi gradient echo sequence is faster and less restricted by RF-SAR limits than methods based on T_1 and T_2, especially at higher field. In this work, the potential for using a T_2^* method for myelin mapping was explored at 7T, taking advantage of the higher SNR and possibly higher contrast; 3T data were acquired as well for determination of field dependence and comparison to previous results (4).

Methods

Seven subjects were scanned on a GE 7T system and 4 on a GE 3T, both with a Nova Medical receive array (32 and 16 coils resp.). A single polarity multi gradient echo sequence was used, with scan parameters: TR 70 ms, TE 2.7-45 ms, with 2.5 ms spacing for 19 echoes, flip angle 30° (at center), 256x96 voxels over 240x180 mm² FOV, 50 repetitions, total scan time 336 s. A single 2 mm slice was acquired parallel to and slightly above the AC/PC line to capture a section of the corpus callosum (CC). The repetitions were averaged, with exclusion of outliers, and fitted voxel by voxel with a mono-exponential decay, excluding the first two TEs from the fit to sensitize it to the slower component. The residue (difference between data and fit) was mapped, and its spatial average as a function of TE was calculated in 3 ROIs: the splenium of the CC, part of the posterior internal capsule (PIC) and a general white matter (GWM) area in the posterior part of the slice. The residue at TE 2.7 ms relative to the fitted decay amplitude was taken as measure of the short component and quantified for 3 and 7 T.

Results and Discussion

The SNR was 30-80 for TE 2.7 ms at 3 T and 70-180 at 7 T. Fig. 1 shows that the residue after fitting with an exponential decay has significant amplitude also for longer TEs and is spatially inhomogeneous, in both amplitude and TE dependence. Fig. 2 shows the average of the 7 T residuals for the three ROIs. CC, with fibers perpendicular to $\mathbf{B_0}$, shows the biggest effect; PIC, with fibers predominantly parallel to $\mathbf{B_0}$, the smallest. Fig. 2 also shows that the time-course of the residual is not consistent with a multi-exponential decay, as is simulated in Fig. 3. Fig. 4 and 5 show the almost linear field dependence of the relative residual at TE 2.7 ms. These findings cannot be explained by relaxation effects from a water fraction restricted by myelin, but rather point to a susceptibility-based mechanism. A myelin associated water fraction should be independent of field strength and orientation and result in a different decay shape. On the other hand, magnetic field inhomogeneities induced by the susceptibility differences associated with axonal fibers would be field and orientation dependent, could show contrast reflecting local fiber structure, and could induce a decay consistent with Fig. 2 as is illustrated by the simulation in Fig. 6.

Conclusion

The observed deviations of the signal decay from a mono-exponential function have a shape, spatial distribution, orientation and field dependence that all point to a susceptibility related source for these effects, rather than originating from restricted water mobility around myelin. Although the susceptibility is related to axonal fibers and likely correlated to myelin, this means that deviations from exponential decay cannot be directly interpreted as local myelin concentration. However, it may be possible to detect abnormal de-myelination by comparing the contrast found in patients to that in healthy subjects.

References: (1) MacKay A, Whittall K, Adler J, Li D et.al. Magn Reson Med 1994;**31**:673-677. (2) Deoni SC, Rutt BK, Arun T, Pierpaoli C, Jones DK. Magn Reson Med 2008;**60**:1372-1387. (3) Yarnykh VL, Yuan C. Neuroimage 2004;**23**:409-424. (4) Hwang D, Kim DH, Du YP. Neuroimage 2010;**52**:198-204.

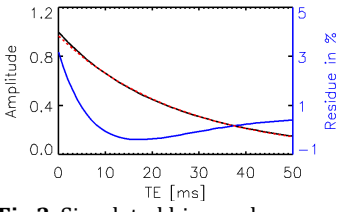

Fig 3. Simulated bi-exp. decay (black), fitted with a mono-exp. function (red) and the scaled up residue (in %, blue). We used amplitudes 0.9 and 0.1 for a R_2^* of 36 and 108 Hz respectively.

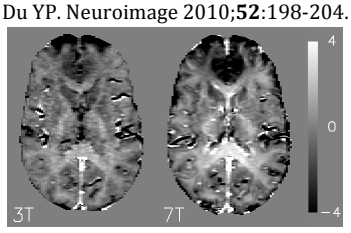

Fig 4. The relative residue (in %) at TE 2.7 ms at 3 and 7 T for one subject, showing the field dependence of the signal deviation from exponential decay.

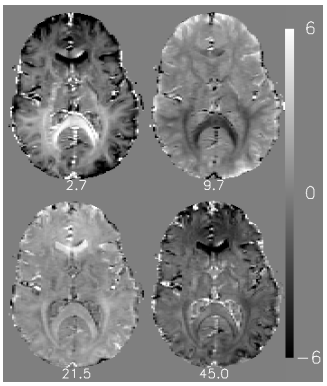

Fig. 1 Relative residue (in %) at 4 TEs after exponential fit at 7 T.

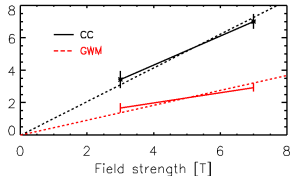

Fig 5. The ROI and subject averaged residual at TE 2.7 ms after exponential fitting, for two ROIs, as function of $\mathbf{B_0}$

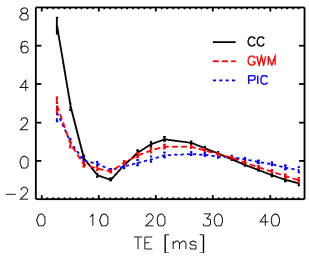

Fig. 2 Averages over 8 studies of the residual after exponential fitting for the three ROIs, with standard errors. The scale is in % of signal at TE = 0.

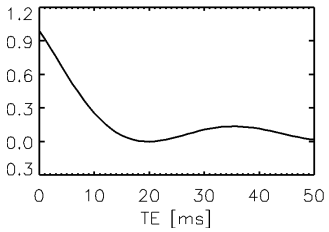

Fig 6. Simulated signal decay in the field of a cylinder placed perpendicular to $\mathbf{B_0}$.