A new quantitative MRI contrast for measuring white matter myelin

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Introduction: Quantitative neuroimaging aims to create acquisition and processing methods that can be used on any MRI scanner to estimate fundamental brain tissue properties. Here, we describe a new quantitative neuroimaging method designed to estimate the fraction of myelin in voxels within the white matter of the human brain. Relying on the established biophysical theory of the hydration layer, we introduce MR acquisition and processing methods that estimate the lipid bilayer concentration in the white matter. The method uses bias corrected proton density (PD) and T1 measurements to estimate the hydration layer fraction (HLF); in the white matter (WM), the HLF is an estimate of the myelin density. We test key aspects of the method and theory by obtaining data from the same subjects using different MRI scanners at different field strengths and different RF coils. Finally, we describe two applications. First, we show how HLF estimates can be combined with diffusion measurements to improve our understanding of individual fiber tracts. Second, we quantify the HLF values in a subject with multiple sclerosis in lesion and in normal appearing brain regions and compare these values with those from a set of normal controls. Quantifying myelin concentration in individual subjects will find useful applications in understanding development, disease, in the human brain.

Methods: 3D-SPGR was acquired on 10 healthy volunteers 1.5T and, 2subject were scan also in 0.5T 3T GE MRI scanner with an 8-channel coil. TR=, 20 ms; TE= 2.6 ms; flip angle α = (4◦, 10◦ 20◦, 30◦) and, 1.5 mm^3 voxel size. A T1 and a M0 (image weighting by coil gain, PD,T 2*) maps were linearly fitted. T2* weight in the M0 map is estimated to be negligible for this short TE. PD was corrected for coil gain inhomogeneity by fitting a slowly varying field over the images. The water PD (PDw) was estimated as the median for CSF ROI (3.5>T1<5). The WF in a voxel (i) is defined as: $WF(i) = PD(i) / PDw$. For scans in 0.5 and 1.5T B1 inhomogeneity was fitted in CSF voxels (WF~1). In this region T1 was fix to be 3.6 sec and B1 was calculate, and a median along the ROI was taken. In 3T magnet the T1 was correct for B1 as describe (Deoni e.t al. 2005). The T1 values are modeled as weighted sum of two fast exchanging pools; the free pool (with T1f=~3.6 sec) and a hydration pool (T1h). T1h was experimentally estimated before to be $T1h=1.83\,x\,f + 25$. f is the relevant magnet filed frequency (Fullerton et. al. 1984). The water T1h fraction (wHLF) is then given by the T1 equation as a weighted sum of the two water pools: $wHLF= (1/T1-1/T1f)\,x\,(1/T1h-1/T1f)$. The HLF in a voxel (i) is then $HLF(i)= wHLF(i)\,x$ WF(i).

Results: The measured PD and T1values are in agreement with those in the literature. A within subjects repeated calculation of the PD, T1, wHLF and HLF maps found to be highly reliable (r~0.8) mean error of ~0 and SD of ~10%. The theoretical used to estimate wHLF found to be reliable as similar values was found in three different magnetic fields and different scanning parameters. **Figure 1** shows an analysis of HLF and FA values in the corticospinal tract (CST). Panel **A** shows the CST estimated by deterministic DTI tractography in blue. Panels **B**, shows the mean HLF and FA values measured at different positions along the CST in 10 different subjects. The FA but note the HLF value declines in the region where the CST and callosal fibers intersect (red arrow). Notice the consistent difference between subjects in the HLF, but not FA, values. **Figure 2** shows a subject with multiple sclerosis (MS), the left panels (**A**) are T2-weighted (T2w) axial slices in MNI coordinates. In the T2w image the MS lesions appear as unusually bright spots. The middle panels (**B**) are z-score maps comparing the HLF values in the MS patient with 10 controls. In the dark red regions the HLF is significantly lower than the mean. Panels **C** (up) shows the arcuate fasciculus (AF) estimated by DTI tractography in blue. The low panel shows the mean HLF values measured at different positions along the AF in 10 control subjects (gray lines) and an MS patient (red line). The black line is the mean and the dotted lines are the +/-2 SD curve for the controls. The HLF values in the MS patient differ from the group in both the lesion and the normal appearing regions. The arrows indicate AF positions at a clear lesion (red) and normal-appearing (green) T2w values.

Discussion H LF is calculated by combining noise corrected T1 and PD maps. Because HLF measurement does not require estimation of additional free parameters it is relatively free from model fitting noise. An advantage of the HLF is that it is easy to calculate in a very high resolution using simple stock sequences. This makes it a good candidate to serve as a standard for clinical WM impairments; for brain structural research and correlations with behaviors; as well as for brain tissues segmentation.

Figure 1

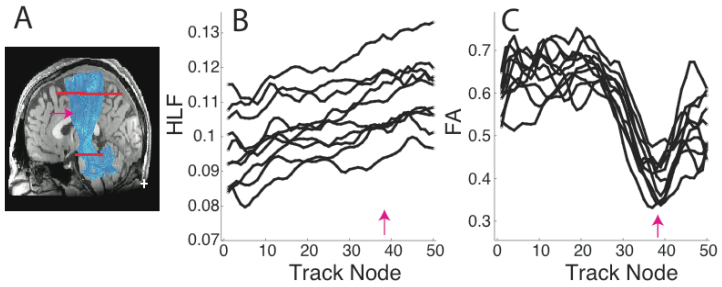

Figure 2