

Absolute Quantification of Myelin related Volume in the Brain

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Introduction. Quantitative Magnetic Resonance Imaging has the major advantage that it handles absolute measurements of physical parameters. Parameters such as relaxation rates R_1 and R_2 and proton density PD are independent of MR scanner settings and imperfections and hence are directly representative of the underlying tissue characteristics. Observed R_1 - R_2 -PD values in the brain can be modeled by 4 tissue compartments: 1. Non-signal-emitting cell tissue (CT), 2. Intracellular Water (ICW), 3. Extracellular Water (ECW) and 4. Myelin related volume (MyV), comprising the myelin sheets and myelin water (MyW). There are strong exchange rates k between the compartments. The relaxation goes via the MyW but the resulting signal is not observed using our sequence due to its high relaxation rate. Hence the measured, visible PD is the sum of ICW and ECW. An increasing amount of MyV is observed as a decrease of PD and a simultaneous increase of R_1 and R_2 .

Fig. 1. The 4 compartment model

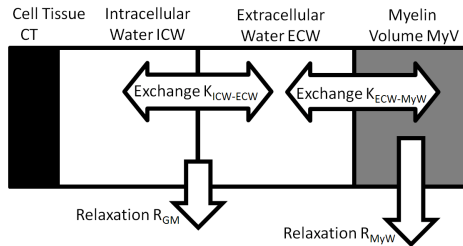


Table 1. Tissue cluster positions for the brain at 1.5T and 3T. Note that the estimated MyW relaxation is the product of the exchange rate $k_{ECW-MyW}$ and the actual MyW relaxation.

Tissue	R_1 (s^{-1}),	R_1 (s^{-1})	R_2 (s^{-1})	R_2 (s^{-1})	PD (%)
	1.5T	3T	1.5T	3T	
CSF	0.24±0.3	0.23±0.3	0.63±0.3	0.95±0.3	100±4
GM	0.92±0.02	0.90±0.03	10.5±0.1	12.5±0.3	85±3
WM	1.70±0.05	1.47±0.07	12.4±0.2	13.9±0.3	64±3
MyW	4.69±0.18	3.40±0.27	19.6±1.1	18.8±1.6	0

Methods. The quantification sequence was a multi-echo saturation recovery sequence using a repetition time $TR = 3.2$ s, 6 echoes at multiples of 15 ms and saturation delays of 128, 384, 1408 and 3072 ms. The in-plane resolution was 1.0 mm, the slice thickness 5 mm, 25 slices were acquired in a scan time of 5:46 minutes. Data of the complete brain of 40 healthy volunteers (30 at 1.5T and 10 at 3T) was fitted using the 4 compartment model resulting in table 1. Based on these values the MyV per voxel was estimated. Ten volunteers were scanned 5 times at different resolutions (1.0, 1.2, 1.4, 1.6, 1.8 and 2.0 mm in plane) to verify independence of acquisition resolution. The scanner was a 1.5T Philips Achieva. Data was analyzed using SyMRI Suite (SyntheticMR AB, Sweden).

Results. Healthy volunteers in age 20-29 had a MyV of 105±17 ml in the brain, at 30-39 101±21 ml, at 40-49 93±19 ml and at 50-59 81±18 ml. The ratio MyV/brain parenchyma was 8.3±0.6, 8.1±1.3, 0.79±0.8 and 0.72±0.7, respectively. The repeated measurements resulted in the same MyV value with an average standard deviation of 1.4 ml, an accuracy in the order of 1-2%.

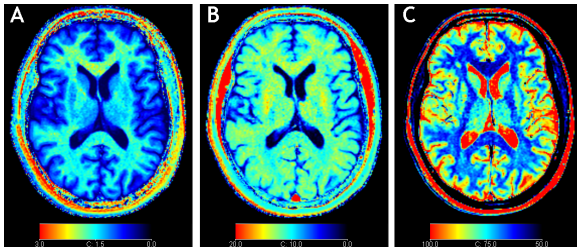


Fig. 2. Example of MR quantification. A: the R_1 relaxation rate (scale 0-3 s^{-1}), B: the R_2 relaxation rate (scale 0-20 s^{-1}) and C: the Proton Density (scale 50-100% water) of an axial slice of the brain.

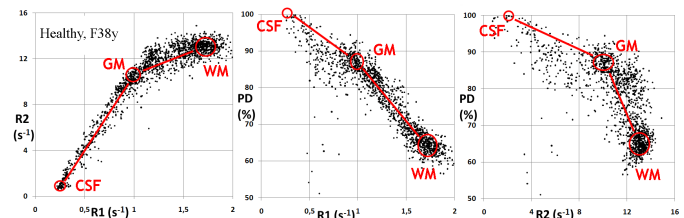


Fig. 3. R_1 - R_2 , R_1 -PD and R_2 -PD projections of the R_1 - R_2 -PD space of 1500 random points in a healthy brain (F38y). The tissue clusters from table 1 are indicated. There is a clear slope from GM towards WM where PD decreases and R_1 and R_2 increase, indicating an increasing myelin related volume.

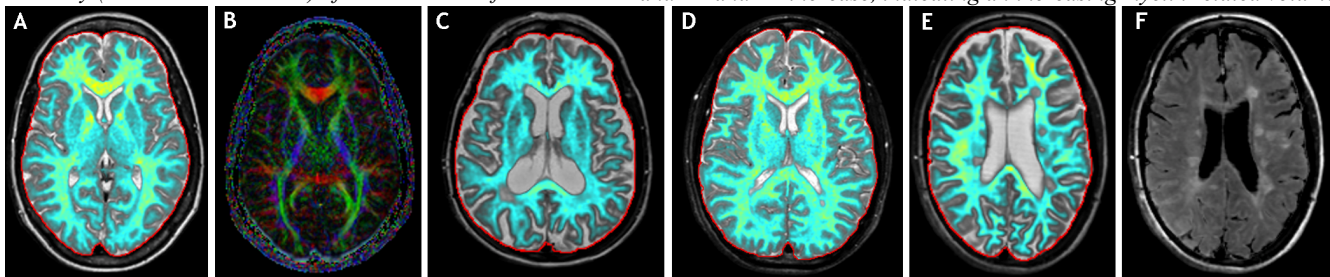


Fig. 4. Examples of absolute Myelin volume calculations where light-blue corresponds to 15% myelinization, up to yellow at 30%.

A: healthy volunteer with B: the FA map of the same slice, where high FA values corresponds to high myelinization. C: dementia patient with both a small white matter volume and a low degree of myelinization. D: young Multiple Sclerosis patient (M32y) with mostly normal myelin except small holes, E: elderly MS patient (F52y) with many holes in the myelin and. F: the corresponding FLAIR image

Conclusion. The absolute myelin related volume can be accurately estimated for the complete brain within a scan time of 6 minutes. This could be a sensitive marker for myelin damage in e.g. dementia and Multiple Sclerosis.