Using multi-parametric quantitative MRI to model myelin in the brain

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Introduction. Myelin content of the brain is an important parameter to study diseases such as Multiple Sclerosis or Alzheimer's disease. A model is proposed here to estimate the myelin content of brain parenchyma from quantitative MRI. QMRI aims at the absolute measurement of physical parameters such as the R_1 and R_2 relaxation rates and proton density PD. These parameters are independent of MR scanner settings and hardware imperfections and hence directly reflect the intrinsic tissue characteristics.

Methods. The quantification sequence[1] was a multi-spin-echo, saturation recovery sequence with 6 echoes of 15 ms and 4 saturation delays of 130, 380, 1630 and 3370 ms with a TR = 3.5 s. The in-plane resolution was 1.0 mm, the slice thickness 5 mm, 30 slices were acquired in a scan time of 7 minutes. The scanner was a 1.5T Philips Achieva (Best, the Netherlands), data was acquired of 30 healthy subjects (mean age 38y, range 21 – 65y) and singular patients. Regions of interest were placed to retrieve the cluster positions of 9 brain structures in the R_1-R_2-PD multi-parametric space using SyMRI Brain Studio (SyntheticMR, Linköping, Sweden).
In the proposed model, the observed R_1, R_2 and PD of each acquisition voxel is the result of a myelin partial volume V_{My} and a cellular partial volume V_{Cl} (Fig. 1), where each partial volume has its own properties in R_1, R_2 and PD. The V_{My} consists of a myelin water pool and a myelin semi-solids pool, the V_{Cl} consists of an intercellular and interstitial water pool and a non-myelin semi-solids pool[2] . A coupled numerical Bloch simulation was performed to calculate the *in-vivo* R_1, R_2 and PD measurements as a function of the two partial volumes. Based on this forward modeling, the myelin partial volume was assigned to combinations of R_1, R_2 and PD. Visualization of the model results was added as a feature in SyMRI Brain Studio (SyntheticMR, Linköping, Sweden).

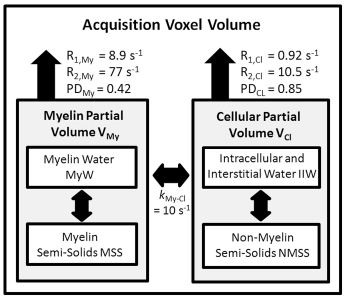


Fig. 1. *Partial volume model of brain tissue: Each voxel consists of a myelin partial volume V_{My} and a cellular partial volume V_{Cl}. There is an exchange $k_{My\text{-}Cl}$ between V_{My} and V_{Cl}.*

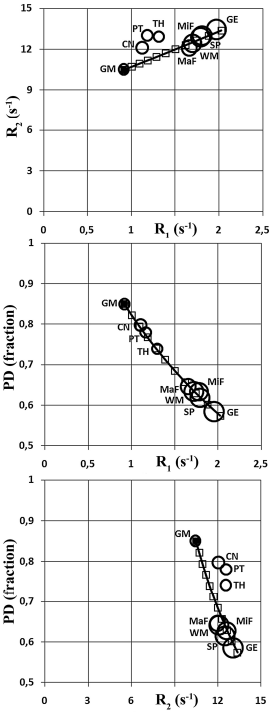
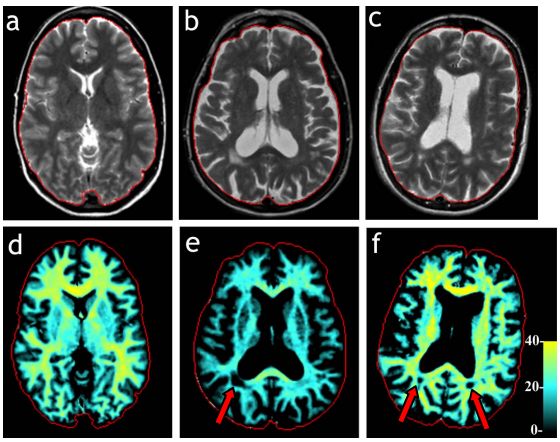


Fig. 2. *The observed R_1-R_2-PD cluster positions of cortical grey matter (GM), caudate nucleus (CN), putamen (PT), thalamus (TH), major forceps (MaF), minor forceps (MiF), genu (GE), splenium (SP) and the average white matter (WM). Added are the simulation results based on the parameter settings in Fig. 1 (square markers).*

Results. The qMRI observations form clusters in R_1-R_2-PD space as displayed in Fig. 2. In the model the V_{My} was varied in the range [0-40%] (and hence V_{Cl} = [100-60%]). The model parameters were adjusted to make the resulting curve go through the observed cluster positions. Using $k_{My\text{-}Cl}$ = 10 s^{-1} and $R_{2,My}$ = 77 s^{-1} from Ref. 2 we obtained $R_{1,Cl}$ = 0.92±0.02 s^{-1}, $R_{2,Cl}$ = 10.5±0.1 s^{-1} and $R_{1,My}$ = 8.9±2.3 s^{-1}. Using these values the average myelin partial volume in healthy white matter was estimated at 30.6±1.2%. Two clinical cases are shown in Fig. 3. A general reduction of myelination was observed in the patient diagnosed with cerebro-vascular degeneration (3b, 3e). MS lesions were clearly seen as strong local reductions of V_{My} (3c, 3f).

Discussion. Presented is a crude model for brain parenchyma where only the ratio of myelin and cellular partial volume was taken as a variable. All other properties were fixed based on observation of a healthy population. A general reduction of myelin can be observed, as well as the strong local reduction of myelin in lesions; thus providing useful diagnostic information on various neurodegenerative diseases.



Conclusion. The myelin partial volume for the complete brain was obtained within a scan time of 7 minutes. This procedure appears to be a sensitive marker for myelin damage in e.g. dementia and Multiple Sclerosis. Further validation of the procedure will be required in order to investigate its applicability.

Fig. 3. *T2W images of a healthy subject (a, F, 38y), a patient diagnosed with cerebro-vascular degeneration (b, F, 73y) and a patient diagnosed with MS (c, F, 40y). The red lines in the images depict the intracranial cavity. The estimated V_{My} is displayed in d, e and f, respectively. The healthy subject had a V_{My} of 29-33% in the white matter, for patient b this was only 19-23%. White matter lesions and MS lesions are seen as strong local reductions of V_{My} (red arrows).*

[1]Warntjes JBM, *et al.* Magn Reson Med 2008;60:320-329.
[2]Levesque R, Pike GB. Mag Reson Med 2009;62:1487-1496.