

A Constrained Estimator of Myelin Water Fraction from Steady-State Data

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Introduction. *Target audience:* Scientists developing protocols and estimation techniques for myelin water fraction. The mcDESPOT method proposed by Deoni¹ et al. uses a two-compartment white-matter model to estimate myelin water fraction and relaxometry parameters from SPGR and SSFP data. Although this approach yields whole-brain coverage in clinically useful times, there is concern about the reliability of the estimates². This work describes a method to constrain estimates with a uniform prior and estimate the model parameters with a gradient descent algorithm. Modifications to the protocol are proposed that improve estimation accuracy. **Methods.** Estimates of each parameter were constrained to the interior of a constraint set by applying a prior probability density given by the difference between two logistic functions as shown in Figure 1. The Levenberg-Marquardt (LM) algorithm was modified to minimize the sum of the log-likelihood and this log-posterior function. Numerical precision was improved by computing the Jacobian of the signal equation analytically and by modifying all libraries to use long-double precision. The acquisition protocol was modified in three ways: 1) The B1 field calibration was performed using actual flip-angle imaging³ (AFI); 2) Phase cycling angles were change from (180°, 0°) to (180°, 45°) to shift the signal null to the periphery of the image; 3) The flip angles acquired were optimized. Two parameterizations were used: an *explicit* model, {T1f, T1s, T2f, T2s, MRT, MWF, ρ_{SPGR} , ρ_{SSFP} , ω } where MWF is the myelin water fraction and MRT is the myelin residence time; and an *implicit* model, {T1f, T1s, T2f, T2s, MRT, MWF, ρ_{SPGR} , $\rho_{SSFP,f}$, $\rho_{SSFP,s}$, ω } where MWF is given by $\rho_{SSFP,f}/(\rho_{SSFP,f}+\rho_{SSFP,s})$. A reduced model was also computed with T1f fixed at 150ms. An initial value of ω was found using a search method with linear models for T1 and T2. These were refined by fitting a one-compartment model with parameters {T1, T2, ρ_{SPGR} , ρ_{SSFP} , ω } to the data with nonlinear least squares. **Data Acquisition.** Data were collected on a 3T GE MR750 with no acceleration. Voxels were 2.5mm cubic and were smoothed with a 2mm Gaussian. Sequence parameters were: **AFI:** TR/TE=20/1ms, TR2/TR1=5, fa=50°, hard RF pulse, spoiler area=35Gms/cm, 64 slices, 64x64, NEX=.75; **SPGR:** fa=[1, 2.7, 4.7, 6.6, 13.3, 21, 30]°, TR/TE=4/1.4ms, hard RF pulse, 96 slices, 96x96, NEX=1 FOV=24cm, pixel size=2.5x2.5mm, no acceleration; and **SSFP:** Two SSFP acquisitions were acquired with phase cycling of [180, 45]° and fa=[8.6, 13, 17.6, 22.1, 30.1, 39.2, 65]°, hard RF, TR/TE=3.1/1.55ms, 96 slices, 96x96, NEX=1, FOV=24cm, no acceleration. Two complete data sets were acquired in a single subject in a single session under an IRB approved protocol. The Mori atlas was used to extract mean white-matter MWF and the genu/splenium ratios.

Results. Images of MWF are shown in Figure 2. Without exception one or more constraints were active at convergence – always MRT and sometimes T2f. Implicitly estimating MWF as a ratio of spin densities yielded reasonable values of both MWF (.11 +/- .022) and the splenium/genu ratio (1.13±.35) while the explicit model yielded values of .034±.005 and ratios of 1.51±.39. Images of T1f converged to values 25-50% higher than starting value for all starting values and did not reflect gray/white differences. Estimates of MWF and T2f varied systematically with the T1f starting value (Figure 3). Although MRT images were insensitive to the starting value, they always converged to the lower bound and did not reflect gray/white differences. Estimates of T2f and MWF covaried with both the MRT lower bound and the T1f starting value. Fixing the value of T1f or MRT yielded degraded image quality. These results held for both acquisitions.

Discussion. These results show that the parameters of the mcDESPOT model can be computed with descent methods and that improved image quality can be achieved with optimal choices of flip angles and phase-cycling angles. It appears from these data that T1f and MRT cannot be reliably estimated. Values of T2f and MWF are dependent on the values of T1f and MRT, so fixing them effectively constrains the values of T2f and MWF.

Conclusions. The parameters of a two-compartment for myelin water fraction can be estimated with a constrained non-linear least-squares algorithm. Estimates of the fast T1 and myelin residence time were unreliable. Estimates of myelin water fraction are visually of high quality but may be a function of several parameters and hence non-quantitative. Nevertheless, they may be a useful indicator of myelin water fraction.

References: 1) Deoni, et al. MRM, 60(6):1372–1387, 2008. 2) Lankford, C. L., & Does, M. D. MRM 2007. 3) Yarnykh, V. L. MRM 57(1):192–200m 2007

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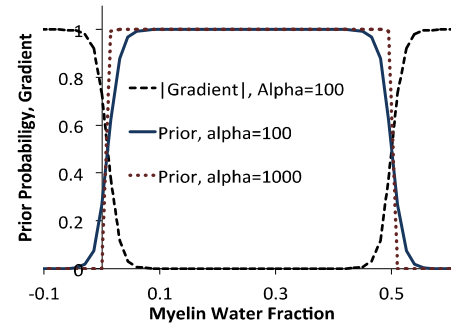


Figure 1. Prior probability density.

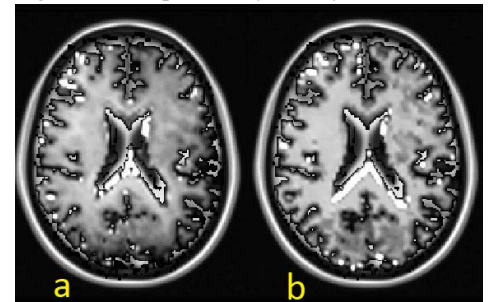


Figure 2. Myelin water fraction for the full model: explicit (a) and implicit (b).

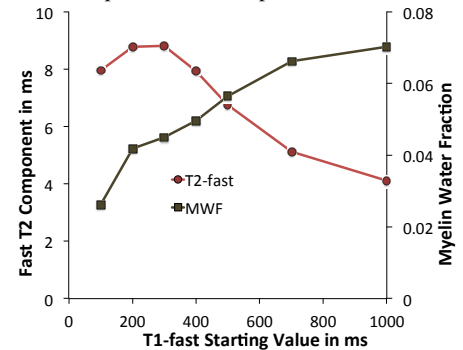


Figure 3. T2f and MWF vs. T1f initial value.

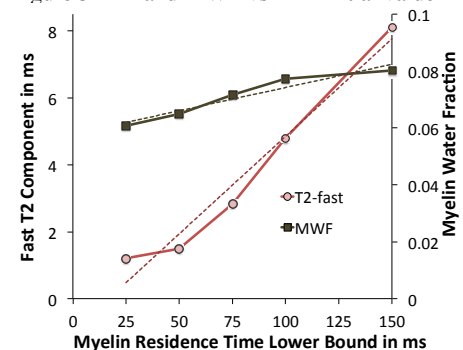


Figure 4. T2f and MWF vs. MRT lower bound.