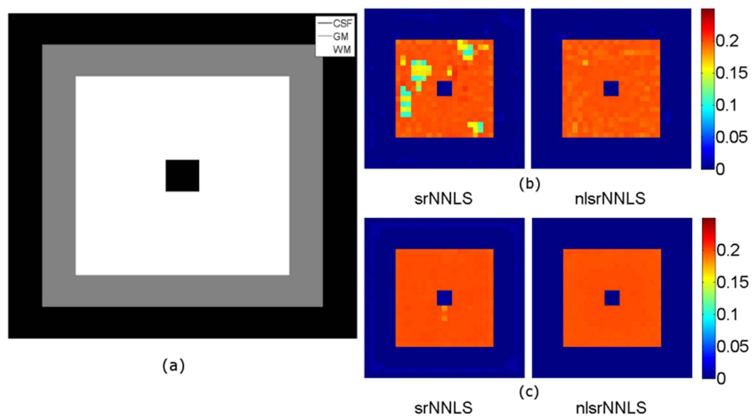
Quantification of Myelin Degeneration in Multiple Sclerosis within Clinical Scan Times.

L. Soustelle[1,2], O. Commowick[1], E. Bannier[1,3], and C. Barillot[1]

[1]*Unité VISAGES U746 INSERM-INRIA, IRISA UMR CNRS 6074, University of Rennes, Rennes, France,* [2]*Université de Strasbourg, CNRS, ICube, FMTS, Strasbourg, France,* [3]*Radiology Dept., University Hospital of Rennes, F-35043 Rennes, France*

Purpose: Multi-echo T_2 relaxometry is a relevant imaging method for Myelin Water Fraction (MWF) quantification in the study of multiple sclerosis (MS). However, to ensure accurate estimation, a large number of echoes are still required that can drive to very long acquisitions. In practice, 32 echo times (TE) ranging from 10 ms to 320 ms and an echo spacing (ESP) of 10 ms are used[1]. Analysis of the decay curve of the consecutive echoes allows the estimation of the T_2 spectrum. The proposed approach makes use of recent spatial regularization methods[2,3] for MWF estimation from clinically compatible acquisitions (typically 11 echoes acquired within 6 minutes with TE_1=ESP=8.4 ms). The algorithms were evaluated on both synthetic and clinical data, illustrating the ability to compute accurate MWF maps from a low number of echoes.

Methods: We assume, as in **[1]**, that the T_2 spectrum of water in the brain has multiple components, classified in the following pools at 3T[4]: myelin-bound water with T_2 values between 15 and 40 ms, intra/extra-cellular water with $T_2 \approx 100$ ms, and cerebrospinal fluid (CSF) with $T_2 > 1500$ ms. According to the model $S_{sig}(t) = \int f(T_2) e^{-t/T_2} dT_2$ for CPMG-like acquisitions, we use a discrete T_2 spectrum model for the analysis, $f(T_2) = \sum_i \alpha_i \delta\,(T_2 - T_{2i})$ with 40 T_{2i} logarithmically spaced from 15 to 2000 ms[1]. Such estimation is performed by Non-Negative Least Squares (NNLS) optimization. The Extended Phase Graph (EPG) algorithm was used instead of the exponential in S_{sig} to account for stimulated echo effect[5]. 2D (31x31 pixels) synthetic data representing 3 tissue classes of the brain is illustrated in Fig.1.a. Myelin-bound water is restricted to white matter (WM), with a simulated spectrum such that MWF equals 0.2 in each pixel. After generating each spectrum according to their respective T_2 values, a synthetic signal is provided for 11 (TE_1=ESP=8.4 ms) and 32 (TE_1=ESP=10ms[1]) equally spaced echoes with a 0.7 B1 deviation on the whole image (highest deviation found on clinical acquisitions). The signals are corrupted by a white Gaussian noise for 10 and 20 dB SNRs. Two strategies are introduced for spatial regularization using L_2-norm for the estimation: spatially regularized NNLS (srNNLS[2]), and non-local srNNLS (nlsrNNLS[3]). The resulting cost function is given by $C = \|SX - Y\|_2^2 + \lambda \|X - P\|_2^2$, with $S_{i,j} = EPG(TE_i, T_{2j}, B_1, ESP)$ and P an *a priori* calculated from previously estimated spectra using regularized NNLS (rNNLS) optimization (where $P = 0$ and λ chosen so that $RMSE_{rNNLS} = 1.02 RMSE_{NNLS}$[1-3]): srNNLS calculates P by averaging spectra in a patch of voxels, and nlsrNNLS calculates P using a non-local algorithm, with a Kullback-Leibler divergence operator to measure the distance between discrete spectra inside a voxel patch. For clinical experiments, 3D T_2 relaxation measurements were performed on a 3T Siemens Verio scanner with the following parameters: matrix size of 192x192, 44 slices, voxel size of 1.3x1.3x3 mm^3. Due to the anisotropy of these dimensions, and for a faster computation time, P was calculated in 2 dimensions.



(d)

SNR (dB)	Relative error 20	Relative error 10	Mean 20	Mean 10	SD 20	SD 10
srNNLS (11 echoes)	0.0060	0.0507	0.1988	0.1902	0.0017	0.0219
nlsrNNLS (11 echoes)	0.0042	0.0161	0.1992	0.1968	0.0007	0.0030
srNNLS (32 echoes)	0.0053	0.0193	0.1984	0.1958	0.0011	0.0034
nlsrNNLS (32 echoes)	0.0035	0.0112	0.1990	0.1969	0.0006	0.0033

Figure 1 Quantitative evaluation. 2D brain tissues simulation (a); MWF estimation at SNR=10 dB (b) and 20 dB (c) (11 echoes); statistics of estimated MWF in WM (d)

Results: Figure 1 shows the robustness of MWF estimation along with two different noise levels and two different spatial regularization methods (srNNLS & nlsrNNLS). Table in Fig.1.d gives relative error, estimated mean and SD of MWF in the WM with these two methods and two different SNRs, both for 11 and 32 echoes. Quantitative evaluation shows that spatial regularization compensates for the loss of information due to echoes reduction. In addition, nlsrNNLS method overcomes srNNLS for low SNR, and results at 11 and 32 echoes are similar with nlsrNNLS. Figure 2 shows a representative axial slice of the estimated MWF of the MS patient with both methods and the corresponding anatomical scan (CPMG at TE=8.4 ms). Even though acquired with only 11 echoes, lesions are clearly visible (arrows) and appear as black voxels or areas with decreased MWF compared to normal appearing WM.

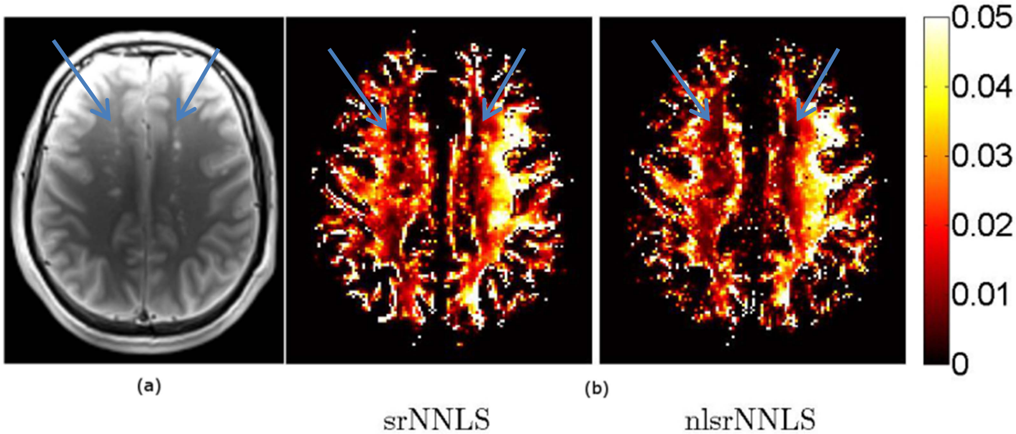


Figure 2 Axial slice of an MS patient (CPMG at TE=8.4ms) (a) and corresponding MWF estimation (b).

Conclusions: We evaluated two recent methods for MWF estimation, using *a priori* information as well as conventional and fast algorithm (NNLS), and a cross-validation strategy. Based on simulated and clinical data results, the nlsrNNLS estimation is more accurate and less penalizing than srNNLS. This regularization provides an efficient way to circumvent an ill-posed problem aspect, in particular with a reduced number of echoes for clinically acceptable acquisition times, allowing for accurate MWF estimation.

References: [1] Whittall et al. JMR 1989, [2] Hwang et al., JMRI 2009, [3] Yoo et al., MICCAI 2013, [4] Kolind et al. MRM 2009, [5] Hennig et al., CMR 1991