Robust myelin water quantification using spatially regularized nonnegative least square algorithm

D. Hwang[1], and Y. P. Du[2]

[1]Electrical and Electronic Engineering, Yonsei University, Seoul, Korea, Republic of, [2]Psychiatry, University of Colorado Denver, Denver, Colorado, United States

Introduction: A quantitative measurement of the myelin content of white matter (WM) can be used as a significant predictor of the prognoses of the clinically isolated syndrome and for earlier diagnosis of WM diseases such as multiple sclerosis (MS). One approach developed to provide valuable information on myelin content is to measure myelin water fraction (MWF) by analyzing T_2 decay curves using a nonnegative least square (NNLS) algorithm [1,2]. This technique has successfully demonstrated the merit of quantitative measurement of MWF in the study of MS. The NNLS algorithm is commonly used with a regularization in the T_2 spectral domain, which will be referred to as *rNNLS* hereafter. The rNNLS algorithm showed an improved performance, but it is still prone to the noise in the measurements [3]. The purpose of our current study is to develop a new analysis approach, referred to as a spatially regularized NNLS (srNNLS) algorithm, for robust MWF estimation with a reduced sensitivity to the noise. In the srNNLS algorithm, the regularization is expanded into the spatial domain in addition to the T_2 spectral domain.

Method: A postmortem MS brain with several focal lesions was scanned with a multi-gradient-echo (MGRE) sequence [4] to acquire free-induction-decay (FID) signals on a 3T MRI scanner (General Electric, Waukesha, WI). The image matrix was 256 x 256, TR = 2 s, FOV = 20 cm, slice thickness = 3 mm, the first echo time = 2.1 ms, and echo spacing = 1.1 ms. The T_2^* spectra were estimated from the acquired FID signals for the individual pixels using the rNNLS and the srNNLS algorithm, respectively. MWF maps were obtained from the estimated spectra and their contrast-to-noise ratios (CNR) over small lesions were compared. The srNNLS algorithm was implemented by minimizing $\{\|As-y\|_2+\mu\|Hs-p\|_2\}$, subject to $s\geq 0$, where A is the system matrix, s is the T_2^* spectrum, y is the T_2^* decay measurements, μ is the regularization parameter, H is the weighting matrix, and p is the *a priori* spectrum. p was estimated from the spectra obtained by the rNNLS algorithm. Simulations with synthetic data were also performed to assess the variability of MWF estimation and the visibility of small lesions due to the measurement noise. The synthetic data were produced with different noise (SNR=75, 100, 150) and contrast levels (C=7.5, 12, 15).

Results: Figure 1 shows the results of simulation studies. In all three cases (a~c), CNR was substantially improved with the use of the srNNLS algorithm. Figure 2 shows the results of the postmortem MS brain studies. The MWF map estimated by the rNNLS algorithm, referred to as MWF_{rNNLS} (b), contained high spatial noise ("hole"-type noise [3]) and the visibility of small lesions (indicated by arrows in T_2-Flair image (a)) was significantly degraded. In contrast, this hole-type noise was substantially reduced in MWF_{srNNLS} (c) with an improved visibility of small lesions. Figure 3 shows CNRs for 7 lesions. CNR was improved by a factor of two with the use of srNNLS algorithm. Figure 4 and 5 shows the effect of regularization strength ($\mu=\alpha\,\mu_{rNNLS}$, where μ_{rNNLS} is the regularization strength in the conventional rNNLS algorithm) on the estimation of MWF maps. The optimal μ was found at α=15.

Discussion: The results of this study demonstrate the effectiveness of the srNNLS algorithm for robust MWF estimation. A substantial decrease in the MWF variability was observed in both simulations and the analysis of *in vitro* MGRE data. The visibility of small MS lesions was substantially improved. In contrast to the regular low-pass filters which reduced the noise with a penalty of reduced spatial resolution, the srNNLS algorithm effectively preserved the visibility of small lesions and sharp boundaries with substantial noise reduction.

References: [1] MacKay A, et al. MRM 1994; 31:673-7. [2] Whittall KP, et al. MRM 1997;37:34-43. [3] Jones CK, et al. MRM 2003;50:206-9. [4] Du YP, et al. MRM 2007;58:865-70.

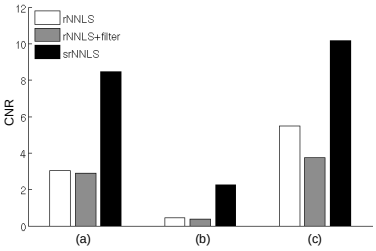

Figure 1. Contrast-to-Noise Ratio (CNR) in simulation studies. (a) SNR=100 & C=15, (b) SNR=70 & C=7.5, (c) SNR=150 & C=12. (C is the original contrast). CNR was substantially improved with the srNNLS algorithm.

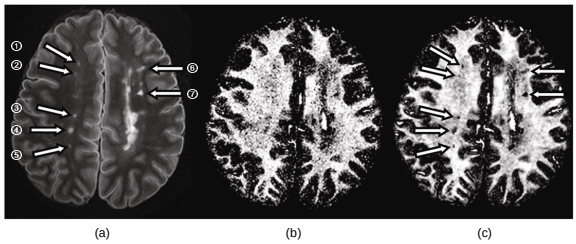

Figure 2. *in vitro* experiments. T_2-FLAIR image (a), MWF_{rNNLS} (b), MWF_{srNNLS} (c) for a fixed MS brain. Several focal MS lesions are indicated by arrows. MWF_{rNNLS} contains high spatial noise and the visibility of small focal lesions is low. MWF_{srNNLS} shows an improved visibility of lesions with a substantial reduction of spatial noise.

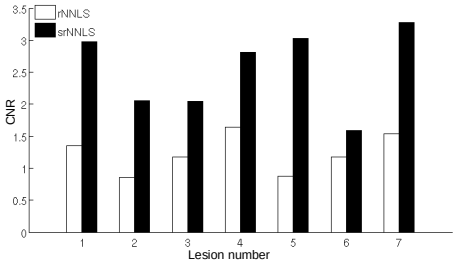

Figure 3. CNR for the MS lesions in Figure 2. In average, CNR was improved by a factor of two when MWF was measured using the srNNLS algorithm, compared to the rNNLS algorithm.

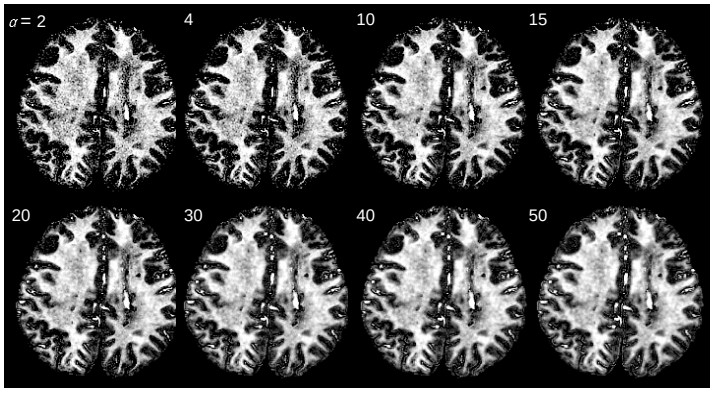

Figure 4. Effect of regularization strength, $\mu_{(srNNLS)} = \alpha \cdot \mu_{(rNNLS)}$, where α = 2, 4, 10, 15, 20, 30, 40, and 50. The MWF map with α = 2 still contains many "holes" and the visibility of small lesions is low. The MWF maps with α = 15 and 20 show an improved visibility of several small focal lesions with sharp boundaries of WM and GM. The maps with α = 30, 40, and 50 still show reasonable visibility of lesions but have introduced blurring effect throughout the images.

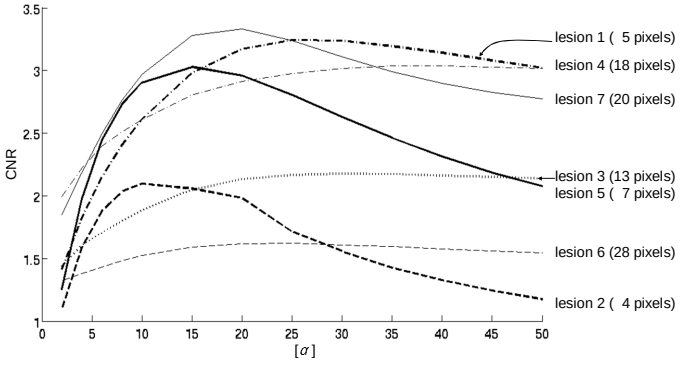

Figure 5. Effect of regularization strength: CNR of focal lesions with different regularization strength, $\mu_{(srNNLS)} = \alpha \cdot \mu_{(rNNLS)}$. The CNR's of large lesions (lesion 3 and 6) slowly increased and reached their plateaus around α = 20 ~ 25. The CNR's of small lesions (lesion 2 and 5) reached their maxima around α = 10 ~ 15, and kept decreasing as α increased further. The optimal range of α can be found between 15 and 20.