AnalyzeNNLS: Software designed to simplify multiexponential decay image analysis

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Introduction: Multiecho MRI studies provide unique insight into tissue microstructure [1,2]; recently this technique has uncovered previously unknown water compartments in pathological white matter [3,4]. Two major hurdles prevent scientists from applying this technique in their research: creating the pulse program and developing the analysis technique. We provide a solution to the latter issue by creating an easy to use, cross-platform software package, called AnalyzeNNLS, capable of analyzing multiexponential decays. AnalyzeNNLS allows scientists to perform region of interest (ROI) analysis on multiecho, multislice data, thus allowing them to focus on the sciences of MRI and biology.

Methods: AnalyzeNNLS was developed using Matlab 7.1 [The Mathworks, Inc] utilizing the Image Processing Toolbox and has been deployed on Windows XP, Macintosh OS X 10.4.7, and Kubuntu Linux operating systems. The general layout is presented in Fig 1. The decay curves are fit using a multi-exponential model consisting of a linear summation of T_2 decays resulting with a T_2 distribution [5]. From the T_2 distribution, shown in the lower right in Fig 1, areas beneath the curve and the centroid of the peaks (gmT_2) can be determined and compared across subjects. The relative area of the peak with the shortest T_2 time, or myelin water fraction, has been shown to correlate with myelin content [1,2]. This application is capable of opening multiecho, multislice image files from 1.5-T GE, 3.0-T Philips, and 9.4-T Bruker scanners. The analyzed data can be saved to disk for later recall and batch processing.

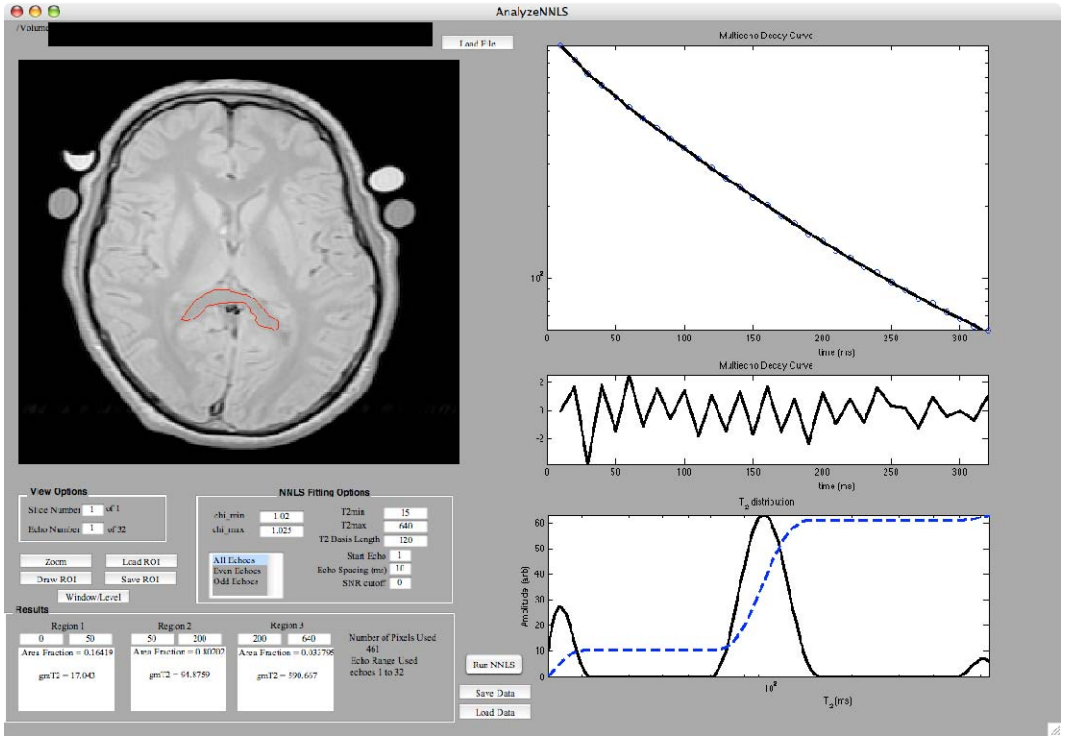

Figure 1: AnalyzeNNLS interface showing a multiecho acquisition; various fitting, display options, and results; decay with fit; residuals; and T_2 distribution.

For testing purposes, a digital phantom was created with six regions that mimic *in vivo* studies. This phantom was Fourier transformed to image space where noise was added at an SNR of 100 and 1000 per pixel. These data were then inverse Fourier transformed back to image space and evaluated against the input parameters. A multiecho acquisition from 1.5-T GE was also included and compared to literature.

	ic	sp	mjf	g	mif
MWF (%)	18	18	13	12	9
gmT_2 (ms)	21	17	15	15	15

Table 1: MWF and gmT_2 from the genu (g) and splenium (sp) of the corpus callosum, minor forceps (mif), major forceps (mjf), and posterior internal capsules (ic).

Results: In general, the peak areas and gmT_2s agreed with the input parameters for the digital phantom. (not shown) The multiecho scan results are shown in Table 1; the order of brain regions with decreasing MWF resembles the results shown in [6]. Variability of these measures can only be determined by performing multiple scans and only one case is shown here. The results were identical across all three operating systems. The ROIs and analysis results were saved to a text file for future recall and batch processing.

Discussion: Multiexponential acquisition and inversion are not trivial tasks. AnalyzeNNLS is designed to work on multiple platforms in order to perform ROI analyses on MRI multiecho experiments. The results show that this software behaves as expected on phantom data and provides similar MWFs to those reported in the literature. This software allows investigators to focus on the science of MRI and the multiple compartments in biology that multiecho acquisitions are sensitive to. AnalyzeNNLS can also be used to help scientists design and refine their multiecho acquisition techniques without the added hurdle of developing their own software to invert multiexponential decays.

[1] Odrobina *et al.* NMR Biomed 18:277-84 (2005). [2] Laule *et al.* MS 12:747-53 (2006). [3] Sirrs *et al.* Radiology 242:236-43 (2007). [4] Laule *et al.* JMRI 26:1117-21 (2007). [5] Whittall & MacKay. JMR 84:134-52 (1989). [6] Laule *et al.* Neurotherapeutics 4:460-84 (2007). We acknowledge financial support from the MSSC, AHFMR, and iCORE, and thank C McCreary and A MacKay.