How much of the reported myelin water component in T2 decays is actually a reconstruction artefact of the main water peak?

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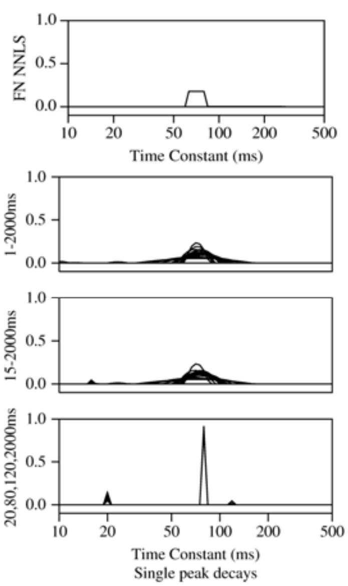
Purpose

To examine the possibility that the regularised nonnegative least squares (NNLS) algorithm, commonly used to reconstruct relaxation spectra from in vivo T2 decays [1-4], may generate artefacts corresponding to the myelin water signal when the source of the T2 decay is a main peak with no myelin component. As much of the pathology that is believed to affect the myelin water also affects the main peak, any confusion between the two signals may lead to questionable conclusions.

Method

Routine application of the NNLS in measuring the myelin water concentration (MWC) uses 32 echoes with a 10ms spacing and yields a signal to noise ratio (SNR) of about 100, as is common in real data sets. [1-4]. The white matter relaxation spectrum was modelled as a biexponential with a 20ms myelin and 80ms main peak. The amplitudes of the two peaks were 0.1 and 0.9 respectively. A relaxation spectrum was generated with only a single peak using a "false negative" NNLS reconstruction algorithm similar to that used by Cover [5]. The false negative algorithm was modified by requiring the reconstructed image be (1) zero for time constants less than 60ms, (2) monotonically increase from 60ms to 80ms and (3) monotonically decrease above 80ms. Twenty realisations of simulated relaxation decays were generated from the single peak spectrum with 32 echoes at 10ms spacing including ideal noise with a signal to noise ratio of 100.

The 20 simulated decays were reconstructed to relaxation spectra with 3 different versions of the regularised NNLS algorithm. All 3 versions approximated the continuous relaxation by a series of monoexponentials, spaced at 40 points per decade, between 1 and 2000ms. The first version of NNLS used the full range, from 1 to 2000ms, of the relaxation spectra. The second version [1-3] restricts the spectrum to 15-2000ms. The third version [4] restricts the spectrum to 4 time constants (20, 80, 120, and 2000ms). Detailed descriptions of all 3 versions are given in Cover [5].



Results

The single peak relaxation spectrum (FN NNLS) has no signal below 60ms. The main peak is more than 25ms wide and has a low shoulder from about 80ms to over 200ms.

The 3 versions of NNLS found many reconstructed spectra consistent with the data. The mean and standard deviations of χ^2 of the 3 versions were 24.4±5.9, 24.5±5.9, and 28.4±7.1, respectively. As would be expected, the more restricted the relaxation spectra, the higher the χ^2. For all 3 versions the mean of the χ^2 was below the expected χ^2 value of 32, indicating good consistency with the data. As is common practice when using NNLS to measure the MWC, the short time constant signal (STCS), defined as the integral of each reconstructed spectrum from 10ms to 40ms, was calculated. The mean and standard deviation of the STCS were 0.042±0.49, 0.014±0.019 and 0.095±0.025, respectively.

Discussion

For the example considered, version 3 of the NNLS generated repeatable myelin water peaks, of the amplitude predicted in the literature, even though the relaxation spectrum used to generate the decays had no signal below 60ms. Version 1give a STCS signal which was about half of what would be expected from a myelin peak. Version 2 gave a small signal which would be considered a non detection. Thus, the amount of MWC is heavily influenced by the choice of the version of the reconstruction algorithm. By modifying the false negative algorithm, it is possible to generate a range of spectra that have no signal below 60ms that will still generate a convincing myelin peak signal.

While versions of NNLS reconstruction algorithm are considered in this example, other multiexponential reconstruction algorithms will generate similar spectra to NNLS and thus maybe susceptible to the same false positive detection of the myelin water signal. A multiexponential reconstruction algorithm, which makes independent measures of the main peak and myelin water signal, has been published [5]. However, the algorithm requires SNR several times higher than the 100 routinely used by the NNLS algorithm, but the higher SNR can be achieved by using substantially larger voxels [5].

In conclusion, when using NNLS, or similar algorithms, to reconstruct spectra from decays with a SNR of 100 it is difficult to know how much of the myelin signal is actually an artefact of the main peak.

Acknowledgements

This work was partially funded by the Netherlands' Virtual Laboratory for e-Science (VL-e) and the VU University Medical Centre.

References

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