# Myelin Selective Magnetization Preparation

A. R. Travis[1], M. D. Does[1,2]

[1]Biomedical Engineering, Vanderbilt University, Nashville, TN, United States, [2]Institute of Imaging Science, Vanderbilt University, Nashville, TN, United States

## INTRODUCTION

Neural tissue is known to exhibit multi-exponential $T_2$ relaxation behavior, which is believed to reflect separate micro-anatomical water compartments in slow exchange. In particular, myelin-associated water is one such compartment and exhibits a characteristic short $T_2$ value in both white matter and peripheral nerve. Efforts have been made to quantitatively map myelin water content by decomposing the transverse relaxation signal into a so-called $T_2$-spectrum and filtering out all but the short-$T_2$ regime (1). This approach is hampered experimentally by sensitivity to $B_0$ and $B_1$ field variation, eddy currents, and the high signal-to-noise ratio necessary for computing a $T_2$-spectrum. A potential alternate approach is to use the multi-exponential $T_1$ characteristics of neural tissue, which has been demonstrated in excised white matter, and *in vitro* and *in vivo* in peripheral nerve (2-4). In this way, magnetization preparation, such as inversion-recovery (IR) or multiple-inversion recovery, may provide a more robust method to quantify tissue myelin content. As a first step toward evaluating the efficacy of such a method, IR and double-IR (DIR) preparations have been used in $T_2$ measurement of peripheral nerve water *in vitro*.

## METHODS/MATERIALS

The amphibian *Xenopus laevis* (African clawed toad) was chosen as the experimental animal. Immediately following euthanasia, 1-2 cm of sciatic nerve was removed from each leg and placed in a 5-mm (o.d.) NMR tube that contained perfluorocarbon solution (fomblin) to prevent tissue drying without adding proton signal. From a total of 11 frogs, various IR-CPMG and DIR-CPMG data sets were acquired at 300 MHz using a 16 cm bore, 7T Varian horizontal animal MRI system. In particular, three types of studies were performed: i) IR-CPMG with a wide range of IR-times ($\tau_{IR}$), in order to characterize the integrated $T_1$-$T_2$ spectrum of nerve water at 7T, ii) IR-CPMG with narrow ranges of $\tau_{IR}$ in order to evaluate the $\tau_{IR}$ required to null each of the three $T_2$ components, and iii) DIR-CPMG over a range of $\tau_1$ and $\tau_2$ times, in order to evaluate the ability to selectively excite only the myelin water $T_2$ component. In all cases, the CPMG portion of the pulse sequence was run with 1024 echoes, 1 ms TE and a four-step phase cycle. A 15 second pre-delay was included prior to every excitation, to ensure the magnetization preparation began from thermal equilibrium. Also, every data set included a CPMG acquired directly from thermal equilibrium, from which all other echo-trains could be subtracted to yield only transverse magnetization decays with non-negative component amplitudes (5). This is important because it allows NNLS processing algorithms to be used to fit $T_2$ spectra from IR- (or DIR-) prepared CPMG data (6).

## RESULTS/DISCUSSION

IR-CPMG data revealed three $T_1$-$T_2$ components with relaxation times ($T_1$, $T_2$) of 1050 ms, 17 ms; 1560 ms, 60 ms; and 1870 ms, 170 ms, and respective signal fractions of 0.21, 0.48, and 0.31, which are consistent with previous studies (3, 4). The second study demonstrated that optimal $\tau_{IR}$ values required to null each of the three $T_2$ components corresponded to $T_1$ values of 876 ± 30 ms, 1540 ± 30 ms, and 2023 ± 80 ms. Differences between these values and those found from the $T_1$-$T_2$ spectra in the first study may be due to processing differences or reflect effects of some inter-compartmental water exchange (4). Using these $T_1$ estimates, $\tau_1$ and $\tau_2$ times required to null both of the longer-lived $T_2$ components using DIR were computed to be 2.64 s and 762 ms (7). Optimal nulling, however, was found with slightly lower values of each (2.48 s and 748 ms), which may also reflect effects of inter-compartmental water exchange. At these adjusted $\tau_1$ and $\tau_2$ times resulting transverse signal decays were found to be comprised of > 90 % signal with $T_2$ < 25 ms, making the preparation largely selective for myelin-water. Figure 1 shows three views of typical transverse magnetization decays from equilibrium and following DIR preparation. Note the slight rebound of signal from zero at TE ≈ 60 ms, indicating some residual long-$T_2$ signal, and the overall drop in signal magnitude expected from removing almost all of the long-$T_2$ signal (and some of the myelin component). Fig. 2 shows NNLS-computed $T_2$ spectra computed from the equilibrium decay (blue) and as computed from the subtraction of the DIR-prepared decay from the equilibrium signal (green). These two spectra almost exactly overlap, except in the myelin component range, which is made clear from the difference between the spectra plotted in red.

The data from these studies indicate that nerve water $T_2$-spectra can be selectively filtered using IR-type magnetization preparations, although further method optimization is required.

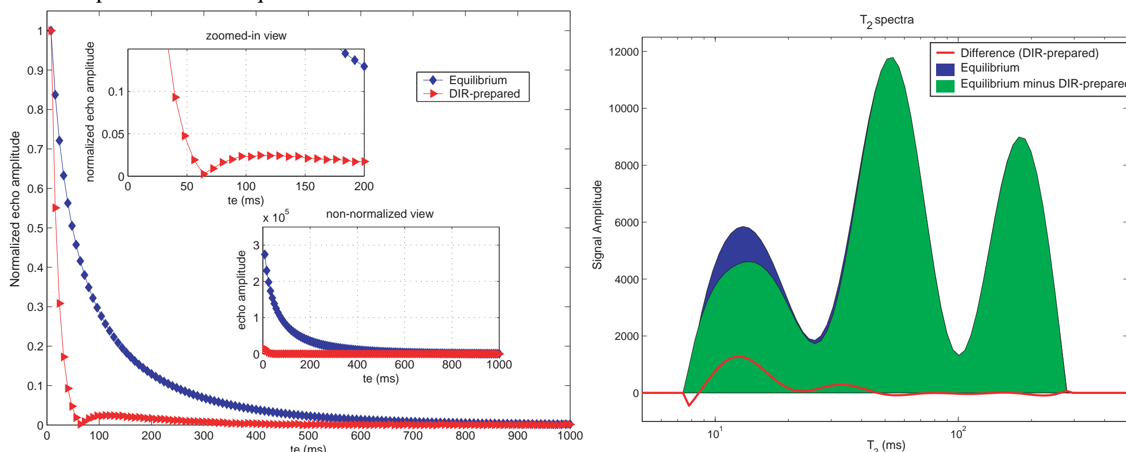


**Fig. 1 (left).** Echo decay curves from equilibrium and DIR-prepared nerve water. Only every eighth echo shown for clarity

**Fig. 2 (right).** $T_2$ spectra computed from equilibrium nerve water decay (blue), and from the difference between the equilibrium decay and the DIR-prepared decay (green). The difference between these spectra (red line) reveals a DIR-prepared signal comprised largely (93.6% in this case) of water with $T_2$ < 25 ms – i.e., myelin water.

**1.** MacKay et al. *Magn Reson Med* 31, 673 (1994). **2.** Harrison et al., *Magn Reson Med* 33, 490 (1995). **3.** Does et al. *Magn Reson Imaging* 16, 1033 (1998). **4.** Does and Gore, *Magn Reson Med* 47, 274 (2002). **5.** Freeman and Hill, *J Chem Phys* 55,1985 (1971). **6.** Whittall and MacKay, J. Magn Reson 84,134 (1989). **7.** Redpath and Smith, *Br. J. Rad*, 67, 1258 (1994).

The authors wish to acknowledge technical support from George Holburn and financial support from the NIH through grant #EB001744.