# MULTI-EXPONENTIAL ANALYSIS OF $T_2$ RELAXATION IN THE HUMAN SPINAL CORD: DIFFERENCES BETWEEN GREY AND WHITE MATTER

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**Introduction:** The ability to produce magnetic resonance images with strong contrast between white matter (WM) and grey matter (GM) in central nervous system (CNS) tissue is crucial for the investigation of a wide range of neurological diseases. In order to determine optimum parameters for contrast differentiation, it is necessary to know both the $T_1$ and $T_2$ relaxation characteristics of each tissue, each of which could have multiple values. Healthy brain and spinal cord (SC) typically exhibit three unique environments in which water protons are found: cerebrospinal fluid (CSF), intra/extra-cellular (I/E) water and myelin water; the different pools of water molecules each have their own spin-spin relaxation rates and cause the overall spin-spin relaxation to become multi-exponential, which gives multiple $T_2$ values [1,2]. Recent literature employing an 8-echo $T_2$ relaxation experiment with a single-exponential fit reported no significant difference in $T_2$ times between WM and GM in the healthy human SC at the C3 level [3]. However, as there is clearly sufficient contrast on conventional $T_2$-weighted images to distinguish between WM and GM, a difference in $T_2$ relaxation time is to be expected. The present study sought to determine differences in $T_2$ relaxation times between WM and GM in the healthy human SC through the implementation of a 32-echo $T_2$ relaxation experiment and multi-exponential fit. In particular, the geometric mean $T_2$ ($GMT_2$; analogous to the amplitude-weighted mean on a logarithmic scale) values were calculated for the I/E water and the entire (global) $T_2$ distribution.

**Methods:** *MR Experiments:* Healthy volunteers (12 subjects, mean age 25y, range 21-30y) were recruited in accordance with the local institutional ethics review board. Subjects were scanned on a 3.0T MRI system (Philips Healthcare, Best, The Netherlands) with a phased array spine coil using only the first four channels. After localizer scans, a multi-echo $T_2$ relaxation experiment was performed using a 3D 32-echo sequence (first echo at 10 ms, echo spacing of 10 ms, TR=1300 ms, six 5 mm thick axial slices perpendicular to the spinal cord, 256×128 matrix, field of view 180 mm×135 mm, single acquisition) [4]. The stack was centered at the C5 vertebra, and oriented perpendicular to the SC.
*Data Analysis:* The 32-echo decay curve for each pixel was decomposed into an unspecified number of exponentials using a regularized non-negative least squares (NNLS) algorithm with 120 input relaxation times spaced logarithmically from 15 ms to 2s [2]. Both $\chi^2$ and solution roughness were minimized such that $\chi^2$ fell between 1.02 and 1.025 times the minimum $\chi^2$ from the NNLS solution. The $GMT_2$ of both the I/E water (defined by the $T_2$ range of 35 – 200ms), and the global distribution (defined by the $T_2$ range of 15ms – 2s) were calculated for each pixel from the $T_2$ distribution output by the NNLS algorithm to generate $GMT_2$ maps. WM and GM regions of interest (ROIs) were drawn on myelin water fraction images (maps of the fraction of the $T_2$ distribution between 15 – 35ms), and the mean $GMT_2$ for each ROI was the average over the ROI on the $GMT_2$ map. Group comparisons were evaluated using a two-tailed Student's t-test, with significance taken as $p \leq 0.05$.

**Results:** The I/E $GMT_2$ was found to be significantly higher in WM than in GM (Table 1); in contrast, the global $GMT_2$ was found to be significantly lower in WM than in GM (Table 1). Figure 1 shows a comparison of the global and I/E $GMT_2$ maps. A significant difference was expected as WM and GM have different compositions and produced visible contrast in $T_2$-weighted images.

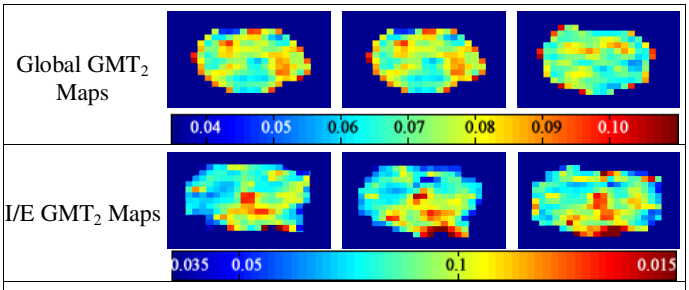


**Figure 1. Examples of global $GMT_2$ maps (top row) and I/E-water $GMT_2$ maps (bottom row) for 3 slices at the C4 level from a healthy subject. Images are on the same physical scale. Each colour bar indicates the scale (in seconds) of the maps above it.**

**Table 1: Geometric Mean $T_2$ ($GMT_2$) in Healthy Adults**
(mean ± standard deviation)

| | GM $GMT_2$ (ms) | WM $GMT_2$ (ms) | Significance b/w GM & WM |
|---|---|---|---|
| **Global distribution** ($T_2$ from 15ms-2s) | 79 ± 8 | 71 ± 16 | **$p < 0.001$** |
| **I/E peak** ($T_2$ from 35-200 ms) | 80 ± 8 | 99 ± 9 | **$p < 0.001$** |

**Conclusions:** This study indicates for the first time that there is a significant difference between WM and GM for both the global and intra/extra-cellular $GMT_2$ in human spinal cord. These differences could help to determine parameters for better contrast in $T_2$-weighted images and to investigate pathology in the spinal cord, such as edema and inflammation. Finally, these results confirm that multi-exponential analysis is a more sensitive method than single-exponential fitting for analysis of $T_2$ relaxation measurements in spinal cord tissue.

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**References:** 1. MacKay, A., *et al. MRM*, 31, 673-677 (1994). 2. Whittall, K.P., *et al. MRM*, 37, 34-43 (1997). 3. Smith, S., *et al. MRM*, 60, 213-219 (2008). 4. Mädler, B. *ISMRM*. 2006:2112