Long T₂ water in multiple sclerosis: What else can we learn from multi-echo T₂ relaxation?

Introduction

Magnetic resonance (MR) T₂ relaxation measurements in vivo can provide specific information about the pathological changes that occur in the brains of people with multiple sclerosis (MS). Multi-echo T₂ relaxation measurements in healthy human brain can generally separate the MR visible proton signal into three components: (1) a very long T₂ component (> 2 s) attributed to CSF, (2) an intermediate T₂ component (~80 ms) attributed to intra/extracellular water and (3) a short T₂ component (~20 ms) assigned to water trapped between myelin bilayers (myelin water) [12, 21].

Such multi-echo experiments have gained in popularity in recent years and have been used extensively to characterise myelin water, geometric mean T₂ and water content in both healthy and diseased white matter [1, 5, 8, 9, 13, 14, 17, 19, 21–23]. Previous T₂ relaxation work in MS has shown abnormalities in brain water content (WC), higher T₂, reduced magnetisation transfer ratio (MTR) and decreased myelin water fraction (MWF) than lesions without a Long-T₂ signal. Those subjects with Long-T₂ lesions had a significantly longer disease duration than subjects without this lesion subtype. A strong correlation was observed between T₁ and Long-T₂ fraction, while a slightly weaker relationship was found for GMT₂, MTR and MWF with Long-T₂ fraction. A potential source of the Long-T₂ signal is an increase in extracellular water. This study supports the usefulness of increasing the data acquisition window of the multi-echo T₂ relaxation sequence to better characterise the T₂ decay in MS.

Abstract

Multi-echo T₂ measurements are invaluable in studying brain pathology in multiple sclerosis (MS). In addition to information about myelin water and total water content, the T₂ distribution has the potential to detect additional water reservoirs arising from other sources such as inflammation or edema. The purpose of this study was to better define the T₂ distribution in MS lesions and normal appearing white matter (NAWM) with particular emphasis on the characterisation of longer T₂ components. Magnetisation transfer (MT), T₁ and 48-echo T₂ relaxation data were acquired in 20 MS subjects and regions of interest were drawn in lesions and NAWM. Twenty-seven out of 107 lesions exhibited signal with a markedly prolonged T₂ (200–800 ms). Lesions with a Long-T₂ signal also exhibited a longer geometric mean T₂ (GMT₂), increased water content (WC), higher T₁, reduced magnetisation transfer ratio (MTR) and decreased myelin water fraction (MWF) than lesions without a Long-T₂ signal. Those subjects with Long-T₂ lesions had a significantly longer disease duration than subjects without this lesion subtype. A strong correlation was observed between T₁ and Long-T₂ fraction, while a slightly weaker relationship was found for GMT₂, MTR and MWF with Long-T₂ fraction. A potential source of the Long-T₂ signal is an increase in extracellular water. This study supports the usefulness of increasing the data acquisition window of the multi-echo T₂ relaxation sequence to better characterise the T₂ decay in MS.

Keywords multiple sclerosis · T₂ relaxation · Long T₂ water · myelin water · brain · MTR

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Cornelia Laule
Irene M. Vavasour
Shannon H. Kolind
Anthony L. Traboulsee
G. R. Wayne Moore
David K. B. Li
Alex L. MacKay

Magnetic resonance (MR) T₂ relaxation measurements in vivo can provide specific information about the pathological changes that occur in the brains of people with multiple sclerosis (MS). Multi-echo T₂ relaxation measurements in healthy human brain can generally separate the MR visible proton signal into three components: (1) a very long T₂ component (> 2 s) attributed to CSF, (2) an intermediate T₂ component (~80 ms) attributed to intra/extracellular water and (3) a short T₂ component (~20 ms) assigned to water trapped between myelin bilayers (myelin water) [12, 21].
Careful multi-echo measurement and analysis of the $T_2$ decay curve has the potential to identify other water reservoirs occurring in white matter pathology such as edema or inflammation. Most recent $T_2$ relaxation experiments in vivo have measured $T_2$ decay curves out to only approximately 300 ms [9, 13, 17, 18, 23]. This methodology is sufficient for accurate quantification of the very short myelin water signal (< 50 ms), where the majority of research efforts have been focused. However, as is demonstrated in Fig. 1, the myelin water pool is not the only component to undergo changes in the presence of white matter pathology. An increase in the geometric mean $T_2$ (GMT2) is often observed in the intermediate water pool in lesions and sometimes NAWM, as is a general broadening of this peak [22]. However, in order to accurately characterize the $T_2$ signal from any intermediate components, one must substantially increase the data collection window. Fig. 2 demonstrates what signal remains for an MS lesion and an area of NAWM after typical 32 echo data collection (TE = 10 ms) is completed.

Several previous studies using both multi-echo $T_2$ relaxation [1, 8, 14] and spectroscopy [6] reported the presence of a longer $T_2$ component in MS lesions. One study at 1.5T investigated a group of 10 MS subjects with known acute MS plaques using a 32 echo multiple spin echo sequence (TE = 30 ms, TR = 4 s) [8]. The $T_2$ relaxation process was a monoexponential function in the acute plaques (average $T_2 = 182$ ms), when measured within 20 days from onset of symptoms. After an average of 78 days, however, the $T_2$ relaxation process clearly became biexponential in all but two patients with an average faster relaxing $T_2$ component of 93 ms and an average slower $T_2$ component of 441 ms. Later some of the relaxation curves reverted to monoexponentiality [8]. Previous work at 0.15T examined a group of 7 MS subjects and controls using a modified CPMG experiment (TE = 6 ms, 128 echoes) and employed a biexponential method of $T_2$ decay analysis [1, 14]. While the $T_2$ relaxation processes were found to be monoexponential in white matter, the $T_2$ relaxation times of NAWM in MS subjects was significantly longer than in controls. However, the $T_2$ decay curves of MS lesions were found in most cases to fit a biexponential function characterised by both a shorter (~82 ms) and a longer $T_2$ component, with the long $T_2$ relaxation times covering a wide range (150–560 ms) [1, 14]. More recently, a study, using 7 TE times ranging from 30 ms to 2 s and a biexponential model, also demonstrated that all acute MS lesions from 8 subjects exhibited two $T_2$ components: one water pool with an average $T_2$ of 87.9 ms and a second component with a longer $T_2$ (average $T_2 = 288$ ms) attributed to extracellular water [6].

To better define the intermediate and long $T_2$ components, important for the characterisation of abnormal white matter, the total data acquisition window of our multi-echo $T_2$ relaxation sequence was lengthened from 320 ms to 1.120 s [10, 15]. The purpose of this study was to describe what, if any, specific long $T_2$ related abnormalities occur in the white matter of subjects with MS and how those abnormalities relate to changes in $T_1$, geometric mean $T_2$, water content, myelin water fraction and magnetisation transfer ratio.