T_2 Determination of the J-coupled Methyl Protons of Tibial Bone Marrow Lipids at 3 T

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Introduction: Proton magnetic resonance spectroscopy measurements of lipids have been shown to be relevant in the study of a number of diseases. Lipid quantification is often based on the 1.3 ppm resonance arising from the methylene (CH_2) chain because of its high signal intensity; however, the peak at 0.9 ppm from the terminal methyl (CH_3) group also contributes valuable information. It has been reported that the CH_2/CH_3 lipid ratio can distinguish between metastases and glioblastomas [1] and can be a measure of response to drug treatment [2]. Accurate quantification of the CH_2/CH_3 ratio requires reliable estimates of T_2 constants. Previous T_2 measurements of lipid peaks by PRESS or STEAM did not correct for J-coupling interactions which are exhibited by most lipid protons. It has been shown that whereas the CH_2 resonance decays monoexponentially as a function of TE (echo time), the CH_3 resonance does not, particularly in response to PRESS [3]. The scalar coupling between the CH_3 protons and the neighbouring CH_2 protons causes the signal from the methyl protons to fluctuate with varying TE making it difficult to determine a representative T_2 for them. The objective of this work is to minimize the effect of J-coupling on T_2 estimates of lipid methyl protons by rewinding their J-coupling evolution in the voxel of interest. The rewinding is achieved by exploiting the chemical shift displacement effect and employing a PRESS sequence whose refocusing pulses have a bandwidth less than the chemical shift difference between the methyl and methylene protons. The method, applicable to spins solely involved in weak coupling interactions, rewinds the J-coupling evolution independently of TE, rendering a decay curve that can be described monoexponentially. The feasibility of the technique was demonstrated *in-vivo* on tibial bone marrow lipids of healthy volunteers.

Methods: All experiments were carried out with a 3 T Philips Intera scanner. A body coil was employed for transmission and a surface coil was used for reception. The scalar coupling constant (J) between the methyl and methylene lipid peaks is ≈ 6.9 Hz [4] and at 3 T, the chemical shift difference (δ) is about 51 Hz, yielding a J/δ of ≈ 0.13, which implies that the spin system is on the threshold of being weakly coupled. Two PRESS sequences were used; in one, 565 Hz bandwidth refocusing pulses (3.2 ms duration) were employed, while in the other the refocusing pulses were replaced by ones with a small bandwidth of 50 Hz (36 ms duration). The frequency of all pulses was set to 0.9 ppm and water suppression was unnecessary. Spectra were acquired from four volunteers in 16 averages from an 8×8×8 mm^3 voxel located in the tibial bone marrow. The data was collected as 2048 complex points sampled at 2000 Hz, and the repetition time was set to 3 s. The sequence was preceded by an outer volume suppression module to minimize signal from outside the volume of interest. To observe the signal modulations caused by scalar coupling twenty four spectra were acquired at TEs ranging from 30 to 300 ms with the regular bandwidth PRESS sequence. For T_2 determination spectra were acquired at five TEs, namely, 100 ms, 140 ms, 180 ms, 240 ms, and 320 ms with both variations of the PRESS sequence. The T_2 of the methylene and methyl protons were determined from the spectra acquired with the regular bandwidth and the narrow bandwidth PRESS sequences, respectively. The resonance areas were plotted as a function of TE and the decay curves were linearized by taking their natural logarithm. The reciprocal of the slope yielded a value for T_2.

Results: Figure 1 displays the signal amplitudes of the CH_2 and CH_3 peaks (from the tibial bone marrow of one of the volunteers) as a function of TE in response to the regular PRESS sequence. The CH_2 decay can be well described by a monoexponential function (linearizing the data yielded a straight line with $R^2 = 0.999$), but the CH_2 signal does not montonically decrease due to J-coupling modulations. Applying the narrow bandwidth PRESS sequence rewinds the J-coupling evolution of the methyl protons and increases their signal as shown in Fig. 2; any methylene signal in the right hand spectra is from outside the voxel of interest. The normalized areas of the methyl peaks in response to both PRESS sequences are plotted in Fig. 3(a). J-modulations are removed with the narrow bandwidth PRESS sequence and the resultant decay curve can be better described by a monoexponential function. Linearizing the curve provides a straight line ($R^2 = 0.973$) and yields a T_2 of ≈ 156 ms for the CH_3 protons. Figure 3(b) shows a plot of the methylene peak areas acquired with the regular PRESS sequence. Linearization gave a T_2 of about 93 ms for the CH_2 protons. Similar results were obtained from the three other volunteers. The mean T_2 for the methyl and methylene protons from all the volunteers was 157 ms (standard deviation of 5.1 ms), and 93 ms (standard deviation of 1.6 ms), respectively.

Conclusion: In this work we have shown how the T_2 of lipid methyl protons can be determined with minimal contributions from J-coupling evolutions. The method is unlikely to be feasible at field strengths below 3 T where the methyl and methylene protons are less weakly coupled (i.e. they are strongly coupled).

References: 1. K.S. Opstad et al., *J. Magn. Reson. Imag.,* **20**, 187, 2004. 2. E.J. Delikatny et al., *Cancer Res.,* **62**, 1394, 2002. 3. G. Hamilton et al., *J. Magn. Reson. Imag.*, **30**, 145, 2009. 4. M. Oostendorp et al., *Clin. Chem.,* **52**, 1395, 2006.

Figures

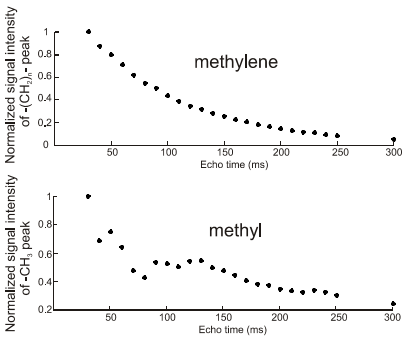

Figure 1: Normalized amplitudes of the CH_2 and CH_3 peaks from the tibial bone marrow of a volunteer in response to the regular PRESS sequence. Spectra were acquired with 24 different TEs.

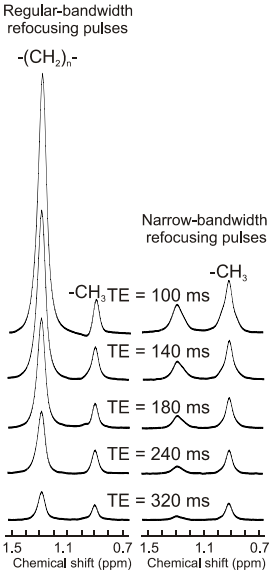

Figure 2: Bone marrow spectra acquired with the two versions of the PRESS sequence at five different TEs.

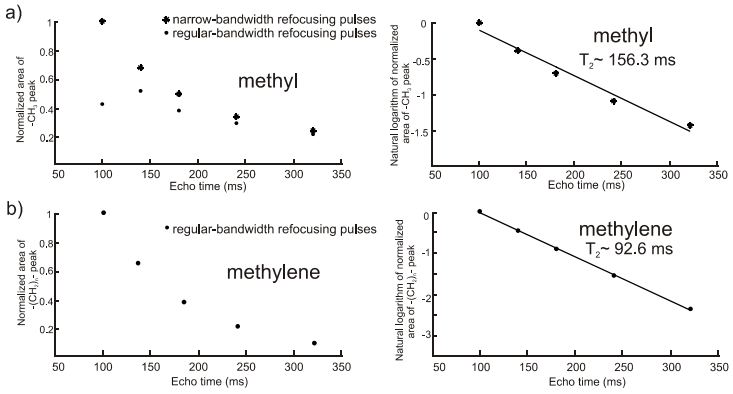

Figure 2: Data corresponds to the spectra shown in Fig. 2. Normalized areas of the a) CH_3 resonances acquired with both PRESS sequences. It is clear that the signal increases when employing the narrow bandwidth refocusing pulses and J-modulations are minimized rendering a decay curve that can be characterized monoexponentially. Taking the natural logarithm of the curve yields a straight line from which a T_2 of 156 ms was calculated. The methylene peak areas obtained with the regular PRESS sequence are plotted in (b). The curve was linearized and the T_2 was calculated to be about 93 ms from the slope of the straight line.