Performance of Bi-Component T2* Fitting of Bound and Pore Bone Water Fractions is Dependent on Field Strength

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Introduction: ^{1}H NMR signal in bone arises from three pools: free water in pores, motionally restricted water bound to matrix, and immobilized ^{1}H nuclei in the collagen molecules themselves. Discrimination between these pools is vital for quantification of bone matrix density via bound water, and for surrogate measures of porosity via pore water. Fortunately, these pools are distinguishable based on T_2 [1]. The two main approaches to differentiation are T_2-selective magnetization preparation [2] and bi-exponential T_2* fitting [3]. As shown in Figure 1, however, T_2* of pore water is shortened by strong internal field gradients arising from the difference in susceptibility between water and bone tissue ($\Delta\chi$ ~ 2.5 ppm SI), complicating separation of bound and pore water, particularly at higher field strengths. An example T_2-T_2* 2D spectrum also illustrating this effect at 9.4T is shown in Fig. 2. To assess the viability of T_2* bi-component fitting as a method for quantifying bound and pore water fractions, we have scanned a set of human cortical bone specimens at 4 field strengths, and validated bi-exponential fitting of the resulting FIDs against μCT porosity and gravimetrically determined matrix density.

Methods:

Specimens: 15 cylindrical samples of human cortical bone (8F, 27-97 y; 7M, 37-93 y) were cut from tibial specimens. The long axis of the cylinder was perpendicular to the anatomic axis of the bone, so this axis can be oriented parallel to B_0 in a solenoidal RF coil.

NMR: 1.5T, 3T, and 7T scanning was performed using custom ^{1}H-free solenoidal RF coils (10 mm diameter, 25 mm length) in whole-body human MRI scanners (Siemens, Erlangen, Germany). Each bone was scanned using a saturation-recovery (SR) FID pulse sequence [5] of the form [90°-SPOIL]$_{12}$-T_{SR}-90°-ACQ. RF pulse duration was 100 μs for saturation pulses and 20 μs for excitation pulses, and readout bandwidth was 250 kHz. 12 T_{SR}s were arrayed exponentially from 3 ms to 6 s. 9.4T scanning was performed on an NMR spectrometer (Bruker, Billerica, MA) using a 5-mm BBI probe with a 1-axis gradient and an SR-FID pulse sequence. 90° pulses were 19-20 μs in duration, and all other parameters were identical to those used at lower fields.

Analysis: Reconstruction and fitting was performed in Matlab (Mathworks, Natick, MA). For T_2* bi-exponential fitting, a sum of two decaying exponentials, $f(t) = ae^{\frac{-t}{b}} + ce^{\frac{-t}{d}} + e$, was fitted to the FID after the longest T_{SR} = 6 s by non-linear least squares. Short-T_2* fraction and relaxation time are given by a/(a+c) and b, respectively; long-T_2* parameters are c/(a+c) and d. Two-dimensional T_1-T_2* bi-component fitting, which should improve accuracy [6], was also performed by fitting $f(T_{SR}, t) = g(1 - e^{\frac{-T_{SR}}{h}})e^{\frac{-t}{k}} + m(1 - e^{\frac{-T_{SR}}{n}})e^{\frac{-t}{p}} + q$ to SR-FID data arrays. Pool fractions are given by g/(g+m) and m/(g+m), T_1s by h and n, and T_2*s by k and p, for short- and long-T_2* fractions, respectively. For validation, bones were scanned by μCT (Scanco, Brüttisellen, Switzerland) at 18.5-μm isotropic resolution, and total and pore volumes were calculated. The fully hydrated samples were then weighed, dried at 105° C for 110 h to remove all bound and pore water, re-weighed, ashed at 600° C for 30 h to burn off all organic matrix, and weighed again [7]. Matrix density was quantified as the difference between dry and ash masses divided by total volume.

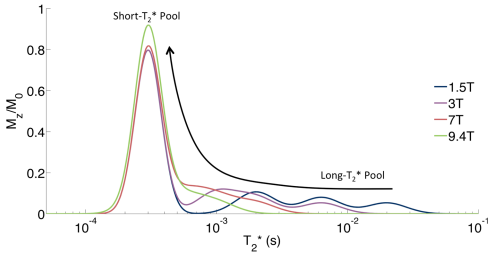

Fig. 1: Schematic T_2* spectra of equilibrium ^{1}H signal at multiple field strengths, showing the shift of pore water signal from the long-T_2* pool to the short-T_2* pool. This shortening of pore water T_2* due to stronger internal magnetic field gradients within pores, complicates discrimination of bound and pore water based on T_2*.

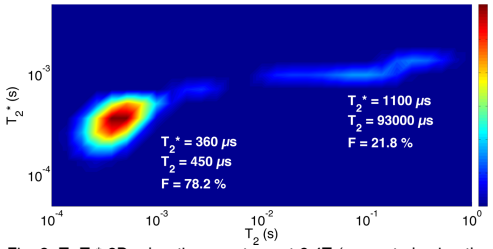

Fig. 2: T_2-T_2* 2D relaxation spectrum at 9.4T (generated using the MERA software package [4]) of a bone specimen taken from a 37 y/o male donor. Two pools, corresponding to bound and pore water, are clearly separated in the T_2 dimension, but much less so in T_2*. This effect is more severe at higher B_0.

	Short		Long	
	Fraction (%)	T_2* (μs)	Fraction (%)	T_2* (μs)
1.5T	69.6±12.7	400±120	30.4±12.7	4100±1200
3T	68.1±21.9	390±120	32.0±21.9	4400±8600
7T	82.3±14.0	370±80	17.7±14.0	1300±420
9.4T	55.1±28.7	300±150	44.9±28.7	890±530

Table 1: Fitted T_2* (by 1D T_2* bi-exponential fitting of FID data) and T_2 (by 2D T_1-T_2 bi-exponential fitting of SR-CPMG data) pool sizes and relaxation times.

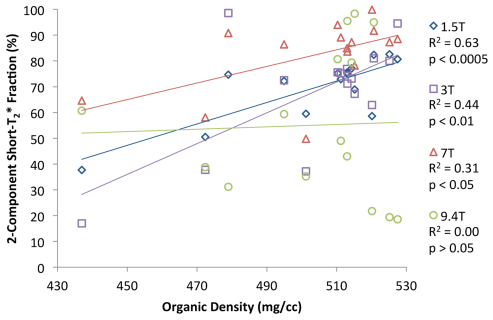

Fig. 3: Scatter plot and correlations of the short-T_2* signal fraction obtained by bi-exponential fitting of FIDs at four B_0 field strengths versus the organic matrix density measured by gravimetry and μCT. Performance of T_2* bi-exponential fitting is dramatically reduced as B_0 increases.

Results: Average FID pool fractions and relaxation times are given in Table 1, and correlations of short-T_2* fractions at four field strengths with organic matrix density calculated from gravimetry are shown in Fig. 3. At 1.5T, short-T_2* fraction is strongly correlated with matrix density (R^2 = 0.63). At 3T, less than 50% of the variance in short-T_2* fraction is explained by matrix density (R^2 = 0.44). The correlation is weaker still at 7T (R^2 = 0.31), and non-existent at 9.4T. Correlations of short-T_2* fractions with porosity are similar to those with matrix density (R^2 = 0.70, 0.50, 0.40, 0.02 at 1.5, 3, 7, and 9.4 T, respectively). Addition of the T_1 dimension yielded marginally stronger correlations with matrix density at low B_0 (R^2 = 0.80, 0.61, 0.16, 0.02) and porosity (R^2 = 0.84, 0.76, 0.25, 0.10).

Discussion and Conclusions: Our results indicate that T_2* bi-exponential fitting of FIDs may be a suitable method for quantifying bound and pore water fractions at 1.5T, but may fail at higher field strengths. At 3T and higher, oscillations appear in the magnitude FID data, presumably due to the contribution of fat [8], which complicate fitting of a bi-exponential function. If FIDs exhibiting these oscillations are identified and excluded (5 out of 15, predominantly elderly females), the short-T_2* fractions derived from the remaining FIDs become strongly correlated with matrix density at 1.5T (R^2 = 0.83) and 3T (R^2 = 0.78), and moderately at 7T (R^2 = 0.61), though a subject-dependent 33% failure rate, disproportionately affecting the elderly females most likely to be studied with this method, may not be acceptable. In practice, this susceptibility-induced shortening of T_2* and oscillations due to off-resonance signal contribution may pose significant challenges to accurate quantification of bound and pore water fractions via bi-component T_2* fitting.

References: [1] Horch RA. MRM 2010;64:680-7. [2] Horch RA. MRM 2012:68;1774-84. [3] Nyman JS. Bone 2008;42(1):193-9. [4] Does M. http://www.vuiis.vanderbilt.edu/ ~doesmd/MERA/MERA_Toolbox.html. [5] Seifert AC. NMR Biomed 2013;26:1158-66. [6] Celik H. JMR 2013;236:134-9. [7] Anumula S. Bone 2008;42(2):405-13. [8] Diaz E. NMR Biomed 2011;25:161-8.

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