Distinguishing Cortical Bone Bound and Pore Water by T2* at Multiple Magnetic Field Strengths

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Introduction: The ^{1}H NMR signals arising from collagen-bound water and mobile pore water can be clearly differentiated based on their T_2 relaxation times at 4.7T (bound water $T_2 \approx 400$ µs, pore water $T_2 > 1$ ms) [1]. Due to the presence of severe susceptibility-induced field gradients arising from bone tissue-pore water interfaces, the difference in T_2^* between bound and pore water is much more ambiguous, with the T_2^* of mobile water in small pores being decreased to a value close to that of bound water. Du, et al. [2] provide evidence that these bone water fractions can be identified based on T_2^* at 3T, while Horch, et al., [1] have found that such differentiation is not possible at 4.7T. Because susceptibility-induced field inhomogeneities are more severe at high field strength, there may be a limit above which differentiation of bound and pore water based on T_2^* is not possible. To assess the separability of bone water fractions with respect to field strength, we have generated and examined T_2^* relaxation spectra of lamb tibial cortical bone specimens at 1.5T, 3T, and 7T.

Figure 1: Saturation recovery pulse sequence

Methods:

Specimens: Three cylindrical pieces of cortical bone (10mm length, 4mm diameter) were cut from the tibial midshaft of lamb shanks obtained fresh from a butcher. Size was limited by a 5 mm NMR tube's inner diameter and by the RF coil's homogeneous region. All data were acquired at room temperature with the osteonal axis parallel to the main magnetic field.

Hardware: **1.5T**: Siemens Magnetom whole-body MRI; **3T**: Siemens TIM Trio whole-body MRI; **7T**: Siemens Magnetom whole-body MRI; **RF coils**: custom-made transmit/receive solenoids with interleaved dual-conductor windings and Teflon support structure, constructed using no ^{1}H-containing materials to avoid contamination of bone ^{1}H NMR signal.

NMR Measurements: A two-dimensional saturation-recovery data set was collected from each specimen. As diagrammed in Figure 1, signal was saturated by a series of six rectangular 90° RF pulses ($t_{RF} \leq 20$ µs), each followed by a spoiler gradient ($t_{spoil} = 2000$ µs, $G = 20$ mT/m). After a saturation-recovery time (t_{SR}) following the final saturation RF pulse, a 90° excitation RF pulse was applied and, following a receiver dead time (44 µs at 1.5T, 160 µs at 3T, 50 µs at 7T), free induction decay (FID) signal was acquired ($N_{pts} = 4096$, dwell time = 4 µs). The 11 saturation recovery times were logarithmically spaced between 3 ms and 6 s.

Figure 2: 1-D T_2^* relaxation spectrum of one lamb tibial cortical bone specimen at multiple magnetic fields

Data Processing: The FID acquired at the longest saturation recovery time was fitted to a sum of 512 decaying exponential functions, with time constants logarithmically spaced between 40 µs and 30 ms, using a non-negative least squares approach and subject to a minimum curvature constraint, producing a T_2^* relaxation spectrum. This method does not require a priori knowledge of the number of relaxation components [3]. The saturation-recovery dataset was also reduced by singular-value decomposition and fitted to a two-dimensional array of 128x128 logarithmically-spaced exponential decay (T_2^*-dimension, 40 µs to 30 ms) and recovery (T_1-dimension, 2 ms to 6 s) functions, also using non-negative least squares and minimum curvature regularization, to produce a T_1-T_2^* relaxation spectrum. All exponential fitting and relaxation spectrum generation were done using the Multi-Exponential Relaxation Analysis v1.0 MATLAB toolbox [4].

Results: 1-D T_2^* relaxation spectra of a single lamb cortical bone at three field strengths is shown in Figure 2, with the expected ranges of bound and pore water T_2^*s indicated. The peak visible at 45 µs at 1.5T arises from within the transmit/receive interface box and appears when no sample is present in the coil. The T_1 and T_2^* relaxation times and relative sizes (excluding the spurious peak at 1.5T) of each distinguishable pool, averaged across all samples, are shown in Table 1, and are assigned to bound (blue) or pore (red), where possible. An example 2-D T_1-T_2^* relaxation spectrum for a single bone at 1.5T is shown in Figure 3, with expected bound and pore water regions indicated. The extremely short-T_2^* component contributed by the transmit/receive hardware is visible but excluded from quantification.

B_0		Pool 1	Pool 2	Pool 3	Pool 4
1.5 T	Fraction (%)	65.8 ± 3.8	2.7 ± 1.6	19.4 ± 1.1	12.0 ± 5.7
	T_1 (ms)	120 ± 0	11.1 ± 2.8	173 ± 15	357 ± 6
	T_2^* (µs)	297 ± 12	337 ± 47	1233 ± 208	3467 ± 404
3 T	Fraction (%)	27.8 ± 2.5	1.9 ± 0.2	58.6 ± 1.5	12.3 ± 3.6
	T_1 (ms)	150 ± 20	14.5 ± 2.1	263 ± 6	573 ± 162
	T_2^* (µs)	190 ± 10	230 ± 14	517 ± 60	2100 ± 346
7 T	Fraction (%)	96.4 ± 0.2	---	---	3.7 ± 0.1
	T_1 (ms)	537 ± 31	---	---	1233 ± 153
	$T2^*$ (µs)	313 ± 32	---	---	1433 ± 252

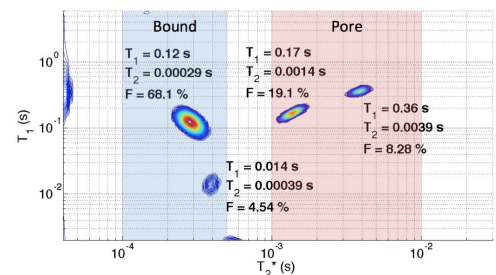Table 1: Identifiable 2-D water relaxation components

Figure 3: 2-D T_1-T_2^* relaxation spectrum of one lamb tibial cortical bone specimen at 1.5T

Discussion and Conclusions: According to previous studies, approximately 60-80% of bulk bone water is bound to collagen in bovine [5] and human [6] cortical bone. These proportions are apparent in the identified relaxation components at 1.5T, with pools 1 and 2 being assigned to bound water and pools 3 and 4 to pore water. At 3T, three components are visible, but the identity of pool 3 is unclear and no combination of pools conforms to the expected proportions. We postulate that a large portion of pore water exists in regions of susceptibility-induced field inhomogeneity, causing T_2^* to be lowered and to become comparable bound water. At 7T, almost all signal exists in a large peak with T_2^* around 300 µs, and no reliable discrimination based on T_2^* is possible. We therefore conclude that identification of bound and pore water based on T_2^* can reliably be performed at 1.5T, but such discrimination would be problematic at 3T and impossible at 7T.

References: [1] Horch RA, et al., MRM 2010;64(3):680-687. [2] Du J, et al., MRM 2012 Mar;67(3):645-9. [3] English, AE, et al., MRM 1991;22:425-434. [4] Does M, Juttukonda M, and Dortch R, http://www.vuiis.vanderbilt.edu/~doesmd/MERA/MERA_Toolbox.html. [5] Diaz E, et al., NMR in Biomed 2012;25(1):161-168. [6] Ong H, et al., JBMR 2012;doi:10.1002/jbmr.1709.