Correlation of [1]H NMR Characteristics and Mechanical Properties in Human Cortical Bone

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Introduction: Modern Magnetic Resonance Imaging methods such as ultra-short echo time (uTE) imaging are capable of imaging proton signals from human cortical bone [1], which shows much promise for non-invasively assessing bone health in ways that current X-ray based methods cannot provide. Since human cortical bone consists of numerous proton and/or water-bearing physiological sites such as collagen, lipids, minerals, and nanoscale-to-macroscale porosity, it is expected that the bone proton signal exhibits a distribution of transverse relaxation (T_2) components [2]. In a previous NMR characterization of human cortical bone specimens [3], it was determined that T_2 components ranging from 50μs to 1s can be attributed to collagen, collagen-bound water, lipids, and mobile water in porous spaces. Herein, we employ this characterization in conjunction with mechanical testing to probe the ability of T_2 relaxometry to predict cortical bone mechanical properties. Sensitivity of T_2 features to mechanical properties in bone would provide a contrast mechanism that many MRI protocols could exploit as a new means for assessing bone health.

Methods: Human cortical bone specimens were harvested from the mid-shaft of seventeen healthy male and female donor femurs (5 young donors, 26.2 ± 5.4 Y.O.; 8 middle-age donors, 52.8 ± 4.2 Y.O.; and 4 old donors, 88.8 ± 7.1 Y.O.). Specimens were machined into 5x2x60mm beams to remove periosteum and endosteum layers, yielding uniform cortical bone. The beams were sectioned into a central 40mm piece for destructive mechanical testing and two flanking 10mm end pieces for NMR and μCT analysis. Mechanical testing was performed under 3-point bending with a 35mm span to determine flexural modulus, yield stress (0.2% linear offset), ultimate stress, and toughness. NMR measurements were performed at 4.7T in a low-proton loop-gap coil with negligible background signal. For each specimen, a CPMG sequence was collected with 100 μs echo spacing, 10000 total echoes, and 90°/180° hard pulses of approximately 7.5/15 μs. CPMG echo magnitudes were fitted with a broad range of decaying exponential functions in a constrained non-negative least-squares sense, producing a so-called T_2 spectrum [4]. A 20μL water marker ($T_2 \approx 3$s) was included with each bone specimen so T_2 spectral components could be quantified in terms of the volume fraction (VF) of bone that an equivalent amount of water would occupy. Finally, μCT images were collected at 6μm resolution, from which apparent bone mineral density (**aBMD**) was derived. All measurements were compared with a Pearson's linear correlation.

Results and Discussion: All human cortical bone specimens exhibited two discrete, sub-millisecond T_2 components and a broad range of T_2 values spanning 1ms-1s. For analysis, these components were grouped into three pools (Fig. 1): a short T_2 pool ($\mathbf{T_{2,A}} \approx 67$μs) of volume fraction $\mathbf{VF_A}$, representing collagen macromolecules; an intermediate T_2 pool ($\mathbf{T_{2,B}} \approx 420$μs, $\mathbf{VF_B}$) consisting of collagen-bound water; and a long T_2 pool ($\mathbf{T_{2,C}} > 1$ms, $\mathbf{VF_C}$) containing a mixture of lipids and free water [3]. The pools' T_2s and volume fractions were compared to μCT and mechanical properties (Table 1); data from a strong correlation set are shown in Figure 2. Interestingly, the pool T_2s had poorer correlations to mechanical data than pool volume fractions. VF_B had the strongest correlation to mechanical properties, indicating that collagen-bound water is beneficial to bone integrity. Surprisingly, VF_B was a better predictor of all bone mechanical properties than aBMD (sensitive only to mineralization), which shows the importance of non-mineralized components to bone strength. VF_C was negatively-correlated to mechanical properties, indicating that stronger bones possess less lipids/mobile (pore-space) water than weaker bones. Importantly, the opposing mechanical correlations of VF_B and VF_C represent competing phenomenon which would confound an MRI-based bone health diagnostic that could not distinguish short- from long-lived T_2 signals.

References: 1) Techawiboonwong, A., et. al. *Radiology* 248(2008): 824-833. 2) Fantazzini, P., et. al. *Magn. Res. Imaging.* 21 (2003): 227–234. 3) Horch, R., et. al. *ISMRM 17th Annual Meeting*, (2009) #1942. 4) Whittall, K., and Mackay, A., *J. Magn. Res.* 84(1989): 134-152.

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Figure 1. Human Cortical Bone T_2 Spectrum and Physiological Origins

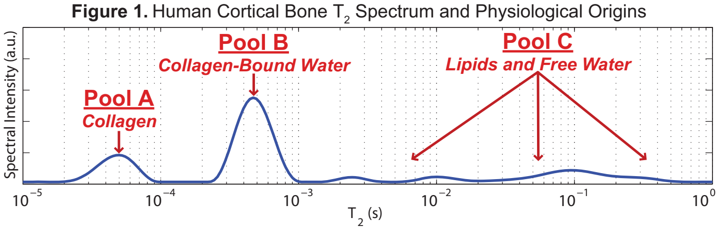
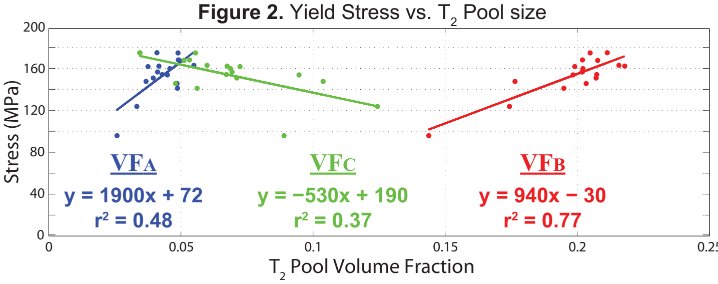


Figure 2. Yield Stress vs. T_2 Pool size



	Age	$T_{2,A}$	$T_{2,B}$	$T_{2,C}$	VF_A	VF_B	VF_C	aBMD
Yield Stress	−	+	+		+	+	−	+
Ultimate Stress	−	+	+		+	+	−	+
Flexural Modulus			+		+	+	−	+
Toughness	−					+		+

Table 1. *Correlation of age, NMR, and μCT to mechanical properties.* Shading indicates Pearson's correlation strength as follows: white for p<0.005, gray for p<0.05, and black for p>0.05 (not significant). Positive/negative correlations are denoted by "+"/"−", respectively. T_2 pool volume fractions were the strongest NMR predictors of mechanical properties, and $\mathbf{VF_B}$ was a stronger predictor of each mechanical property than **aBMD**—a current "gold standard" for assessing bone health.