Relaxometric Characterization of Human Cortical Bone

R. A. Horch[1,2], R. D. Dortch[1,2], J. S. Nyman[3], D. F. Gochberg[2,4], and M. D. Does[1,2]

[1]Biomedical Engineering, Vanderbilt University, Nashville, TN, United States, [2]Vanderbilt University Institute of Imaging Science, Vanderbilt University, Nashville, TN, United States, [3]Orthopaedics & Rehabilitation, Vanderbilt University, Nashville, TN, United States, [4]Radiology and Radiological Sciences, Vanderbilt University, Nashville, TN, United States

Introduction:

Magnetic Resonance Imaging methods such as ultra-short echo time (uTE) imaging are capable of collecting proton signals from human cortical bone [1], which consists of collagen networks (osteoid), mineralized calcium phosphate microcrystals (hydroxyapatite), and porous channels (Haversian canals). In cortical bone, water exists in an ensemble of microenvironments and may be tightly bound to hydroxyapatite surfaces, loosely associated with the collagenous osteoid, or freely diffusing in the Haversian spaces. As such, the proton NMR signal arising from cortical bone may be best characterized by a distribution of relaxation components [2], potentially confounding uTE imaging and other NMR measurements that provide relaxation-based contrast. To this end, both T_1 and T_2 relaxation properties of human cortical bone are characterized herein to quantify multi-exponential relaxation and field dependence.

Methods:

A series of human cortical bone samples were harvested from femurs of healthy male and female donors. The samples were machined in PBS to 5x5x10mm dimensions to remove periosteum and endosteum layers, thus producing uniform cortical bone, which was blotted dry and immersed in Fomblin, a susceptibility-matched fluorocarbon oil with no proton NMR signal. To characterize multi-exponential T_1 and T_2 relaxation components and magnetic field strength dependencies, separate NMR experiments were performed at 0.5, 4.7, 7, and 9.4 T as follows: a CPMG pulse sequence with 100 µs echo spacing and 90°/180° hard pulses of approximately 7.5/15 µs was performed with 4000 echoes to measure T_2 relaxation characteristics; a single hard inversion pulse followed by a recovery period and subsequent CPMG sequence as above (IR-CPMG) provided two-dimensional T_1-T_2 measurements with the recovery period duration varied from 20 ms to 2.5 s; and IR-CPMG sequences with low-power (soft) inversion pulses yielded T_1-T_2 measurements without fully inverting short-lived signals, probing magnetization transfer effects among relaxation components. CPMG echo magnitudes were fitted with a broad range of decaying exponential functions in a non-negative least-squares sense, subject to a minimum energy constraint, which produced a so-called T_2 spectrum. IR-CPMG data was reduced by singular-value decomposition [3] prior to two-dimensional non-negative least squares fitting to a range of decaying exponentials, producing a so-called T_1-T_2 spectrum. All NMR measurements were performed in a custom-machined Teflon "loop-gap" RF coil, which did not contribute fast-relaxing proton signals as would traditional coils constructed from protic engineering plastics.

Results and Discussion:

Human cortical bone exhibited a broad range of transverse relaxation time constants, approximately spanning 100 µs - 500 ms with the majority of T_2 spectral intensity falling below 1ms (Figure 1). Major T_2 spectral features, such as the two dominant components at approximately 100 µs and 500 µs, exhibited minor shifts between 0.5 and 4.7T main field strengths, indicating there is little field dependence in cortical bone transverse relaxation. The T_1-T_2 spectrum obtained from a hard IR-CPMG (Figure 2), in which there is maximum simultaneous inversion of all proton pools, indicates that the shortest-lived T_2 component is best characterized with a T_1 of approximately 20 ms, while the majority of cortical bone water signal originates from proton pools with a T_1 of approximately 500 ms. However, the soft IR-CPMG T_1-T_2 spectrum (Figure 3) exhibits two dominant T_1 components at 10 ms and 500 ms, both with a T_2 of 500 µs. Since the soft-IR preparation (150 µs pulse width) results in a relaxation-weighted inversion, the presence of the 10 ms T_1/500 ms T_2 component in Figure 3 indicates the cortical bone water compartments characterized by 100 µs and 500 µs T_2s are undergoing magnetization transfer. Results from CPMG and IR-CPMG T_1-T_2 characterizations of human cortical bone water at 0.5T and the high fields of 4.7, 7, and 9.4 T will be presented, with emphasis on field-related changes to relaxation rates and apparent magnetization transfer.

References: 1) Techawiboonwong A, Song HK, Leonard MB, Wehrli FW. "Cortical bone water: in vivo quantification with ultrashort echo-time MR imaging." *Radiology* 2008; 248(3):824-833. 2) Fantazzini P, Garavaglia C, Palombarini M, Brown RJS, Giavaresi G, Giardino R. "Analysis of H-1-NMR relaxation time distributions in L1 to L6 rat lumbar vertebrae." *Magnetic resonance Imaging* 2004; 22(5): 689-695. 3) Venkataramanan L., Yi-Qiao Song, Hurlimann M.D. "Solving Fredholm integrals of the first kind with tensor product structure in 2 and 2.5 dimensions." *IEEE Trans. Sig. Process.* 2002; 50(5):1017-1026.

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Figure 1: T_2 Spectrum for Human Cortical Bone

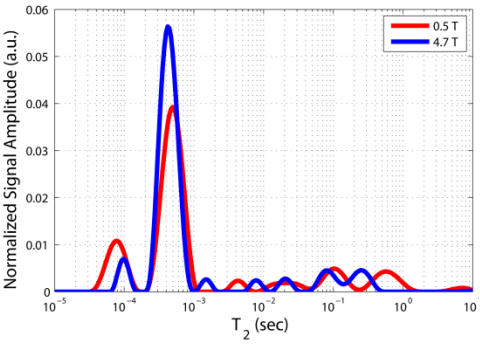

Figure 2: T_1-T_2 Spectrum of Human Cortical Bone at 4.7T, ***hard*** inversion pulse (IR-CPMG)

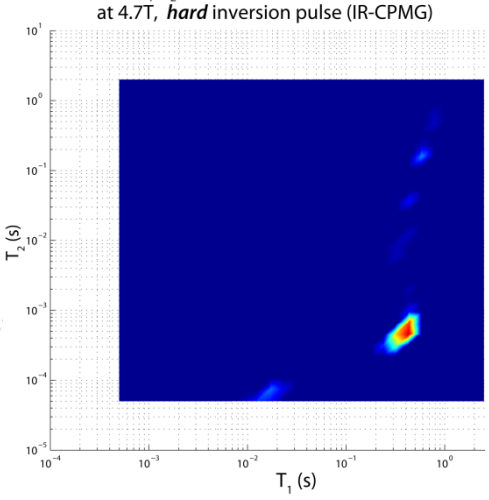

Figure 3: T_1-T_2 Spectrum of Human Cortical Bone at 4.7T, ***soft*** inversion pulse (IR-CPMG)