Cross-relaxation parameter quantification in cortical bone from repeated binomial excitations

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Purpose: Evidence of magnetization transfer (MT) was recently shown in cortical bone between collagen-bound water protons and collagen methylene protons[1]. A quantitative assessment of cross-relaxation parameters is of interest considering the observation of Horch et al.[2] that the amount of collagen-bound water protons (M_0^b) was related to cortical bone mechanical properties. The cross-relaxation parameters were quantified using off-resonance saturation[3]. However, this approach is limited by the high Specific Absorption Rate and the long acquisition time. The purpose of this work was to quantify the cross-relaxation parameters in cortical bone using a scheme easily integrated in an imaging sequence.

Materials and Methods: Femoral bovine cortical bone was obtained from local butcher, 11 transverse sections were cut from the diaphysis over approximately 10 mm thickness. Experiments were run on a home-assembled 4.7 T scanner. Inversion-recovery (IR) was used to follow longitudinal relaxation with 31 inversion times using two pulse widths (pw): 10 µs (TE = 55 µs) and 100 µs (TE = 100 µs), and CPMG to follow transverse relaxation with TE = 0.75 ms at both pw. A third order selective binomial excitation[4] was implemented to saturate the longitudinal magnetization of protons with a specific T_2 called T_{2sel} with a minor perturbation of the long-T_2 proton magnetization. To attain a steady state, the binomial excitation was repeated after a delay (11.2 ms) and for a determined number of excitations (Nbin = 100-1500). A hard 90° RF pulse followed by a 100 µs dead time was applied to measure M_z^a; M_0^a was similarly measured after TR = 15 s. Experiments were simulated with a matrix approach[5] for a two-pool model using the usual cross-relaxation parameters[6] with home-developed software written in Matlab (MathWorks, Natick, MA).

Results: At pw = 10 µs, IR data could be described as a monoexponential decay, whereas at pw = 100 µs, the IR data were compatible with a biexponential decay. This behavior was comparable for all examined samples. A biexponential decay for the long pw experiment is in agreement with two characteristic times[7] describing the return to equilibrium of M_z^a with the two-pool model. Data at both pw could be reproduced by simulation of the two-pool model. The model parameters were initialized as follows: $T_1^a = T_1^b$ = time of the monoexponential fit of IR data at pw = 10 µs, $T_2^a = T_2^*$, then T_2^b, R and M_0^b were searched to minimize the Root Mean Square Error (RMSE) between simulation and experimental data. CPMG data were analyzed as a decreasing tri-exponential function and were not sensitive to MT. Indeed the mean fast T_2 component was equal to 0.466 ms (±0.07 ms) at pw = 10 µs and to 0.488 ms (±0.1 ms) at pw = 100 µs, with similar relative fraction (≈ 90%). To simulate the repeated binomial experiment, T_1^a was initialized from IR monoexponential decay at pw = 10 µs and T_1^b was set = T_1^a. Four parameters (T_2^a, T_2^b, M_0^b and R) were set to minimize RMSE between experiments and simulations. The saturation data in cortical bone samples were systematically much lower than the one-pool simulation (Fig. 1), and the two-pool model with $T_1^a = T_1^b = 0.4$ s, $T_2^a = 1.9$ ms, $T_2^b = 13$ µs, $M_0^b = 0.24$, $R = 72$ s^{-1} was in a fair agreement with data. Increasing T_{2sel} caused a decrease of M_z^a/M_0^a mainly due to direct saturation. Therefore the largest difference between the one-pool simulation and the data could be found for the shortest T_{2sel} (9 µs) which was also the closest value to T_2^b. Fig. 2A shows as iso-contour lines RMSE between data of Fig. 1 and simulations for different M_0^b and R values, on a two-pool system. All iso-contour lines tended to be vertical for $R > 100$ s^{-1} therefore $R > 100$ s^{-1} cannot be accurately predicted. For lower R the iso-contour lines generally looked like hyperboles. Accuracy on T_2^b and T_2^a was better (Fig. 2B). Table 1 shows cross-relaxation parameters of cortical bone samples deduced from IR and repeated binomial excitation experiments.

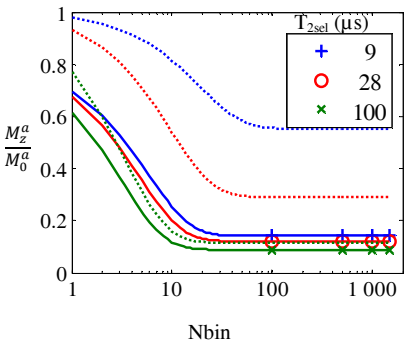

Fig. 1: Saturation in a cortical bone sample (symbols), one-pool simulation (dotted lines) and two-pool simulation (lines)

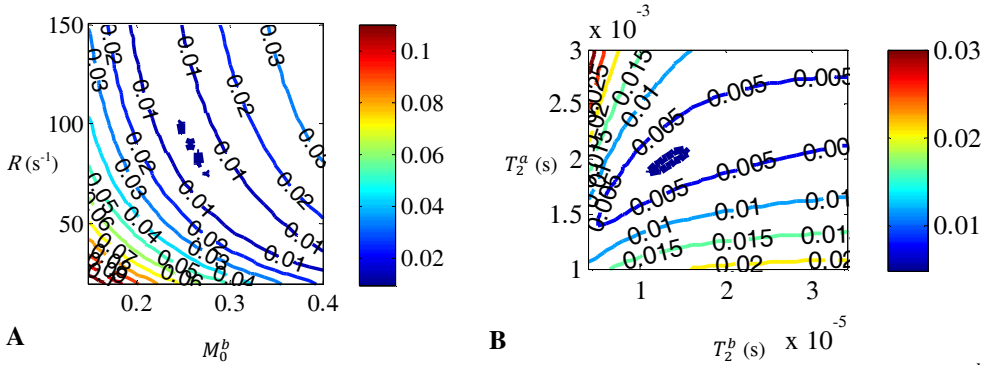

Fig. 2: RMSE for the cortical bone sample as iso-contour lines around optimal values for R and M_0^b (A) and T_2^a and T_2^b (B) minimizing RMSE (RMSE$_{min}$= 0.002)

Table 1: Cross-relaxation parameters (mean±std.) of the 11 investigated cortical bone samples from IR and repeated binomial excitation experiments

	$T_1^a = T_1^b$ (s)	T_2^a (ms)	T_2^b (µs)	M_0^b (%)	R (s^{-1})
Inversion-Recovery	0.40±0.01	0.20±0.02	11±0.36	50±4	155±19
Repeated binomial excitation	0.40±0.01	1.86±0.31	14±3	25±5	89±39

Discussion and Conclusion: T_1^a from IR data was close to 0.4 s in agreement with literature[1] and T_2^b deduced from both experiments were comparable. M_0^b could not be precisely determined from the IR data. Indeed, as 180° excitation was not repeated, M_z^a was less perturbed by M_z^b. M_0^b from repeated binomial excitation simulation was in agreement with past findings[1]. The optimal T_2^a from repeated binomial excitation being longer than the fast T_2 from CPMG is tentatively attributed to susceptibility inhomogeneities. IR can be used to detect MT (large M_0^b and short T_2^b). However to quantify cross-relaxation parameters, a repeated binomial excitation can be easily integrated into a UTE sequence and should be used.

References: **1.** Horch RA et al. Magn Reson Med 2010;64:680-687. **2.** Horch RA et al. PLoS ONE 2011;6:e163592011. **3.** Bouazizi-Verdier K and Guillot G. In: Proceedings of the ISMRM, 2014 (#3995). **4.** Pachot-Clouard M and Darrasse L. Magn Reson Med 1995;34:462–469. **5.** Müller DK et al. J Magn Reson 2013;230:88–97. **6.** Henkelman RM et al. Magn Reson Med 1993;29:759–766. **7.** Edzes HT and Samulski ET. J Magn Reson 1978;31:207–229.