Cross-relaxation parameters in cortical bone from combined VFA-UTE and off-resonance saturation

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Purpose: Cortical bone porosity can be evaluated by UTE-MRI [1-2]. Magnetization Transfer (MT) effects have been observed in cortical bone between collagen-bound water and free water [3-4]. Since porosity determination involves T1 correction, the method used for T1 measurement should be critically assessed, taking the cross-relaxation effects into account [5]. Significant transverse relaxation during RF pulse complicates the analysis of inversion-recovery experiments, and has been shown to lower the observed T1 value in Variable Flip Angle (VFA) experiments [6]. The purpose of this work was to determine quantitative cross-relaxation parameters in cortical bone from the combined results of VFA-UTE and off-resonance saturation experiments.

Materials and methods: Femoral bovine cortical bone was obtained from local butcher. Transverse sections were cut from the diaphysis over approximately 10 mm thickness. Agar gel (4% concentration) and 0.2 mM $MnCl_2$ solution were used as references. All experiments were run on a home-assembled 4.7 T scanner. UTE images were acquired as described in [2] with TE = 51 µs, a hard RF pulse of 100 µs duration, at different flip angles (10°-130°), and at different repetition times TR (58 ms, 500 ms and 1 s). T1 was evaluated from the VFA-UTE images in cortical ROIs delimited by their T2 value (<1 ms). An independent off-resonance saturation experiment [5] was performed with a long RF pulse duration (5 s), six B1 amplitudes and 27 frequency offset values, followed by a hard 90° pulse of 100 µs duration. Cross relaxation parameters were defined as in [5]: T1 and T2 values of both pools (T1a, T2a, T1b, T2b), restricted protons magnetization (M0b) and exchange rate of longitudinal magnetization between the two pools (R). VFA experiments were simulated for a two-pool model, cross-relaxation effects being taken into account during TR and RF excitation, with home-developed software written in Matlab (MathWorks, Natick, MA). Signal intensity from free water was checked to be in a steady state after 40 repetitions, so data were collected at repetition #100.

Results: T1 of cortical bone, measured experimentally by VFA-UTE, was increasing with TR (Fig. 1A). The mean values (±std) over 5 samples are shown in Table 1. The complex shape of the off-resonance saturation curves in cortical bone (Fig. 2) could be fitted to the two-pool model with a Gaussian line-shape for the restricted protons [5], and the Root Mean Square Error (RMSE) was lower than 0.025 for the cross-relaxation parameters reported in Table 2. No MT was observed in the $MnCl_2$ solution as expected. Off-resonance saturation in agar gel was quantitatively in excellent agreement with reported values [5], with a RMSE < 0.02, consistently with our 0.5% measurement uncertainty. VFA experiments were simulated using the parameters reported in Table 2. Simulations (Fig. 1B) showed the same trend as experiments. T1 values (±95% confidence interval) fitted from the simulated data are shown in Table 1.

Table 1. T1 values for different TRs

	T1 (ms) at TR=58 ms	T1 (ms) at TR=500 ms	T1 (ms) at TR=1 s
Experiment	294 (±9)	427 (±13)	499 (±80)
Simulation	340 (±20)	390 (±6)	430 (±4)

Table 2. Cross-relaxation parameters of a cortical bone sample

T1a (ms)	T2a (ms)	T1b (ms)	T2b (µs)	M0b	R (s^{-1})
540±10	1.2±0.1	520±10	11±0.1	0.5±0.01	30±1

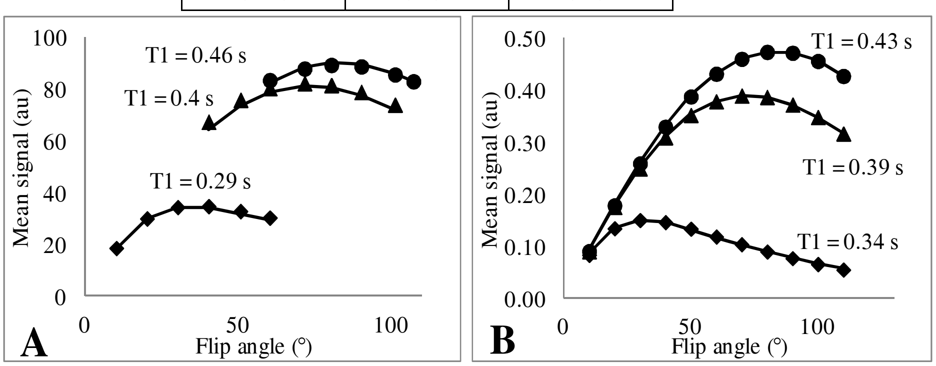

Fig. 1: Mean signal intensity (symbols) and fits (lines) in cortical bone as a function of flip angle: diamonds: TR=58 ms, triangles: TR=500 ms; circles: TR=1 s: A: UTE experimental data (same sample as Fig. 2), B: simulation.

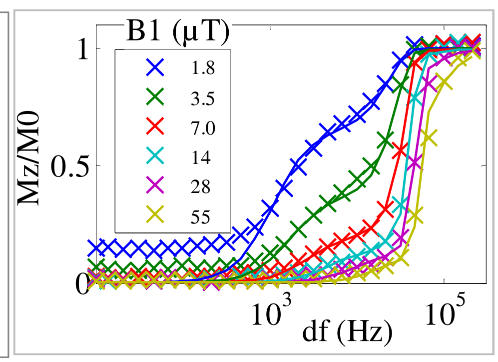

Fig. 2: Off-resonance saturation in a cortical bone as a function of frequency offset (df): data: symbols, fit: lines.

Discussion and conclusion: The T1 values deduced from the VFA-UTE data were systematically lower than the T1a value consistent with the off-resonance experiment, which can be attributed to cross-relaxation effects. The two-pool model parameters giving RMSE < 0.025 were not unique, we retained those for which the VFA simulations were in closest agreement with experimental VFA-UTE data. The confidence interval for T1 values fitted from simulated data was the smallest at long TR, from stronger signal variation, whereas the dispersion of the experimental data showed the opposite trend. A possible explanation could be variability between sample porosity distributions. At B1 = 1.8 µT, only partial saturation was observed in the off-resonance saturation experiment (Fig. 2), behavior also observed in the reference samples and attributed to B0 inhomogeneities. Simulations showed that the uncertainty on the two-pool model parameters was lower when describing VFA experiment than when minimizing off-resonance saturation RMSE, particularly the T1b value uncertainty was reduced. However our simulation of VFA experiments was performed with two Lorentzian line-shapes, which probably explains the remaining discrepancy with VFA-UTE. The T1 value for porosity determination should be chosen taking into account the specific sequence parameters (TR, flip angle, RF pulse duration) which strongly influence the effective relaxation rate.

References: [1] Techawiboonwong A. et al. Radiology (2008) 248:824-833 [2] Bouazizi-Verdier K. et al. In: Proceedings of the ESMRMB (2013) [3] Horch R. A. et al. Magn Reson Med (2010) 64:680-687 [4] Springer F. et al. Magn Reson Med (2009) 61:1040-1048 [5] Henkelman R. M. et al. Magn Reson Med (1993) 29:759-766 [6] Springer F. et al. J Magn Reson (2010) 206:88-96.