Magnetic Field Dependence of 31P Relaxation in Cortical Bone

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Introduction: Bone mineral density (BMD) is typically measured by dual energy x-ray absorptiometry (DXA), which provides a measure of projected (2D) apparent density. In contrast, quantitative computed tomography (QCT) measures 3D density, but this density is still apparent in that it is a measure of mineral mass divided by total volume, including osteoid and pore volume, rather than osteoid alone. Furthermore, QCT involves a high radiation dose. Phosphorus is a major component of the apatite-like mineral that confers bone its compressive strength [1]. It has recently been shown that solid-state ^{1}H and ^{31}P radial MRI have the potential to quantify both matrix and mineral mass per unit volume of bone tissue, from which true bone mineral density can be computed [2-4]. However, solid-state ^{31}P MRI in bone is challenging due to its extremely short transverse and exceptionally long longitudinal relaxation times, adversely affecting signal-to-noise ratio. SNR in MRI usually increases with field strength, but because the relaxation properties of phosphorus in bone become dramatically more unfavorable as field strength increases, this common assumption may not be valid and further investigation is warranted. In this study, we used a single set of lamb cortical bone specimens and a standardized set of coils and pulse sequences to measure the T_1 and T_2 relaxation times of bone phosphorus at field strengths ranging from 3 to 11.7T in order to gain insight into the mechanisms of relaxation and determine the optimal field strength in terms of achievable SNR.

Methods:

Specimens: Five cylindrical pieces of cortical bone (10mm length, 4mm diameter) were cut from the tibial mid-shaft of lamb shanks obtained fresh from a butcher. Size was limited by a 5mm NMR tube inner diameter and by the RF coil's homogeneous region. All data were acquired at room temperature.

Hardware: **3T**: Siemens TIM Trio whole-body MRI; **4.7T**: Varian DirectDrive horizontal-bore animal MRI; **7T**: Siemens Magnetom whole-body MRI; **9.4T**: Bruker Avance III vertical-bore NMR; **11.7T**: Varian DirectDrive vertical-bore NMR. **RF coils**: custom-made transmit/receive solenoids with dual-conductor windings (3T, 4.7T, 7T) or vendor-supplied saddle-coil/gradient probes (9.4T, 11.7T).

T_1 measurements: Due to the difficulty in generating sufficiently short 180° RF pulses, saturation recovery rather than inversion recovery was used. This consisted of non-localized sequential [SAT–t_{SR}–ACQ] blocks, where SAT refers to six rectangular 90° RF pulses, each followed by a spoiler gradient, i.e., [90°–G_{SPOIL}]x6, and ACQ refers to a pulse-acquire FID measurement, i.e., [90°–t_{DEAD}–t_{DAC}]. During the SAT preparation, generation of stimulated echoes was not a concern because the duration of G_{SPOIL}≥3ms>>T_2*. At all fields, 90° flip angles were achieved with pulses of duration <12μs and receiver dead times t_{DEAD} were ≤30μs. Here, the duration of the DAC gate t_{DAC} was 10.24ms (N_{pts}=2048, BW=200kHz). The saturation recovery time t_{SR} was incremented by powers of two (4ms–512s at 3T, 4.7T, 7T; 4ms–1024s at 9.4T, 11.7T), and the entire set of blocks was repeated and two data points at each t_{SR} averaged.

T_2 measurements*: A simple pulse-acquire FID measurement was performed using four signal averages, i.e., [ACQ–TR]x4, with TR=256s at 3T, 4.7T, 7T and TR=512s at 9.4T, 11.7T. ACQ was identical to that used above for T_1 measurements.

Deuterium Exchange: One bone sample was thoroughly blotted dry and then immersed in 3mL of 99.9% D_2O saline at 4°C for 72h, and T_1 measurement was performed at 7T.

Data Processing: Data were Fourier transformed and phased. A Lorentzian function was fitted to the single ^{31}P peak in each real-component spectrum (mean R^2=0.94). T_1 was calculated by fitting an exponential function to the peak amplitudes at each t_{SR}, as shown in Figure 1 (mean R^2=0.99). T_2* was calculated from the Lorentzian line width (FWHM). Due to the rapid transverse relaxation of solid-state phosphorus, T_2* can be assumed approximately equal to T_2. To estimate SNR, measured relaxation times were incorporated into the gradient-echo signal equation. A TR=250ms was chosen and the Ernst angle was calculated based on measured T_1 values. Signal was calculated using receiver dead times (TE) ranging from 0μs to 200μs. SNR was calculated for both coil-dominated and sample-dominated noise by multiplying the signal by $\omega^{7/4}$ and ω, respectively. Fitted lineshapes, with areas scaled by calculated sample-dominated SNR at TE=30μs, are shown in Figure 2.

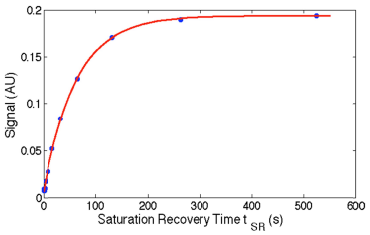

Fig. 1: Representative saturation recovery points and fitted curve at 7T.

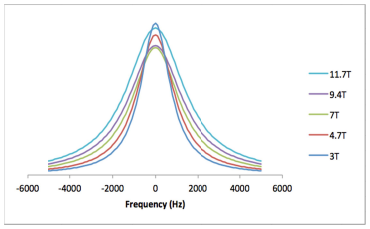

Fig. 2: Lineshapes illustrating broadening at increasing field strength.

Results: As field strength increases, T_1 was found to increase and T_2 to decrease monotonically, as shown in Figure 3. In the coil-dominated noise case, calculated SNR increases with field strength. In the sample-dominated noise case, SNR increases with field strength when TE<130μs, but decreases with increasing field strength when TE>130μs. Calculated SNR trends, each normalized to the value at 3T, are shown in Figure 4 for several representative values of TE.

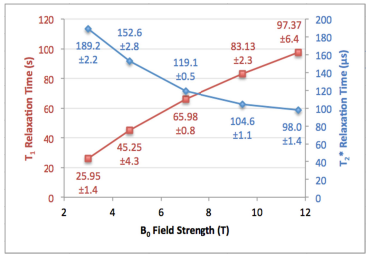

Fig. 3: T_1 and T_2 relaxation times with respect to field strength.

Discussion and Conclusions: Phosphorus in bone exists in a rigid crystalline structure. Therefore, the virtual absence of motional averaging leads to extremely short T_2 (and thus broad resonance lines), dominated by chemical shift anisotropy and dipole-dipole interaction. This also means that local magnetic fields due to dipole-dipole interactions involving nearby ^{1}H and ^{31}P nuclei contain very little power at the ^{31}P Larmor frequency to cause longitudinal (T_1) relaxation. ^{1}H-^{31}P dipole-dipole interaction is the dominant T_1 relaxation mechanism, as evidenced by the increase in ^{31}P T_1 from 66s to 180s at 7T following replacement of exchangeable protons with deuterons. Although the relaxation properties of bone phosphorus do become significantly more unfavorable at higher field strengths, as long as RF pulse and receiver dead time are sufficiently short (<<T_2*), and readout bandwidth is sufficiently large so that sample points at k-space center are acquired before 130μs, then SNR increases with B_0 for both sample-dominated and coil-dominated noise. Such conditions are often already met in solid-state imaging techniques such as UTE. The difference between sample- and coil-dominated noise regimes also suggests an advantage of using a small, highly sensitive receive coil. While other factors must be considered, such as the greater SAR and increased point spread function blurring known to occur at higher field strengths, these results suggest that under appropriate conditions there is an SNR advantage of high field strength for solid-state imaging of cortical bone phosphorus.

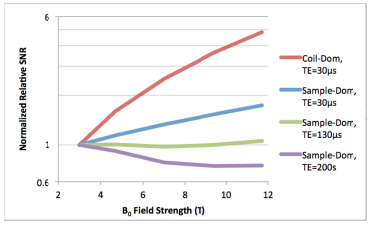

Fig. 4: Normalized calculated SNR for sample- and coil-dominated noise with respect to field strength, at several TEs.

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Acknowledgements: NIH AR50068, Translational Bio-Imaging Center at the Penn Institute for Translational Medicine and Therapeutics, NIH 5T32EB009384-03.