Can bound and mobile bone water be distinguished by T2* at 9.4T?

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Introduction

Ultra-short echo time (UTE) MRI is a powerful tool for non-destructive study of bone water (BW) that can provide insight into bone micro-architecture[1]. In particular, differentiating between bound BW, which is associated with collagen, and mobile BW, which resides in the pore space, may allow for assessment of porosity and degree of mineralization. Nyman *et al.*[2] used T_2^* NMR relaxometry to identify collagen protons, bound BW, and mobile BW at low field (0.6T). Recently, Diaz *et al.*[3] performing a bi-exponential fit of the BW signal decay as measured with UTE to quantify bound and mobile BW at 3T. In this work, we attempt to investigate the potential of T_2^* relaxometry to quantify bound and mobile BW at 9.4T by performing three-component exponential fits of FIDs from human bone specimens. The results of these fits were compared with bone porosity (P_o), BW concentration (BWC) as well as bound and mobile BW fractions measured previously with a D_2O exchange deuterium (^2H) NMR method[4]. The advantage of the deuterium NMR method is that bound and mobile BW fractions can be unambiguously determined without multi-exponential fitting, which is an ill-posed problem.

Materials and Methods

24 bone specimens were harvested from the posterior, medial, lateral, and anterior sides of mid-tibia from 6 donors (3M, 3F, 27-83 y) from the Musculoskeletal Transplant Foundation. All NMR experiments were performed on a 9.4T spectrometer (DMX-400, Bruker Instr.). FIDs were acquired for all specimens (64 scans, τ_{90}=4.6μs, TR=2s, dwell time=5μs). The normalized magnitude FIDs were fit to a three-component exponential function as the short dwell time allowed for detection of collagen protons: $f_a\exp(-t/T2^*_a) + f_b\exp(-t/T2^*_b) + f_c\exp(-t/T2^*_c)$, where f_i and $T2^*_i$ are the relative fraction and T_2^* values of the three components (i=a,b,c). Fitting was performed in Matlab (Mathworks) with the constraint $f_a+f_b+f_c=1$. Only the first 4 ms of the FIDs were used for fitting in order to match previous reports[2,3].

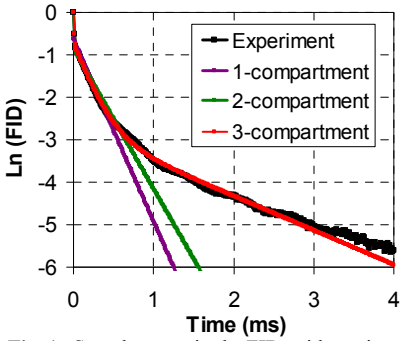

Fig 1. Sample magnitude FID with various multi-exponential fits.

A D_2O exchange method was used previously to independently measure BWC and bound and mobile BW fractions[4]. Each bone specimen was immersed in 99.8% D_2O saline for >72hrs. Total BW content was calculated by measuring the amount of H_2O that had exchanged into the D_2O saline[5]. After D_2O immersion, deuterium inversion recovery NMR was used to quantify bound and mobile BW (inversion time (TI): 50μs to 4s). Deuterium T_1 of bound BW was found to be shorter than mobile BW because of restricted motion and is identified based on its doublet splitting due to non-averaged quadrupole interaction (T_1 = 4-5ms vs 150-200ms). As a result, the spectrum at $TI=T_{null,\ bound\ BW}$ will consist predominantly of mobile BW and can be used to unambiguously separate and quantify bound and mobile BW in the deuterium NMR spectra. 3D μ-CT images (reconstructed at 16 μm^3) were also acquired of the specimens and the images processed with ImageJ (NIH) to calculate total bone volume and P_o. BWC is calculated by dividing total BW by the total bone volume.

Results and Discussion

Fig. 1 shows a logarithmic plot of a sample FID with result of one, two, and three-component exponential fits. It can be readily seen that the three-component fit best describes the FID. The weak oscillations in the FID arise from off-resonance lipid protons. Further investigation is needed to analyze its effect on the multi-exponential fits.

Table 1. Average Measurements and Fitting Results

	Measurements				Fitting Results					
Donor (age, sex)	**BWC (%)**	**Bound %**	**Mobile %**	**P_o (%)**	**f_a**	**$T2^*_a$ (μs)**	**f_b**	**$T2^*_b$ (μs)**	**f_c**	**$T2^*_b$ (ms)**
27, F	21.2±1.6	79.5±3.5	20.5±3.5	2.6±0.6	0.54±0.02	6.9±0.5	0.39±0.05	227±42	0.07±0.03	0.8±0.1
65, F	37.5±1.6	65.8±2.6	34.3±2.6	12.5±2.3	0.48±0.01	6.9±0.7	0.46±0.01	244±64	0.06±0.02	1.3±0.2
83, F	60.1±19.7	59.3±9.6	40.8±9.6	23.9±8.1	0.31±0.05	3.9±0.8	0.56±0.04	138±18	0.13±0.03	0.9±0.2

Bound %: Bound BW fraction; Mobile %: Mobile BW fraction; P_o: bone porosity

Table 1 summarizes measurements and fitting results, which were averaged for each donor. For brevity, only female donor values are shown. Male donors showed similar behavior. P_o increased with age as expected[6], which led to increases in BWC and mobile BW fraction. All fits showed good agreement with the FIDs (R^2>0.96). $T2^*_a$ values are consistent with collagen protons[7]. $T2^*_b$ and $T2^*_c$ are roughly 200 μs and 1 ms. These values approximately agree with bound and mobile BW T2* values reported in (2) and (3). Furthermore, if f_b and f_c are renormalized without f_a, as collagen protons were not detected by the method in (2), the average f_b and f_c are 0.85±0.4 and 0.15±0.4, which are in fair agreement with values reported in (2). Table 2 shows correlation coefficients, *r*, calculated between the measurements and relative fractions of the fitted components. All correlations were significant (p<0.05). The strong negative *r* of f_a with BWC and P_o, and its positive *r* with bound BW fraction, again suggests that component 'a' represents collagen protons. f_b, f_c, and f_b+f_c all show positive *r* with BWC, which suggests that components 'b' and 'c' represent BW. However, both f_b and f_c show positive *r* with mobile BW fraction and P_o, and negative *r* with bound BW fraction. This suggests that components 'b' and 'c' both represent mobile BW since bound BW would have a negative *r* with P_o and mobile BW fraction[4]. Component 'c' may represent BW in larger pores given its longer T_2^*[8]. Further investigation is needed to understand how the bound BW signal contributes to the overall FID.

Table 2. Correlation Coefficients, *r*

	f_a	f_b	f_c	$f_b + f_c$
BWC (%)	-0.90	0.87	0.40	0.90
Bound %	0.78	-0.64	-0.56	-0.78
Mobile %	-0.78	0.64	0.56	0.78
P_o (%)	-0.93	0.82	0.55	0.93

Bound %: Bound BW fraction; P_o: bone porosity
Mobile %: Mobile BW fraction

Conclusion

This work investigated the potential of using three-component exponential fits to quantify bound and mobile BW at 9.4T. The results here show that while the exponential fitting does model the BW signal decay very well, the three components correlate only with collagen protons and mobile BW. This suggests that T2* relaxometry may not distinguish between mobile and bound BW at 9.4T.

References: 1. Techawiboonwong A *et al*., *Radiology*, **248**:824 (2008). 2. Nyman JS et al, *Bone*, **42**:193 (2008). 3. Diaz E *et al.*, *NMR Biomed*, Early View (2011). 4. Ong HH *et al.*, *Proc of 18th ISMRM Meeting* (2010). 5. Fernandez-Seara *et al*., *Biophys J*, **82**:522 (2002). 6. Bousson et al, *Radiology*, **217**:179 (2000). 7. Edzes H, et al, *Nature*, **256**:521 (1977). 8. Brownstein KR and Tarr CE, *Phys Rev A*, **19**:2446 (1979). **Acknowledgements:** NIH R01 AR50068