Free and bound water quantification of cortical bone

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INTRODUCTION

Bone is a composite material consisting of mineral (~45% by volume), organic matrix (~35% by volume) and water (~20% by volume). Bone water occurs at various locations and in different states. It is associated with the mineral phase, bound to the organic matrix, and a significant fraction occurs in more or less free form in the microscopic pores of the Haversian and the lacuna-canalicular systems (1). A measure of free water concentration can potentially provide a surrogate measure of bone porosity, while a measure of bound water reflects collagen content (2, 3). However, current techniques including DEXA and CT can only detect the mineral component, while completely ignoring the contribution from organic matrix and water. Here we propose to use bi-component analysis of UTE images to quantify T2* and fractions of the free and bound water components in cortical bone.

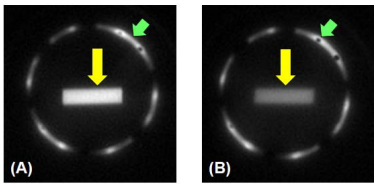

Fig 1 UTE MR images of a wet bovine cortical bone before (A) and after (B) air-drying for three days shows significant bone signal (long arrows) after air-drying, suggesting that significant bone signal is from bone bound water. The UTE sequence also detected high signal from the 1-inch coil (short arrows).

MATERIALS AND METHODS

Cortical bone has an extremely short T2/T2* relaxation time and appears as signal void with any clinical MR imaging sequences. We have developed an ultrashort echo time (UTE) sequence with a nominal TE of 8 μs that is 100-1000 times shorter than conventional TEs, allowing us to detect and quantify T2* of free and bound water within the cortical bone that otherwise presents as signal void (2-4). A short hard pulse of 32 μs was used for signal excitation to minimize signal decay during excitation. Multi-component fitting is very sensitive to signal-to-noise ratio (SNR), the number of components, minimum TE, the number of echoes, and the separation of T2/T2* (5). The two-component model, together with other factors such as a near zero TE of 8 μs and an order of magnitude difference in T2* values of the free and bound water components, are expected to significantly reduce the sensitivity to SNR. Furthermore, background noise was estimated through maximum likelihood (MLE) distribution fitting of background noise histogram. The UTE signal decay was normalized before the fitting so that the sum of the amplitude of the two components equal to 1. As a result, the normalized time-domain UTE signal intensity (SI*) at echo time TE can be simplified as shown in equation [1]:

$$SI^*(TE) = F_b \times e^{-TE/T^*_{2,b}} + (1-F_b)\times e^{-TE/T^*_{2,f}} + \text{noise} \qquad [1]$$

There are only three fitting parameters: T2* of free water ($T^*_{2,f}$) and bound water (T^*_{2b}), and fraction of bound water (F_b) or free water (F_f= 1-F_b). Total bone water concentration can be measured through comparison of UTE MR signal of bone with that of a calibration water phantom (from a separate scan) (3), which is a mix of distilled water (20%) and D_2O (80%) doped with $MnCl_2$ with T2*~400 μs. T2 effect is neglected since our UTE sequence has a minimal TE of 8 μs and T2* of the water calibration phantom approaches that of bone. As a result, bone water concentration (BWC) in terms of reference water concentration (RWC) can be calculated as follows:

$$BWC \approx \frac{I_{bone}}{I_{ref}} \times \frac{(1-e^{-TR/T_{1,ref}})}{(1-e^{-TR/T_{1,bone}})} \times \frac{(1-\cos\alpha\times e^{-TR/T_{1,bone}})}{(1-\cos\alpha\times e^{-TR/T_{1,ref}})} \times RWC \qquad [2]$$

Free and bound water concentrations are calculated by integrating water fractions determined by equation [1] with BWC from equation [2]. T1 difference between free and bound water components is neglected.

In total 5 bovine cortical bone segments were subject to bi-component fitting of UTE images acquired with: TR = 200 ms, FOV = 10 cm, matrix = 256×256, 255 projections, 20 or more TEs ranging from 8 μs to 8 ms, 1-inch transmit/receive (T/R) coil. The protocol was also applied to five healthy volunteers and five patients with osteoporosis (OP). A more localized 1 cm T/R coil was used for in vivo study. The total scan time ranges from ~50 min for in vitro and ~20 min for in vivo studies. The non-negative least-square (NNLS) algorithm was used for fitting of signal from a region-of-interest (ROI) placed in tibial cortex. The bovine specimens were subject to μCT imaging (9×9×9 μm^3) to calculate bone porosity, and a drying protocol (3, 6): 3 days air-drying at room temperature to measure free water and 24 hours oven-drying at 100 °C to measure bound water using a precision balance.

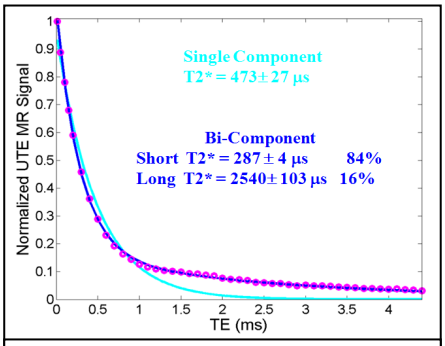

Fig 2 Bi-component curve fitting of UTE signal from bovine cortical bone demonstrates a bound water T2 of 271 μs and fraction of 25%, and free water T2 of 3004 μs and fraction of 75%.*

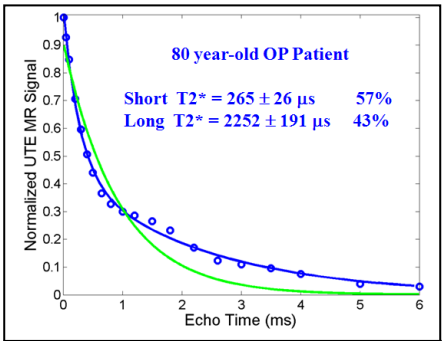

Fig 3 Bi-component analysis of 10 patellae. These results suggest that the T2 of the bound water is more sensitive to early degeneration than T2* of the*

RESULTS and DISCUSSION

Figure 1 shows UTE images of a bovine specimen before and after air-drying. Gravimetrical method shows 9.1% bone water loss by volume during air-drying, with another 17.3% water loss during oven-drying. Equation [2] shows that wet bovine bone had 16.5% bone water by volume, which was reduced to 8.5% after air-drying, suggesting 8% free water and 8.5% bound water. Figure 2 shows single- and bi-component fitting of the T2* decay. There is a clear short T2 component with a T2* of 287 μs and long T2* of 2540 μs, with a fraction of 84% and 16%, respectively, suggesting 4.1% free water and 12.4% bound water. μCT shows a bone porosity of ~3%. There are several possible reasons accounting for the differences in free and bound water fractions measured from different techniques: 1) it is likely that air-drying for three days results in more than just free bone water loss (6); 2) oven-drying at 100°C may result in more than bound water loss; 3) free water in small pores may behave more like bound water due to surface relaxation mechanisms; 4) T1 for free and bound water may be different, thus equation [2] is not accurate; 5) bi-component is an over-simplified model, especially considering that four distinct proton populations have been reported by Horch et al in a recent NMR study of cortical bone specimens (7). Figure 3 shows an example on single- and bi-component analysis of an 80-year old female patient, where bone signal decay is better characterized by the bi-component model which shows a short T2* of 265 μs and long T2* of 2252 μs, with a fraction of 57% and 43%, respectively. Volunteers have long T2 water fractions in the range of 20-30%. There is a marked increase in free water fraction likely due to increased bone porosity. For in vivo bi-component analysis, it is critical to use a localized coil for signal reception to minimize long T2 water and fat contamination, and also a large number of TEs to minimize fitting errors. Patient motion is a major limitation.

CONCLUSIONS

The bi-component T2* analysis of UTE images allows us to quantify T2*, fractions and volume percentile concentrations of bound and free water in cortical bone in vitro and in vivo, and to non-invasively assess bone porosity (the amount of free water) and organic matrix (the amount of bound water) using clinical MR scanners.

REFERENCES 1. Wehrli FW, et al, NMR in Biomed 2006. 2. Wu Y, et al, MRM 2003. 3. Techawiboonwong A, et al, Radiology 2008. 4. Du J, J Magn Reson 2010 (in press). 5. Reiter DA, MRM 2009 6. Nyman JS, et al, J Biomechanics 2006. 7. Horch RA, et al., MRM 2010.