Validation of bound and free water measurement using bi-component analysis of UTE images of cortical bone

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INTRODUCTION

Recently proton magnetic resonance (MR) spectroscopy has been used to measure water distribution in cortical bone [1, 2]. Horch et al. [2] investigated the origin of MR signal relaxation components in human cortical bone using multi-component analysis of the free induction decay (FID) and Carr-Purcell-Meiboom-Gill (CPMG) signal, and found four distinct proton populations from five microanatomical sources: free water, collagen-bound water, collagen and mineral hydroxides, collagen and lipid methylene. However, these techniques can only be applied to small samples. They are not applicable in vivo. Ultrashort echo time (UTE) sequences allow us to quantify water within cortical bone in vivo [3, 4]. Collagen and lipid methylene as well as water associated with bone mineral have extremely short T_2s (T_2* < 12 μs) [2] and are undetectable with MRI. Our data indicate that UTE sequences detect signals from both water bound to organic matrix and free water [5]. In this study we aim to validate the bound and free water measurements use bi-component analysis of UTE images of bovine cortical bone samples.

MATERIALS AND METHODS

In total 19 bovine cortical bone segments (~20×15×4 mm^3) were subject to bi-component fitting of UTE images acquired with the following parameters: TR = 200 ms, FOV = 8 cm, matrix = 256×256, flip angle = 10°, a short rectangular pulse (32 μs) for non-slice selective excitation, 20 TEs ranging from 8 μs to 8 ms, 51 seconds per image, 1-inch T/R coil, total scan time of 17 minutes. Total bone water concentration was quantified by comparison of signal intensities from bone with that from an external reference phantom. Volume concentrations for bound and free water components were calculated by integrating water fractions determined from bi-exponential fitting with total water concentration. The samples were divided into three groups for the following three experiments:

(1). Sequential drying experiments: 7 bovine bone samples were subjected to UTE MR measurement of bound and free water content, and gravimetric measurement of bone water loss in a laboratory oven at room temperature for 0 min (wet bone), 30 min, 60 min, 90 min and 3 days (five different degrees of free water loss), and oven-drying for 24 hours at 100 °C (bound water loss). Percent water loss by weight was calculated based on weight change. UTE measured free water loss was correlated with gravimetric bone water loss during sequential air-drying, and UTE measured bound water loss was correlated with gravimetric bone water loss during oven-drying.

(2). D_2O-H_2O exchange experiment: D_2O is heavier than H_2O and provides no MR signal. Exchange between D_2O-H_2O is able to provide information on bone water concentration. 6 bovine bone samples were subjected to UTE measurement of bound and free water content and gravimetric measurement of bone weight change at a series of exchange times until equilibrium was achieved with no significant bone weight increase. Total bone water content was calculated based on the total weight gain. Then the samples were subject to air-drying for 3-days. The total weight loss provided information on free water concentration. The samples were put in H_2O for another exchange experiment to calculate bound water content based on weight change.

(3). ^{3}HHO-H_2O exchange experiment: ^{3}HHO is radioactive and heavier than H_2O. 6 bovine bone samples were subject to UTE measurement of bound and free water content. 3 samples were placed in ^{3}HHO until equilibrium was reached. The other 3 samples were subject to air-drying for 3 days and then placed in ^{3}HHO until equilibrium was reached. Changes in radiation and weight provided two independent measures of bound/free water concentration. The UTE measured bound/free water contents were compared with results from both radiation and gravimetric measurements.

RESULTS and DISCUSSION

Figure 1 shows bi-component analysis of a wet bovine bone, 30 minutes and three days after air-drying, respectively. Bi-component analysis shows that the long T_2* water fraction gradually decreased from 14.8% for wet bone to 6.0% for air-dried bone for 30 minutes. After three days air-drying, only a single short T_2* component was left, consistent with complete loss of free water and signal only detectable from the residual bound water.

Figure 2 shows the correlation between UTE MR measured free water loss and gravimetric bone water loss of 7 bovine cortical bone samples during sequential air-drying. There is a high correlation (R = 0.9084; P < 0.0001) between these two measures, indicating that UTE bi-component analysis can reliably estimate free bone water.

Figure 3 shows free water fraction from UTE bi-component analysis of a wet bovine cortical bone, the same bone 6 hours and 24 hours after D_2O-H_2O exchange, as well as radiation measurement of ^{3}HHO-D^2O exchange for 24 hours. The free water fraction remains fairly constant before and after D_2O-H_2O exchange, suggesting that both bound and free water are subject to chemical exchange. Water bound to the mineral phase of cortical bone is expected to participate in the isotope exchange but at a much slower rate [6]. We limited the exchange times to less than 24 hours to minimize this source of error.

The excellent agreement between these techniques suggests that UTE bi-component analysis provides accurate measurements of bound and free water in cortical bone. This has allowed us to assess organic matrix via bound water [7], and bone porosity via free water [3] using a clinical MR scanner. Future study will focus on correlation of the UTE measurements of bound and free water T2*s, relative fractions and volume concentrations with biomechanical properties of cadaveric human cortical bone samples, as well as in vivo applications in osteoporosis (OP).

CONCLUSIONS

The UTE sequences detect both bound and free water in cortical bone. The bi-component analysis of UTE images allows us to reliably quantify bound and free water using clinical MR scanners.

REFERENCES

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4. Du, et al, JMR 2010. 5. Du, et al, MRM 2011. 6. Fernandez-Seara, et al., Biophys 2002. 7. Wu, et al, MRM 2003.

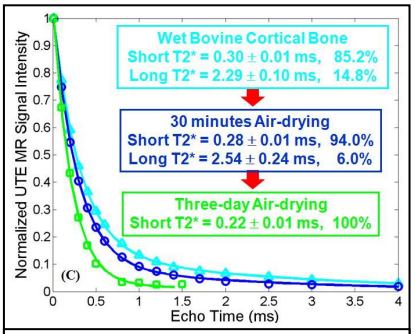

Fig 1 *Bi-component fitting of a bovine cortical bone at three drying stages: wet bone, air-drying for 30 minutes and three days. Free water dropped from 85.2% by volume for wet bone to 6.0% after 30 minutes air-drying, and 0% after three-days air-drying.*

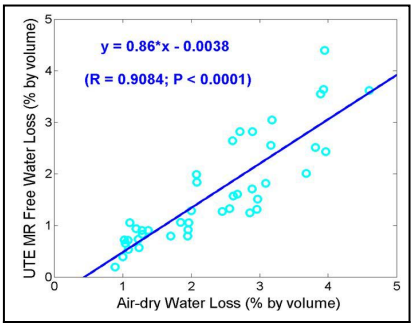

Fig 2. *A high correlation was observed between UTE free water loss and gravimetric water loss. UTE water loss is lower probably because residual surface water only contributes to gravimetric water loss.*

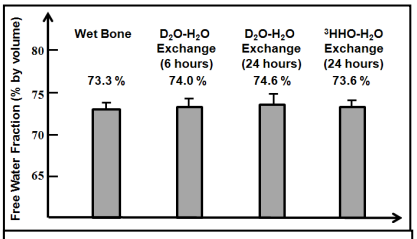

Fig 3 *Free water fraction measured by UTE bi- component analysis of a wet bovine cortical bone, 6 and 24 hours after D_2O-H_2O exchange, as well as radiation measurement of ^{3}HHO-H_2O exchange for 24 hours.*