Ultrashort Echo Time Magnetization Transfer (UTE-MT) Imaging of Cortical Bone

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INTRODUCTION

Magnetization transfer (MT) imaging is one way of indirectly assessing pools of protons with extremely fast transverse relaxation [1]. However, conventional long TE MT imaging sequences are not applicable to short T2 tissues such as cortical bone [2], which has multiple water components including water loosely bound to the organic matrix (T2* ~ 0.3 ms), water tightly bound to mineral (T2* ~ 10 µs or less), and free water residing in the pores of cortical bone (T2* ~ 1-3 ms) [3-6]. Ultrashort echo time (UTE) sequences can detect signal from short T2 species with T2*s of a few hundred microseconds or longer (e.g., water loosely bound to the organic matrix and free water in cortical bone, tendons, ligaments, etc.), but tissues with extremely short T2*s (e.g., mineral bound water, collagen protons, membranes, etc.) remain "invisible". The combination of UTE with MT (UTE-MT) provides a valuable option to assess different bone components. In this study we evaluated UTE-MT imaging of cortical bone and its application in assessing cortical porosity and biomechanical properties of cadaveric human bone samples using a clinical whole body 3T scanner.

MATERIALS AND METHODS

A 2D UTE-MT sequence was developed on a clinical 3T scanner (GE Healthcare Technologies, Milwaukee, WI). The UTE sequence employed a short half pulse excitation followed by 2D radial ramp sampling with a minimal nominal TE of 8 µs. The MT pulse was a Fermi pulse (duration = 8 ms, maximal saturation flip angle = 1000°) which provided a much improved spectral profile than a rectangular square pulse, and much higher efficiency than conventional Gaussian or sinc pulses in suppressing short T2 signals. The 2D UTE-MT sequence was first applied to a piece of rubber and bovine cortical bone (both have similar T1s and T2*s), and then to cadaveric human cortical bone samples. In total 122 rectangular (~4x2x40 mm) cortical bone samples were resected from cadaveric (n=38, 30-94 yrs, 65.7±16.3 yrs) femora and tibiae using a precision saw. The UTE-MT imaging protocol included: TR=300 ms, TE= 8 µs, FOV=4 cm, slice thickness=3cm, MT pulse power=1000°, a series of MT frequency offset (Δf=1.5,3,5,10,20 kHz). A home-built birdcage coil (~2.5 cm in diameter) was used for signal excitation and reception. The bone samples were placed in a 20 ml syringe filled with perfluorooctyl bromide (PFOB) during MR imaging to maintain hydration and minimize susceptibility effects at air tissue junctions. Images were analyzed to determine the magnetization transfer ratio (MTR) at each frequency. For each sample, porosity was determined using µCT at 9 µm resolution. Four point bending-to-failure biomechanical test was performed to obtain measures of Young's modulus, yield stress, and failure stress. MTR was plotted as a function of MT pulse frequency offset Δf and MT power (θ) for the rubber phantom and bovine bone samples. The relation between MTR, cortical porosity, and biomechanical properties of human cortical bone samples was assessed.

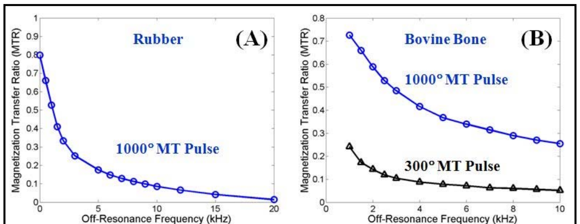

***Fig 1** UTE MTR of rubber (A) and bovine cortical bone (B) as a function of MT pulse frequency offset Δf, and MT pulse power, θ. MTR increases with MT power and decreases with Δf. MTR is consistently lower in rubber than in cortical bone, probably due to the mineral bound water and collagen protons which make a significant contribution to the MTR of cortical bone, but not rubber.*

RESULTS AND DISCUSSION

Clinical MT sequences show near zero signal for both rubber and cortical bone, which have very similar relaxation times with T1s of 262 ± 15 ms vs. 246 ± 9 ms and T2*s of 355 ± 12 µs vs. 356 ± 8 µs, respectively. The UTE-MT sequence provides high quality images and MTR maps of both rubber and cortical bone. **Figure 1** shows the UTE MTR of the rubber phantom and a bovine cortical bone sample at different frequency offsets and MT pulse powers. Although the rubber phantom and bovine bone sample have similar T1s and T2*s, their MTR vs. frequency offset behaviors are very different, reflecting the fact that rubber only has protons similar to bound water, while cortical bone has both bound and free water with distinct relaxation times.

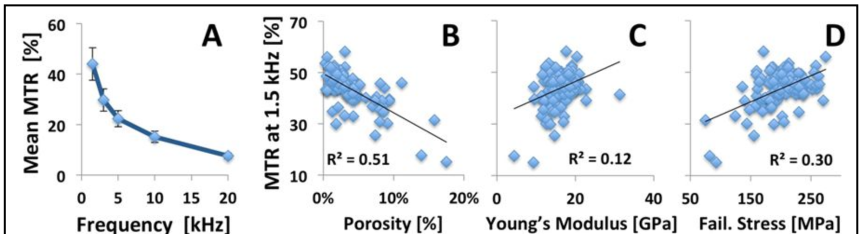

***Fig 2** UTE-MT imaging of 122 human cortical bone samples: MTR vs. MT pulse frequency offset (A), and correlation between MTR (at 1.5 kHz) and µCT cortical porosity (B), Young's modulus (C) and failure stress (D). MTR is negatively correlated with porosity, and positively correlated with Young's modulus and failure stress.*

Figure 2 shows MTR as a function of frequency offset for a human bone sample, as well as the relation between MTR and cortical porosity, Young's modulus and failure stress of 122 human bone samples. MTR decreased significantly ($p<0.001$) with Δf (**Fig.A**) due to reduced direct saturation effect at increased Δf. MTR under all Δf correlated significantly with both cortical porosity and biomechanical properties, with the strongest correlation observed at Δf=1.5 kHz. At this frequency, MTR correlated strongly and negatively with porosity (**Fig.B**, R^2=0.51) and positively with Young's modulus (Fig.C, R^2=0.12), failure stress (**Fig.D**, R^2=0.30) and yield stress (R^2=0.33).

Table 1 shows correlation statistics of the 122 human cortical bone samples. These results suggest that UTE-MT can potentially evaluate free water residing in the microscopic pores and water bound to the organic matrix of cortical bone, and provide information about cortical porosity and biomechanical properties of cortical bone.

	MTR 1.5 kHz	MTR 3 kHz	MTR 5 kHz	MTR 10 kHz	MTR 20 kHz
Porosity	R^2 =0.51, P<1e-20	R^2 =0.49, P<1e-19	R^2 =0.48, P<1e-18	R^2 =0.48, P<1e-18	R^2 =0.46, P<1e-17
Young's Modulus	R^2 =0.12, P<1e-4	R^2 =0.11, P<2e-4	R^2 =0.11, P<3e-4	R^2 =0.11, P<3e-4	R^2 =0.09, P<6e-4
Yield Stress	R^2 =0.30, P<1e-10	R^2 =0.28, P<2e-10	R^2 =0.28, P<3e-10	R^2 =0.28, P<2e-10	R^2 =0.25, P<5e-9
Failure Stress	R^2 =0.33, P<4e-12	R^2 =0.34, P<2e-12	R^2 =0.34, P<2e-12	R^2 =0.35, P<1e-12	R^2 =0.31, P<2e-11

***Table 1** Correlation between UTE-MT measured MTR and cortical porosity, Young's modulus, yield stress and failure stress. MTR is highly negatively correlated with µCT porosity at all Δf, with R^2 slightly reduced from 0.51 at 1.5 kHz to 0.46 at 20 kHz. MTR is weakly positively correlated with Young's modulus at all Δf, with R^2 slightly reduced from 0.12 at 1.5 kHz to 0.09 at 20 kHz. MTR is moderately positively correlated with yield stress and failure stress at all Δf, with R^2 around 0.3. p values are less than 0.0001 for all the correlations.*

CONCLUSIONS

UTE-MT assessed MTR provides information on bound and free water in cortical bone and is significantly correlated with cortical porosity and biomechanics, and therefore provides a new approach to evaluate bone quality non-invasively.

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