The Suppression Ratio as a Surrogate Marker of In Vivo Cortical Bone Porosity

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INTRODUCTION- Cortical bone contains a significant amount of water that can be detected and quantified by ultra-short echo-time (UTE) MRI [1, 2]. The two most significant fractions consist of water bound to collagen and mobile water located in the spaces of the lacuna-canalicular and Haversian pores [3]. The latter fraction is of particular interest clinically as it scales with pore volume, which is known to expand during aging, and particularly so in osteoporosis [4]. Hence, if pore water could be quantified, it would be possible to estimate porosity indirectly without a need to spatially resolve the pores, which is not possible *in vivo*. One approach to separate the two types of water is based on bicomponent analysis of the FID, the rationale being that pore water possesses longer T_2* values [5]. While this method is effective *ex vivo*, it is difficult and time consuming to achieve *in vivo*. Here we propose an alternate method to obtain a surrogate measure of porosity in the form of the suppression ratio, i.e. a ratio of the unsuppressed to the soft-tissue suppressed UTE signal intensity.

METHODS- Image Acquisition: The left mid-diaphyseal tibia (38% from the lateral malleolus) of 18 healthy females (27-81 years old) was imaged at 3T (TIM Trio; Siemens Medical Solutions) using an 8-channel Tx-Rx knee coil. The subjects were recruited from a previous study that utilized a 3D hybrid radial UTE technique to measure bone water concentration (BWC) [6]. In the present study, three soft tissue suppression schemes for UTE MRI were employed in order to cancel and/ suppress signal from the long-T_2 species: 1) dual-echo UTE (echo subtraction using two different TE values), 2) dual-band (DB)-UTE (saturation via dual band UTE pulses and 3) Inversion-recovery (IR)-UTE (inversion by adiabatic inversion pulses) as described previously [7]. Imaging parameters common to all three sequences were: FOV = 180x180 mm^2, slice thickness = 5mm, TR/TE$_1$/TE$_2$ = 300 ms/50μs/4.6ms, FA = 60°, sampling frequency bandwidth = ±125 kHz, and 288 readout points for each half radial projection that resulted in a reconstructed matrix size of 512 x 512 and in-plane resolution = 0.35x0.35 mm^2. In the DB-UTE method, an optimized dual-band saturation pulse was used, which was designed using Shinnar-Le Roux tools with complex Parks McClellan algorithm [8] with: Pulse duration = 15ms, flip order = 300, FA(water/fat) = 100°/110°, Suppression bandwidth = 120 Hz on resonance, 320 Hz at fat resonance centered at 430 Hz at 3T and ripple values of 0.5%. In IR-UTE, an optimized hyperbolic secant pulse was used with: Pulse bandwidth/duration = 1kHz/20ms, with frequency shift of 270 Hz towards the lipid peak in order to cover both, fat and water peaks. The pulse amplitude was set to allow 30% B1 variation and TI = 100 ms. The acquisition time was 5 min 12s for each sequence.
Reconstruction and Analysis: As a first step, sampling density compensation weighting was performed. The weighting was computed based on gradient mapping which measured the k-space trajectories. Next, acquired k-space data were remapped onto Cartesian grids using Greengard's regridding algorithm prior to 2D IFFT. The final magnitude image was generated as the square-root of the sum-of-squares of the multi-coil images. Suppression ratio (SR) maps for both, IR- and DB-based techniques were computed as a ratio of the dual-echo UTE images (TE=50 μs) to the corresponding images (TE=50 μs) of both the IR and DB methods. Manual segmentation of the periosteal and endosteal cortical boundaries to generate a cortical bone mask was performed on the IR suppressed images, as cortical bone contrast is uniform and well-demarcated in IR-UTE [7]. This mask was then propagated on to the DB-suppression ratio maps and mean suppression ratios were extracted as a global cortical bone parameter for both the IR and DB techniques. Histogram analysis was performed to enable visualization of the distribution of suppression ratios per subject. The subjects also underwent scanning by peripheral quantitative computed tomography for the assessment of cortical bone mineral density (BMD).

RESULTS and DISCUSSION- Figure 1 shows representative axial mid-tibia IR- and DB-based SR parametric maps and the corresponding histograms from a young (A-B, 33 year-old), middle-aged (C-D, 50 year-old) and elderly (E-F, 75 year-old) subject. Both, the IR and DB techniques demonstrate an increase in SR with age (R^2=0.39-0.48, p≤0.005) as seen in the maps and histograms. Furthermore, in young subjects, the SR histograms are relatively symmetric. In contrast, in older subjects (**Figure 1 C-F**), besides a shift in the mean values, the histograms become increasingly asymmetric with long tails toward high SR values suggesting the presence of large pores with long T_2* values. Overall, the mean DB-based SR was 15% lower than the IR-based SR (p<0.01, paired *t*-test). A strong inverse association was observed between cortical BMD and SR (**Figure 2**; R^2 =0.53-0.59, p<0.001). This relationship indicates that increased porosity in general occurs at the expense of the loss of osteoid, which in the case of constant mineralization density would scale with volumetric BMD. Unsurprisingly, a weaker association was found between cortical BMD and total BWC (R^2 = 0.40, p<0.01) compared to that with SR, owing to the fact that total BWC consists of both, bound and pore water fractions, which have opposing relationships with porosity. SR and total BWC were only weakly correlated (R^2=0.25-0.31, p<0.05), which is in line with the notion that in younger subjects, the majority of bone water is collagen-bound [3]. A limitation of the analysis is the use of manual segmentation of the periosteal and endosteal boundaries. Accurate segmentation of the endosteum is critical due to the ruffled boundary that arises from endosteal trabecularization. Future work should also incorporate registration between scans to account for subject motion. Increased SR may correlate with an increase in the fraction of large pores (>100 μm) associated with longer T_2* values expected in mobile water pools. Recent *in vitro* studies have highlighted the presence of short and long T_2* components in cortical bone [9].

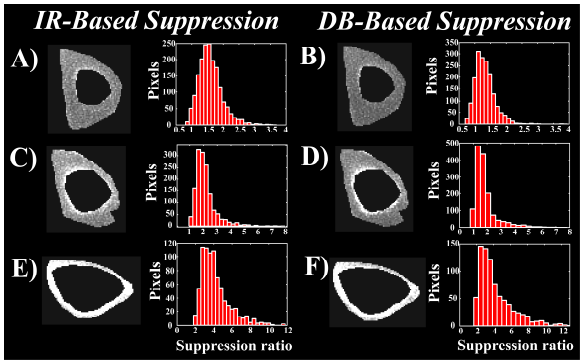

Figure 1: Comparison of axial inversion recovery (IR) and dual-band (DB)-based cortical (mid-tibia) bone water suppression maps and histograms from young (33 year old; A, B), middle-aged (50 year old; C, D) and elderly (75 year old; E, F) female subjects.

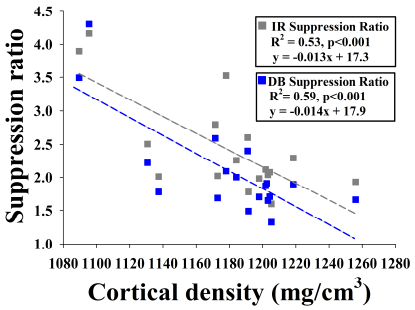

Figure 2: Plot of cortical density vs. suppression ratio for the inversion recovery (IR) and dual band (DB)-based suppression techniques in 18 women (27-81 years).

CONCLUSION- Preliminary results suggest that the suppression ratio may serve as a surrogate parameter for cortical porosity *in vivo*. Proof of such an association will require comparison with quantitative μCT in bone specimens where porosity can be measured by image processing.

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