

Ultra-Short Echo-Time (UTE) Imaging Based Estimation of Cortical Bone Stiffness

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Introduction:

Accurate prediction of osteoporotic fracture risk and timely detection of treatment efficacy depend on the ability to assess bone's mechanical competence *in vivo*. However, most work so far has focused on trabecular structure while cortical bone has been neglected since it is believed to remodel more slowly and also because most fractures occur at sites dominant in trabecular bone. Nevertheless, it is well known that intracortical remodeling occurs, resulting in increased porosity and impaired strength with advancing age [1]. Also, high-resolution MR images of distal extremities have been shown to be suitable for the generation of micro-finite element (μ FE) models that allow quantification of age- and treatment-related mechanical changes [2, 3]. However, typically bone produces a signal void in conventional MRI sequences in which echo times are on the order of milliseconds thereby precluding detection of the proton signal arising predominantly from water possessing very short $T2^*$ ($<500\mu s$) [4]. Consequently, bone tissue properties such as Young's modulus are typically assumed to be constant (~ 15 GPa) and homogeneous when generating μ FE models [5, 6]. Recent advances in 3D ultra-short echo-time (UTE) MRI now offer the potential to estimate true bone tissue fraction as 1-BWF where BWF is bone water fraction [7, 8]. Here, we investigated the feasibility and practicality of using BWF maps derived from UTE images of the tibial diaphysis as input to a μ FE model in order to assess age-related variations in cortical bone stiffness in a healthy volunteer cohort.

Methods:

Image acquisition - The tibial diaphysis of ten healthy volunteers (7 female and 3 male; 22-79 yr of age) were imaged using a 3D hybrid radial UTE (3DHRUTE) sequence at 3T (Siemens Tim Trio, Erlangen, Germany), with a $180 \times 180 \times 90$ mm³ FOV (third dimension along axial direction), 500 radial projections of 256 readout points, dwell time 6 μ sec ($BW_{read-out} = 650$ Hz/pixel), and $TR=20$ msec yielding $0.31 \times 0.31 \times 4.5$ mm³ voxel size in 6.6 mins with a 8-channel Tx/Rx knee coil. High-resolution gradient-echo (GRE) images of the same FOV were also obtained at $0.18 \times 0.18 \times 1.5$ mm³ voxel size.

Processing of UTE images - After regriding reconstruction of the UTE images, the cortical bone region was disconnected from soft tissue and fatty marrow by detecting the periosteal and endosteal boundaries (Figure 1). Subsequently, BWF of each voxel in the cortical bone was computed by following a previously established protocol [8] in which the voxel intensities were compared to that of an external reference phantom attached anteriorly to the subject's tibial midshaft. The tissue bone volume fraction (BVF) of each voxel was computed as $BVF = 1 - BWF$.

3D μ FE Analysis - To create a finite-element mesh, each voxel in the BVF map was modeled as a hexahedral (brick) finite element with dimensions corresponding to the voxel size [9] after interpolating to $0.18 \times 0.18 \times 1.5$ mm³ voxel size to enhance the apparent resolution and match the voxel size of GRE images. The bone tissue material properties were assumed isotropic and linear elastic with each element's Young's modulus (YM) given by $YM = (15 \text{ GPa}) \times (BVF)$ and Poisson's ratio 0.3 for all elements resulting in the *scaled* FE model. A partial threshold was applied by setting finite elements with $BVF < 20\%$ to zero in order to remove the contributions from image noise. Subsequently, axial stiffness of the central 48 mm cortical region was estimated via μ FE analysis by applying simulated compression ($\sim 1\%$ strain) along the bone's longitudinal axis [10]. The resulting linear system was then solved by minimizing strain energy. Finally, axial stiffness was obtained as the ratio of the resulting stress on the proximal face to the applied strain.

Processing of GRE images - The same cortical bone region in the high-resolution GRE image was segmented in a similar manner as detailed before by using an operator-guided segmentation program resulting in a binary mask. A *binary* FE model was then generated by setting each voxel's Young's modulus and Poisson's ratio to 15 GPa and 0.3, respectively. Subsequently, the axial stiffness of the cortical bone segment was computed via μ FE analysis. Finally, the mean cortical thickness on each axial imaging slice was computed by modeling the endosteal and periosteal boundaries in each image as concentric circles whose radii were estimated from the respective areas.

Results and Conclusions:

The variation of BWF along the mid-tibial cortex for two healthy subjects (35 and 79-yr old) with 29% and 40% mean BWF, respectively, is shown in Figure 1. The minimum BWF values were observed around the site of maximum cortical thickness ($\sim 38\%$ proximal to distal endplate). Further, BWF was greater in the older subject, a trend observed for the entire cohort ($R^2 = 0.61$; $p < 0.01$). The mean cortical bone thickness derived from segmented GRE images of the 79-yr old was only 3% less than that of the younger subject (Figure 2) while the μ FE-derived cortical stiffness values were able to discriminate the mechanical competence of the two subject with a larger margin. The axial stiffness of the younger subject derived from the binary μ FE model was about 6% greater than that of the older subject. On the other hand, the difference in axial stiffness values between the two subjects increased to about 19% when the scaled μ FE model was utilized. Mid-tibial cortical stiffness computed on the basis of UTE images (scaled model) decreased with advancing age ($R^2 = 0.27$; $p = 0.1$) while no such trend was observed ($R^2 = 0.03$; $p = 0.6$) for those obtained from GRE images (binary model). In summary, the scaled μ FE model seems to provide more discriminating power for age-related changes in axial stiffness of the cortical bone compared to binary model or cortical thickness measurements. Finally, the preliminary data highlights the potential benefits of incorporating UTE-based estimates of bone tissue volume fraction into the μ FE modeling to estimate cortical bone's mechanical competence *in vivo*.

References:

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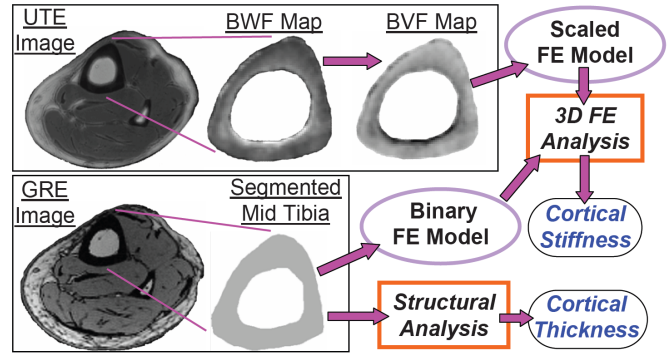


Figure 1: Illustration of the image acquisition and processing flow for computing cortical stiffness and thickness of mid tibia on the basis of UTE and gradient-echo images via μ FE and structural analysis.

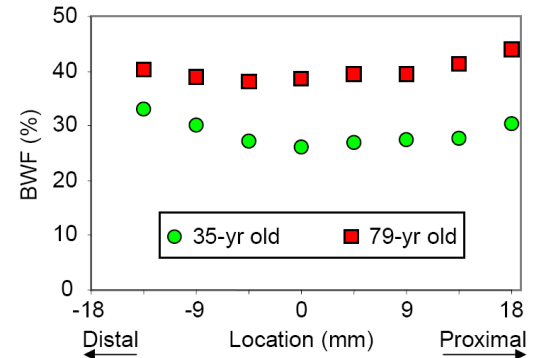


Figure 2: BWF along tibia for two female subjects with zero location representing the site of maximum cortical thickness ($\sim 38\%$ proximal to distal endplate).

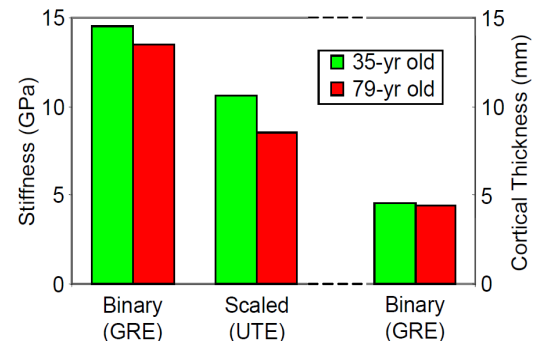


Figure 3: Comparison of axial stiffness of the mid-tibial cortex computed from GRE-based *binary* and UTE-based *scaled* μ FE models and cortical thickness computed from segmented GRE images for the same two subjects in Figure 2.