Detection of Short-Term Temporal Changes in Mechanical Properties of Bone in Early Postmenopausal Women using μMRI

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Introduction Most osteoporotic fractures occur at anatomic sites predominant in trabecular bone (TB), including wrist, vertebrae or ribs [1]. There is growing evidence that, next to bone volume fraction, the architecture of the trabecular network determines the bone's mechanical competence. However, it is less well understood which of the myriad of structural measures are most important in predicting bone strength. It would therefore be desirable to have a more direct measure of bone strength. In particular, it would be of interest to know whether drug intervention improves bone strength. Recent advances in computational biomechanics now allow estimation of mechanical parameters based on 3D image information obtained in vivo as input into a micro-finite-element (μFE) model to assess treatment efficacy [2]. Here, we submitted 3D spin-echo images from the distal-tibial metaphysis in early postmenopausal women to μFE analysis using a custom-designed software [3] to evaluate the hypothesis that estradiol preserves the elastic moduli whereas the absence of estrogen supplementation leads to a reduction in mechanical competence.

Methods Sixty-five early postmenopausal women, 45-55 yr of age, were recruited for the study. Thirty-two of them chose estrogen supplementation (estradiol group); the remainder did not (control group). Micro-MRI of the distal tibia was performed at baseline and 12 and 24 months thereafter to determine the temporal changes in the TB at 137 x 137 x 410-μm^3 voxel size using a customized RF coil and 3D FLASE (fast large-angle spin-echo) [4] sequence at 1.5-T field strength (General Electric Signa, Milwaukee, WI). Navigator echoes acquired simultaneously with the image data were used to retrospectively correct for translational subject motion during the scan [5]. Motion-corrected k-space data was Fourier transformed yielding 32 image slices. The number of subjects who provided adequate image quality for the baseline to 12(24)-month interval was 28(23) for the control group and 23(19) for the estradiol group. Subsequently, a local thresholding procedure was applied [6], yielding an image in which the gray value of each voxel equals the fractional marrow content with 100% and 0% intensity representing pure marrow and bone, respectively. The marrow-volume fraction maps were *sinc*-interpolated by a factor of 3x3x3, yielding 45.7 x 45.7 x 137-μm^3 voxels. The 12- and 24-month repeat images of each subject were registered in 3D [7] to match the corresponding baseline volume using tri-linear interpolation. Finally, 10 x 10 x 5-mm^3 cuboid sub-volumes were automatically extracted from the center of the TB region for micro finite-element (μFE) analysis with image voxels being converted to hexahedral finite elements. Micro-FE models were generated by converting each voxel into hexahedral finite elements. The Young's modulus and Poisson's ratio of pure bone tissue were chosen as 15 GPa and 0.3, respectively, and the Young's modulus of each finite element was set proportional to the intensity of the corresponding voxels. Finally, Young's moduli (E_{11}, E_{22}, E_{33}) and shear moduli (G_{23}, G_{31}, G_{12}) of the sub-volume were calculated using a μFE solver developed in authors' laboratory by performing three compressive and three shear tests and solving for the compliance matrix [3]. The mean change in parameters from baseline to 12 and 24 months was computed for both control and treatment group using JMP software (Version 7.0; SAS Institute; Cary, NC).

Results and Conclusions The mean relative change from baseline to 12 and 24 months in mechanical parameters and bone-volume fraction (BV/TV) derived from μMRI-based μFE analysis are listed in Tables 1 and 2 for control and estradiol subjects, respectively. Notably, the change in BV/TV was not significant from baseline to both follow-up time points in either group. On the other hand, the decrease in mechanical parameters was statistically significant for E_{11}, E_{33}, and G_{11} at 12 months and for all six parameters at 24 months in the control group, paralleling changes in network topology observed previously in the same patients [8]. In contrast, the mechanical parameters in the estradiol group did not change significantly at either time point relative to the baseline value. This observation supports the hypothesis that the maintenance of estrogen levels preserves the trabecular network's mechanical competence. In this work, we have provided compelling evidence for using μMRI-based *in vivo* μFE analysis for detecting short-term temporal changes in mechanical parameters in TB in response to estrogen supplementation and decline in hormone levels.

	Relative change Baseline to 12 mo (%)		Relative change Baseline to 24 mo (%)	
Parameter	Mean value	*P*	Mean value	*P*
BV/TV	-0.99	0.071	-1.07	0.098
E_{11}	-5.53	0.006	-5.14	0.005
E_{22}	1.44	0.309	-3.71	0.018
E_{33}	-3.01	0.013	-3.55	0.003
G_{23}	-1.51	0.231	-3.64	0.005
G_{31}	-4.60	0.002	-4.41	0.002
G_{12}	0.22	0.850	-2.93	0.005

Table 1: Temporal changes in mechanical parameters in the control group.

	Relative change Baseline to 12 mo (%)		Relative change Baseline to 24 mo (%)	
Parameter	Mean value	*P*	Mean value	*P*
BV/TV	-0.35	0.677	0.718	0.524
E_{11}	2.89	0.490	3.79	0.442
E_{22}	0.96	0.655	-1.63	0.596
E_{33}	0.27	0.901	0.10	0.966
G_{23}	2.38	0.322	0.37	0.907
G_{31}	1.75	0.554	1.64	0.647
G_{12}	0.45	0.792	-0.58	0.795

Table 2: Temporal changes in mechanical parameters in the estradiol group.

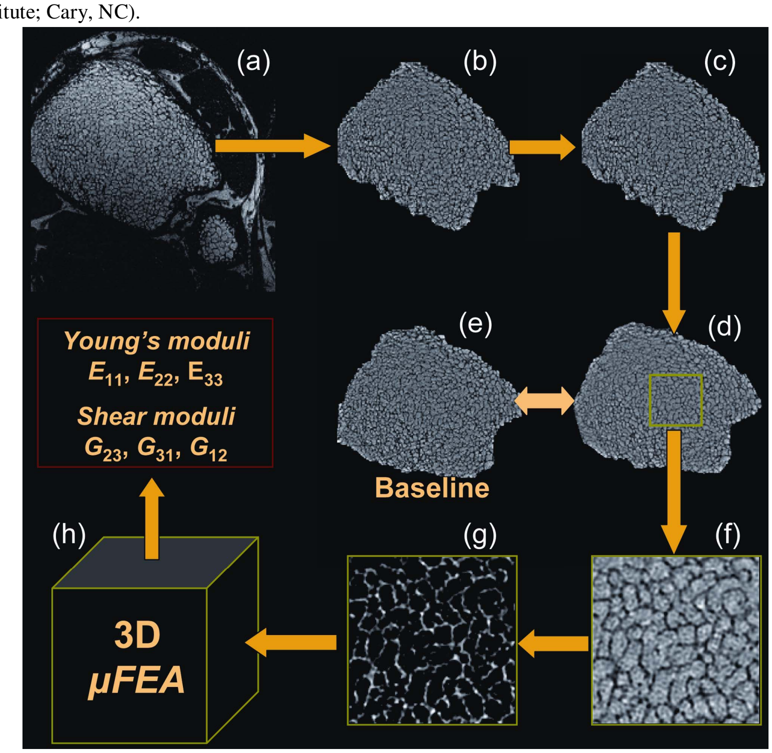

Figure 1: Illustration of the processing steps required for the μMRI-based estimation of mechanical properties of distal tibia: (a) one cross-sectional image from 3D volume; (b) intensity normalized with TB region isolated; (c) 3x3x3 *sinc*-interpolated yielding a voxel size of 45.7 x 45.7 x 137 μm^3; (d) registered in 3D to baseline (e); (f) region of interest selected; (g) intensity inverted; (h) parameters calculated via μFEA.

References [1] National Osteoporosis Foundation. [2] Zhang et al., J Bone Min Res, 2008:**23**. [3] Magland et al., Proc Am Soc Bone Min Res, 2008. [4] Ma et al., Mag Res Med, 1996:**35**. [5] Song et al., Magn Res Med, 1999:**41**. [6] Vasilic et al., IEEE Trans Med Imaging, 2005:**24**. [7] Magland et al., Proc ISMRM, 2006. [8]Wehrli et al., J Bone Min Res, 2008:**23**.

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