Micro-mechanical Modeling in the Nonlinear Regime for Assessing Indices of Bone Strength from High-Resolution MR Images

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Introduction: Osteoporosis is a common bone disorder characterized by decreased bone strength that leads to increased risk of fracture. Assessment of osteoporotic fracture risk on the basis of in-vivo images would be of considerable clinical interest. High-resolution MR (µMR) image-based linear micro-finite element (µFE) modeling has been used to estimate bone elastic parameters [1], but it cannot directly assess bone strength and fracture risk. In contrast, nonlinear analysis has the potential of providing more direct predictions of bone failure behavior [2,3]. Bone strength represents the maximum stress that bone can hold before failure, thereby depending on not only yield but also post-yield properties.

In this work, we present a program for nonlinear µFE modeling of trabecular bone (TB) strength and failure mechanisms based on in-vivo µMR images as input into the model. The algorithm was implemented through iteratively executing a computationally efficient algorithm for linear µFEA [4] in conjunction with establishment of a strain-based criterion for adjusting TB tissue-level modulus. To assess its performance, the serial reproducibility and reliability of TB yield and post-yield parameters were evaluated in view of applying the technique to the study of the effect of intervention in patients at risk of fracture.

Methods:

Image acquisition and processing: In-vivo µMR images of the right distal radius from twenty women (ages: 50-75) had been acquired previously [5] at three time points (over an 8-week period) using a 3D FLASE sequence [6] with a 137x137x410 μm^3 voxel size at 1.5T field strength. All images were first corrected for subject motion and follow-up images were retrospectively registered to baseline images. The resulting images were then masked to isolate the TB region and processed to generate grayscale bone volume fraction (BVF) maps [4] as input into the nonlinear model.

Nonlinear µFE model: TB yield and post-yield parameters were estimated by solving a series of nonlinear systems with incrementally applied deformations (simulated as increased strain values) using an iterative algorithm. Tissue-level modulus depends on each element's deformation and is adjusted at each iteration according to

$$E(\epsilon_{tissue}) = ((sech((\epsilon_{tissue} * 50 + 0.53)^{1.4}))^{0.6} + 0.05) * 15GPa$$

where ϵ_{tissue} is the tissue-level effective strain calculated for each element using $\epsilon_{tissue} = \sqrt{2 * SED/E}$, E=15 GPa and *SED* stands for strain energy density, which is obtained from solving a linear system using the computationally optimized linear solver [4]. Boundary conditions were set to represent axial compression with no friction along the transverse directions.

Stress-strain curves were obtained as the best-fitted cubic polynomial to the points of applied strains and resultant stresses. The apparent yield stresses and strains were then obtained based on the 0.2% offset rule [3]. The ultimate stress was taken as the maximum stress of the stress-strain curve, and fracture toughness was calculated as the area under the stress-strain curve from zero to the ultimate strain point. Coefficients of variation (CV) and intra-class correlation coefficient (ICC) were calculated as metrics on reproducibility and reliability.

Results and Discussion: Micro-FE models contained an average of 65.2 thousand elements requiring 13.7 minutes on average for analyzing 61 strain levels on a desktop computer with four dual processors (i7-2600 3.40 GHz CPUs) and 8 GB of RAM. Good visual reproducibility and anatomical alignment are illustrated by the cross-sectional images as well as their BVF maps from a subject at three scan time points (Fig. 1), suggesting accurate registration. Examples of simulated stress-strain curves (Fig. 2) demonstrate within-group similarities and between-subject variations in the simulated results. The mean (±S.D.) of the estimated yield stress, yield strain, ultimate stress, ultimate strain and fracture toughness were 3.09 ± 1.01 MPa, 0.78 ± 0.05%, 3.48 ± 1.05 MPa, 1.35 ± 0.28% and 32.77 ± 12.22 kPa, respectively. ICCs ranged from 0.986 to 0.994 with an average value of 0.991 and mean CVs ranging from 1.0 to 5.6% with an average of 3.5%, indicating that between-subject variances dominated over within-subject variances for all estimated parameters. Further, test-retest plots (Fig. 3) depict high correlation ($R^2 \geq 0.94$) between estimates at baseline and follow-ups, consistent with the computed ICCs and CVs.

Conclusion: A new nonlinear µFE model for TB yield and post-yield properties was developed and its performance evaluated. Results suggest that the yield and post-yield parameters derived from the nonlinear model have adequate reproducibility to evaluate treatment effects in interventional studies within short follow-up periods.

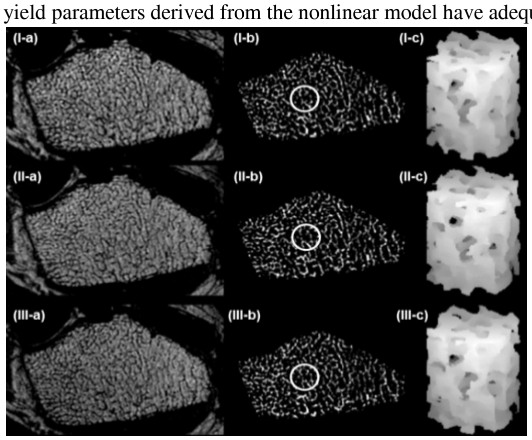

Fig. 1. (a) Cross-sectional µMR images, (b) BVF maps and (c) magnified 3D volume renderings of a small sub-region for a subject at three scan time points: (I) baseline; (II) follow-up 1; (III) follow-up 2, visually illustrating similarities across.

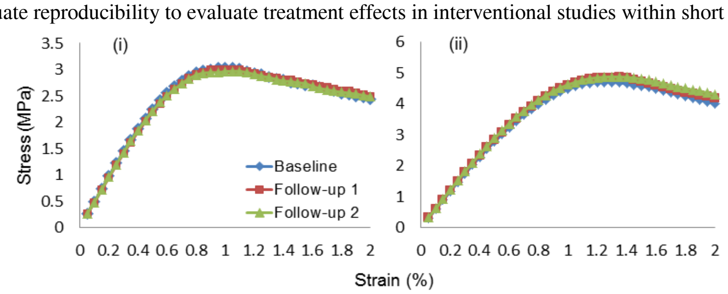

Fig. 2. Simulated stress-strain curves from two subjects at three time points (blue: baseline; red: follow-up 1; green: follow-up 2).

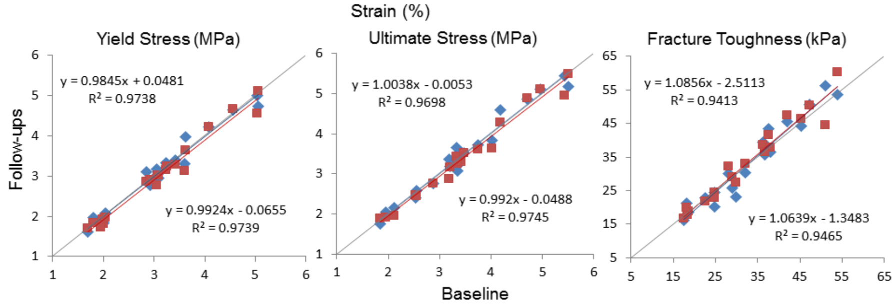

Fig. 3. Test-retest plots (blue: follow-up 1 versus baseline; red: follow-up 2 versus baseline; light grey: the line of identity) showing high reliability in all estimates ($p < 0.0001$).

References: [1] Wehrli, JBMR, 2010; [2] Verhulp, J. Biomech, 2008; [3] Niebur, J Biomech, 2000; [4] Magland, PLoS ONE, 2012; [5] Lam, Bone, 2011; [6] Magland, MRM, 2010.

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