Implications of Testosterone Treatment on Trabecular Bone Elastic Constants Assessed by Micro-Finite Element Analysis of In Vivo Images

F. W. Wehrli[1], X. S. Liu[2], X. H. Zhang[2], B. Vasilic[1], P. J. Snyder[3], and X. Guo[2]

[1]Laboratory for Structural NMR Imaging, Department of Radiology, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania, United States, [2]Department of Biomedical Engineering, Columbia University, New York, New York, United States, [3]Departments of Radiology and Medicine, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania, United States

Background and Motivation

The strength of trabecular bone (TB) is significantly determined by its architectural make-up characterized by parameters of scale, orientation and topology. During recent years micro-MRI technology has advanced to the stage where in vivo assessment of TB micro-structure has become possible, thereby allowing quantitative characterization of TB network architecture (*1*). However, it is currently not known which of the structural parameters are optimal in reflecting the bone's mechanical competence or which are most sensitive as indicators of disease progression or regression in response to treatment. Here, we examined the hypothesis that antiresorptive treatment of men with gonadal steroid deficiency (male hypogonadism) results in an increase in the elastic constants of TB.

Methods

MR images were acquired at 1.5T at a voxel size of 137x137x410 μm^3 from the distal tibia of 10 hypogonadal and 10 eugonadal men with a 3D spin-echo sequence. The subjects were scanned at baseline, 6, 12 and 24 months during treatment with testosterone as described in (*2*). The images then were subjected to a processing chain starting with navigator motion correction, followed by bone volume fraction mapping and subvoxel processing, yielding a final voxel size of 68.5x68.5x103 μm^3. Cylindrical cores of 7.5 mm diameter and 5.1 mm height were isolated from the subvoxel-processed images after registering the 24-month repeat data to the baseline images. After binarization of the images, cubic VOIs of 5x5x5 mm^3 were extracted in such a manner that their faces were aligned with the imaging coordinate system (XYZ), which deviated only slightly from the three anatomic axes as shown in Fig. 1 (mainly due to positioning errors).

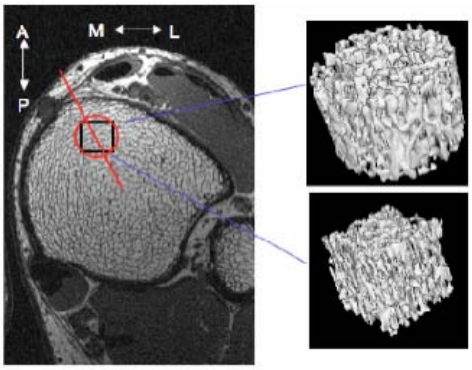

***Fig. 1** Left: Cross-sectional image through the distal tibial metaphysis with antero-posterior (AP) and medio-lateral (ML) direction indicated; right: isolated core and inscribed cube used for µ-FE analysis after BVF mapping, subvoxel processing and binarization.*

The processed VOI images then served as input into a micro finite-element (µ-FE) program after a 1:1 conversion of the bone voxels to 8-node brick elements. The bone tissue properties were chosen as isotropic, linearly elastic with a Young's modulus of 15 GPa and a Poisson's ratio of 0.3. Using an element-by element pre-condition conjugate gradient solver, six FE-analyses were performed for each specimen, representing three compression tests and three shear tests (*3*). The anisotropic stiffness tensor of the VOI was calculated first in the image coordinate and then transformed to the anatomic coordinate system. Based on the diagonalized stiffness tensor, elastic material constants (three Young's moduli, E_{zz}, E_{yy}, E_{xx} and three shear moduli, G_{xy}, G_{yz}, G_{xz}) were calculated.

Results

Structural differences between the two groups at baseline have been reported previously, indicating a more connected plate-like network in the eugonadal men (*4*). Similarly, in the present study, all six elastic constants were significantly greater in the eugonadal group (by 36-70%, p=0.000001 to 0.001). Although there were changes in the structural parameters (*2*) in the hypogonadal group in response to treatment at all time points, changes in the elastic constants were only found after 24 months. Fig. 2 shows TB virtual cores from one subject with the largest treatment effect at baseline and after two years of testosterone treatment, visually showing improved structural integrity. On the average, the Young's moduli E_{xx} and E_{zz} were found to have increased 8.6% (p=0.004) and 4.3% (p=0.04), respectively, while the shear modulus G_{xz} had increased 5.7% (p=0.02, Fig. 3).

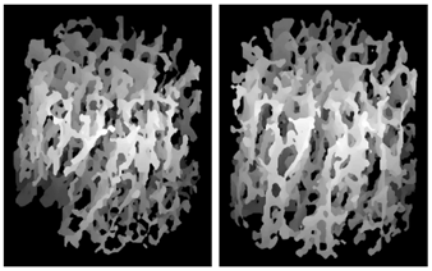

Fig. 2 Micro-MRI-derived virtual core of TB at baseline and 24 months of testosterone treatment.

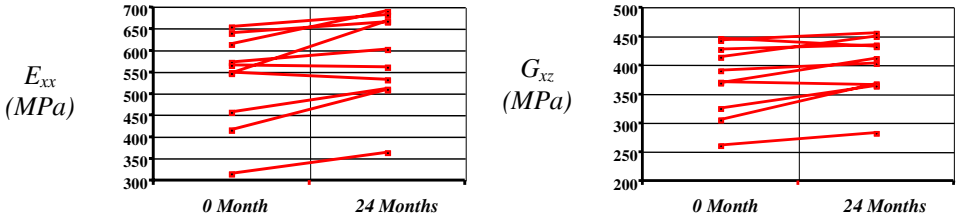

Fig. 3 Changes in one of the Young's and shear moduli in response to treatment.

Conclusions

The data indicate that treatment-induced changes in trabecular bone elastic constants and thus strength can be captured by µ-FE analysis based on 3D images obtained by micro-MRI. Even though the distal tibia is not a typical osteoporotic fracture site, osteoporosis is a systemic disorder and drug-induced changes in architecture at this load-bearing surrogate site are likely to parallel those at anatomic sites susceptible to fracture such as the vertebrae or proximal femur.

References

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Acknowledgments

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