Quantitative Micro-MRI Demonstrates Significant Effects on Trabecular Bone Architecture in Response to Antiresorptive Therapy

F. W. Wehrli[1], G. A. Ladinsky[1], B. Vasilic[1], B. S. Zemel[1], A. C. Wright[1], H. K. Song[1], P. K. Saha[1], H. Peachy[1], P. J. Snyder[1]

[1]University of Pennsylvania, Philadelphia, PA, United States

Introduction

It is well known that age-related reduction in bone mass is accompanied by structural alterations that further aggravate the mechanical consequence of bone loss. Data from bone biopsies suggest that during normal aging, and more so during osteoporosis, trabecular plates are converted to rods, which eventually fracture and disconnect [1]. This etiology, however, has so far not been confirmed by data obtained *in vivo*. Advances in MR image acquisition and processing techniques now have made possible direct imaging of trabecular microarchitecture and assessment of the topological changes that occur during the pathogenesis and treatment of patients. Here we provide evidence for the postulated architectural changes in response to antiresorptiive treatment and show that these effects can be visualized in individual patients.

Methods

Subjects studied were women, ages 45-55 years in early menopause (amenorrhea 6-24 months, FSH>30 mIU/mL if not on estrogen), divided into a control group comprising women who chose not to take estrogen and a treatment group comprising women who chose to take estrogen (referred to as the HRT group). All subjects were given supplemental calcium to provide a daily intake of 1500 mg calcium/day. HRT subjects received estradiol 0.05mg/day via patch; medroxyprogesterone 2.5mg daily was given to women with an intact uterus. DXA was performed on the spine and hip and MRI scans were performed of the distal radius and distal tibia at baseline, 12 months and 24 months. Custom-built coils were used for MRI of the wrist (transmit/receive birdcage coil) and ankle (dual-element receive-only surface coil).

MRI (General Electric Signa 1.5T) was performed using a 3D FLASE pulse sequence [2] (flip angle 140°, TR/TE 80ms/9.5ms, NEX=1, FOV=7cm, BW=7.81kHz), to achieve a voxel size of 137x137x410 μm^3. The data were then subjected to a processing chain starting with navigator motion correction, followed by bone volume fraction mapping [3], and subvoxel processing [4], yielding a final voxel size of 68.5x68.5x103 μm^3. The images from the different time points were registered to the baseline scan and the ROI isolated using an automated masking routine. After binarization, the three-dimensional trabecular bone (TB) network was then skeletonized resulting in a structure where plates of bone are converted to 2-dimensional voxel surfaces (*S*) and rods to linear curves (*C*), which can be classified by digital topological analysis (DTA) [5]. Intermediate structures called profile elements (PE), which are essentially double-layered curves, are also classified. DTA can also identify voxels pertaining to junctions (*J*=*SS*+*CC*+*SC*) between surfaces (*SS*), between curves (*CC*), and between surfaces and curves (*SC*). Finally, composite parameters were evaluated: S/C (the ratio of all *S*-voxels divided by all *C*-voxels) as well as an erosion index (EI, the ratio of voxel densities that decrease divided by those that increase with osteoclastic resorption). Statistical analysis was then performed to compare the changes from baseline for the control and treatment groups.

Results and Conclusion

Fig. 1 shows preliminary data for the one-year changes from baseline in both groups. It is noted that in the control group BMD at the spine and hip decreases slightly (1-3%) while MRI of the tibia shows an increase in the PE (7.6%), *C* (9.1%), *J* (5.5%) and EI (7.7%), and the surface/curve ratio consistently decreases by 8.7%. By contrast, none of the parameters in the HRT group exhibit significant changes from baseline. Fig. 2 shows an enlarged section from the registered 3D-rendered images (Fig 3) clearly demonstrating remodeling-induced changes in network topology in a control subject after one year. These observations are commensurate with an etiology of postmenopausal bone loss that entails fenestration of trabecular plates and their conversion to rods. The work shows that detailed quantitative information on the temporal changes in bone remodeling can be obtained and that these observations can be made *in vivo* in individual subjects.

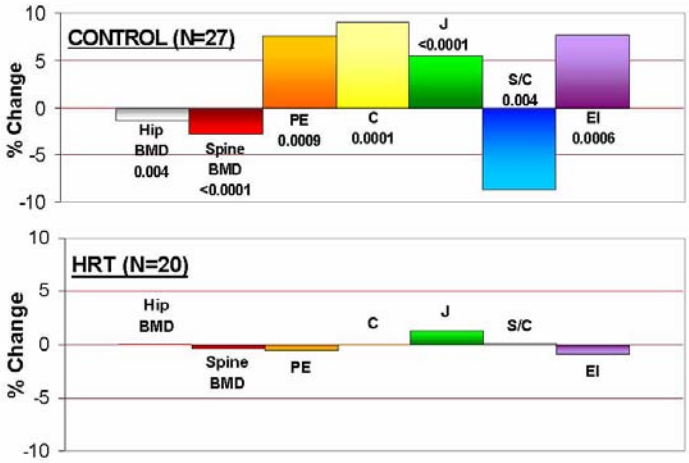

Fig 1: Changes over one year from baseline in the MRI-derived topological parameters for the trabecular bone network in the tibia and for the BMD *via* DXA of the spine and hip.

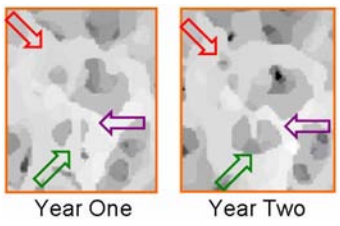

Fig. 2: Magnified view of trabecular bone changes observed in the 1.5x1.5x1.5 mm^3 subvolume indicated in the virtual cores shown in Fig. 3: trabecular strut erosion (lower arrows), new pit formation (upper), trabecular thinning (right).

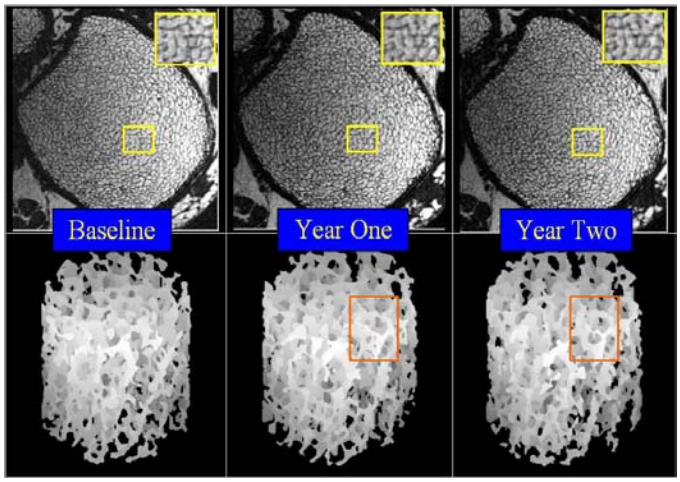

Fig 3: Time series of images from one of the control subjects clearly showing feature similarity in the tibia cross sections (top row) with 3D virtual TB cores extracted from the same locus in these images (lower row).

Acknowledgements: NIH R01AR41443, T32DK07006 & Novartis

References

[1] Borah B, et al. Bone 2004; 34(4): 736-46.
[2] Ma J, et al. Magn. Reson. Med. 1996;35(6):903-10.
[3] Vasilic B and Wehrli FW. IEEE Trans. Med. Imaging, in press.
[4] Hwang SN and Wehrli FW. Magn. Reson. Med. 2002;47(5):948-57.
[5] Gomberg BR, et al. IEEE Trans. Med. Imaging. 2000;19(3):166-74.