In-vivo Micro-MRI of Trabecular Bone in the Ovariectomized Rhesus at 3T

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Introduction

Osteoporosis is currently assessed using bone mineral density (BMD) measurements, but BMD does not characterize the microarchitecture of trabecular bone which may better predict fracture risk [1]. Microscopic MRI (μ-MRI) reveals detailed trabecular structure and has the potential to characterize its architecture and thereby give an additional measure of 'bone quality'. In this study, trabecular bone μ-MRI was used to examine bone architecture in sham operated and ovariectomized (OVX) rhesus monkeys as a model for osteoporosis and compared to traditional BMD measurements. The endpoints calculated were apparent Bone Volume Fraction (app. BVF, %), Trabecular Number (app. TrN, 1/mm), Trabecular Thickness (app. TrTh, mm), and Trabecular Separation (app. TrSep, mm). Our long term goals are to evaluate the precision, sensitivity-to-change, and specificity of μ-MRI as a tool for diagnosis and evaluation of disease modifying therapies in osteoporosis.

Methods

Six age- (11-18 years) and weight- (6.6 - 9.0 kg) matched rhesus monkeys (3 OVX-8 years post-surgery, 3 sham) were anesthetized with 1.5% isofluorane, mechanically ventilated, and imaged using a Siemens 3T Trio and a small Animal Coil (10cm Tx/Rx birdcage, Clincial MR Solutions, Brookfield, WI). A FLASH localizer sequence was used for positioning the distal radius, distal femur, and proximal tibia, respectively followed by a high resolution 3D-FISP sequence with the following imaging parameters: 160x160x340 μm resolution, TR/TE = 15/6.44ms, 320x448 imaging matrix, 18 slices, FA = 60°, BW = 180Hz/px, 30 averages and a total imaging time of 33:31minutes for each anatomical location. Data was analyzed with MATLAB software, and for this preliminary study analysis was confined to regions of interest (ROI) chosen at the center of the slice pack (proximal to the joint line for the radius and medial femoral condyle, distal in the tibia) in each area as a circle of the largest radius still fitting within the trabecular region. Bone Volume Fraction was calculated as discussed by Majumdar et al. [2] and Newitt et al. [3] assuming partial volume effects of both marrow and bone. The threshold was then determined iteratively by adjusting the threshold value and matching the calculated binary BVF to the app. BVF. From the binary image, app. TrN was calculated at each voxel in the ROI as the number of trabecular crossings made by eight lines passing at angles through that voxel up to a given radius. App. TrSep and app. TrTh were derived from these two quantities.

For each location and morphological parameter, a two sample Student's t-test was used to test for significance of mean difference between the sham and OVX groups. BMD was assessed in the whole body, spine (L1-L4), and the femur of each subject using a General Electric Lunar Prodigy DEXA and analysis software.

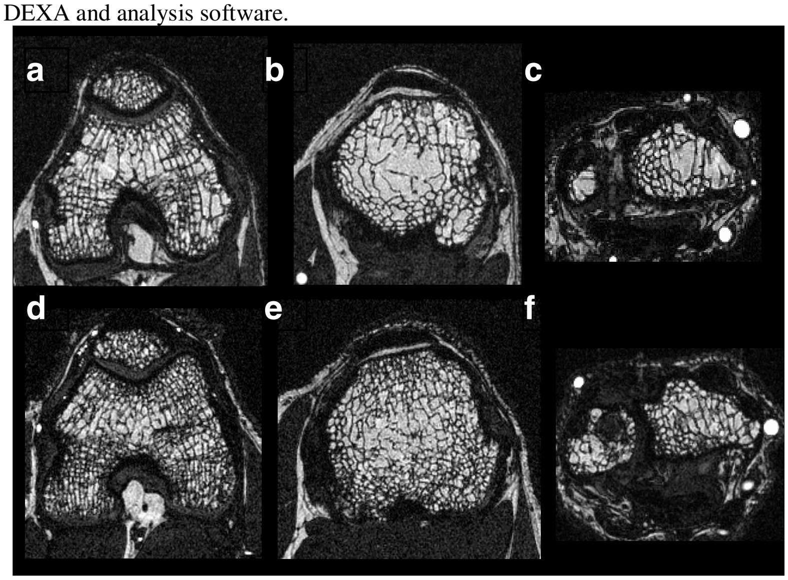

Figure 1a-f. In-vivo μ-MRI images of rhesus monkey distal femur, proximal tibia, and distal radius (left-to-right) showing trabecular structure at a resolution of 160 μm. The top three images (a-c) are in an 8-year post-OVX rhesus and the bottom three images (d-f) are in a sham operated rhesus.

Results

Figures 1a-c and 1-d-e show representative high resolution images in the femur, tibia, and radius for an OVX rhesus and a sham rhesus respectively. In each location, the images reveal an apparent decrease in trabecular number and separation in the OVX animals

Table 1 contains the mean and standard error of the mean for the above morphological parameters as well as BMD measurements. Even in this preliminary small study there was a significant difference ($p<0.05$) between the two groups in the femur for app.TrN and app.TrSep and a clear trend towards significance for all tibial measurements as well as app.TrSep measurements. It is noteworthy that data was only analyzed at one slice location using a small ROI compared to the total trabecular volume and this may contribute to the inter-subject variability that was observed.

Discussion

These novel μ-MRI studies on bone morphology in the OVX rhesus model suggest that this technique may have value in assessing bone disease and in drug discovery and development. Studies are ongoing and data is currently being collected on several more subjects with full volumetric evaluation across the entire slice pack.

The data suggest that μ-MRI can evaluate key parameters of bone structure extending our ability to assess bone pathology beyond simple BMD measurement.

Table 1. Mean and standard error of the mean for morphological parameters in OVX and sham rhesus.

	app.BVF	app.TrN (1/mm)	app.TrTh (mm)	app.TrSep (mm)
Tibia: Sham	0.45±0.01	1.14±0.02	0.39±0.03	0.54±0.03
OVX	0.40±0.05	1.00±0.11	0.43±0.01	0.70±0.18
Femur: Sham	0.57±0.04	1.20±0.06†	0.54±0.07	0.33±0.02†
OVX	0.56±0.01	1.03±0.04†	0.62±0.04	0.39±0.01†
Radius: Sham	0.58±0.04†	1.18±0.09	0.56±0.05	0.33±0.05
OVX	0.43±0.04†	1.12±0.09	0.49±0.03	0.46±0.06

	Whole Body BMD	L1-L4 BMD	Femoral BMD
Sham	0.61±0.04†	0.81±0.06†	0.81±0.07
OVX	0.52±0.01†	0.63±0.01†	0.69±0.05

$^{\dagger}p<0.05$

References 1. Wehrli, FW et al, *Topics in Magnetic Resonance Imaging.* 13(5):**335**-355, 2002. 2. Majumdar, S et al, *Journal of **Bone** & Mineral Research.* 12(1):111-118, 1997. 3 Newitt, D et al, *Osteoporosis International*, 12:6-17, 2002.