INTRODUCTION: Osteoporosis is a disease of the remodeling imbalance between bone formation and resorption [1]. Accelerated bone resorption is believed to be a major pathogenic mechanism in postmenopausal bone loss. Antiresorptive and anabolic drugs hold the potential to retard to the premenopausal range, the somewhat elevated levels of bone turnover found in such women. Bone mineral density (BMD) is a poor predictor of fracture risk and does not provide insights into bone quality, a secondary marker for elucidating changes in trabecular bone (TB) microarchitecture [2]. Furthermore, at present, remodeling induced changes upon treatment can only be observed by bone biopsy and there only in paired biopsies from different anatomic sites. High resolution μMRI-based virtual bone biopsy (VBB) techniques permit quantification of TB microarchitectural changes at peripheral skeletal sites such as the distal tibia [5]. Here, we present initial data from an ongoing longitudinal clinical study at 3T designed to evaluate the effectiveness of teriparatide (PTH) against zoledronic acid in 30 postmenopausal women with osteoporosis. A subset of the patients were also evaluated at 7T. We report some of the baseline data by examining inter-modality associations including finite-element (μFE) derived axial stiffness calculations and structural parameters and their relationships to densitometric variables as well as initial longitudinal data in a few subjects studied so far.

METHODS: The left distal tibia of 30 postmenopausal women (ages, 58-84) with osteoporosis were scanned with a 4-channel receive array using 3D fast large angle spin echo (FLASE) [3] on a Siemens 3T Tim Trio system. The patients were then randomized to treatment by either PTH (N=15, 20 µg daily, s/c) or zoledronic acid (N=15, 5 mg i.v. annually). A subset of these patients (N=5) were also scanned on a Siemens 7T whole body system with a shielded Helmholtz transmit coil with a decoupled 4-element phased array identical to the RF coil used at 3T. The patient was scanned with a 4-channel receive array using a decoupled 4-element phased array identical to the RF coil used at 3T. Follow-up scans were performed once, at 12 months at 3T and twice, at 6 months and 12 months at 7T. An earlier follow-up scan was performed at 7T (6 months) as we expected to utilize the SNR increase at the higher field strength for enhanced detection sensitivity. Each baseline image was manually masked to isolate the tibial TB region. The full tibial cross-section masks were subjected to VBB processing [7] involving BVF mapping, skeletonization and topological analysis (DTA). Parameters quantifying scale and topology included BVF, surface/cut (S/C) ratio and erosion index (EI). FE analysis was performed on the full tibial TB mask with image voxels converted to hexahedral finite elements [8]. 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 BVF of the corresponding voxels. Finally, compression loading was simulated along bone’s axis direction by applying a strain (~0.1) to the proximal face of the FE model and keeping the distal face constrained. Axial stiffness was computed as the stress/strain ratio. Follow-up images were identically masked and full 3D transformations (3 rotations and 3 translations) were determined between baseline and follow-up images using a fast, rigid body registration algorithm [9]. Prior to application of the transformation, the follow-up images were upsampled in k-space by a factor of three and subsequently downsampled again after mapping the images to the grid of the baseline images. These images were accordingly subjected to VBB processing. The patients also underwent scanning by dual energy x-ray absorptiometry (hip, femoral neck and spine) and peripheral quantitative computed tomography (pQCT, distal tibia) for serial assessment of BMD.

RESULTS: BVF derived from 3T data was moderately correlated with BMD (r=0.001, hip (R²=0.38) and femoral neck (R²=0.24)). Figure 1 shows a plot comparing BVF and trabecular density as measured by pQCT in 30 patients scanned at 3T using 3D FLASE. A moderate correlation was observed between the measures reflecting that 38% of the variability in trabecular bone can be attributed to the variation in BVF. Figure 2 highlights a comparison of BVF and axial stiffness at 3T (A) and 7T (B). The baseline data from both, 3T and 7T, resulted after processing in a 3D grayscale image of 137x137x410 µm³ voxel size with each voxel representing bone volume fraction (BVF), bone vol. (BV)/total vol. (TV). Follow-up scans were performed once, at 12 months at 3T and twice, at 6 months and 12 months at 7T. An earlier follow-up scan was performed at 7T (6 months) as we expected to utilize the SNR increase at the higher field strength for enhanced detection sensitivity. Each baseline image was manually masked to isolate the tibial TB region. The full tibial cross-section masks were subjected to VBB processing [7] involving BVF mapping, skeletonization and topological analysis (DTA). Parameters quantifying scale and topology included BVF, surface/cut (S/C) ratio and erosion index (EI). FE analysis was performed on the full tibial TB mask with image voxels converted to hexahedral finite elements [8]. 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 BVF of the corresponding voxels. Finally, compression loading was simulated along bone’s axis direction by applying a strain (~0.1) to the proximal face of the FE model and keeping the distal face constrained. Axial stiffness was computed as the stress/strain ratio. Follow-up images were identically masked and full 3D transformations (3 rotations and 3 translations) were determined between baseline and follow-up images using a fast, rigid body registration algorithm [9]. Prior to application of the transformation, the follow-up images were upsampled in k-space by a factor of three and subsequently downsampled again after mapping the images to the grid of the baseline images. These images were accordingly subjected to VBB processing. The patients also underwent scanning by dual energy x-ray absorptiometry (hip, femoral neck and spine) and peripheral quantitative computed tomography (pQCT, distal tibia) for serial assessment of BMD.

CONCLUSION: The data in this ongoing treatment study show internal consistency between structural, mechanical and densitometric measures and suggest that the hypothesized changes in these parameters can be quantified.


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Figure 1: Comparison of BVF (3T FLASE) and BMD measurements (pQCT) at the distal tibia in 30 patients.

Figure 2: Comparison of BVF and TB axial stiffness in baseline data within 30 patients at 3T using 3D FLASE (A) and 5 patients at 7T with 3D FSE-OSC (B).

Figure 3: Representative co-registered axial images and cores of a 67-year old patient randomized to Zoledronic acid acquired with 3D FLASE at 3T (A, B) and 3D FSE-OSC at 7T (C-E).