Trabecular Structure Measured with the MRI-based Virtual Bone Biopsy at a Surrogate Site Contributes to Vertebral Fracture Load Independently of Spinal BMD

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Background and Motivation

Although low bone mineral density (BMD) is a well-established risk factor for osteoporotic fracture, BMD describes only about 60% of overall fracture risk. Recent data suggest that half of women sustaining osteoporotic fractures had BMD T-scores ≤-2.0, and a significant portion had BMD in the range considered normal (*1*). These observations have, during the past 10 years, spurred the search for other predictors of fracture susceptibility, often summarized under the concept "bone quality" (*2*). Based on histomorphometry from bone biopsies, several studies have provided evidence for structure as an independent risk factor for osteoporotic fractures. (*3*). The emergence of noninvasive imaging methods – notably high-resolution MRI and CT – has provided an additional incentive to explore the role of micro-architecture as a determinant of fracture risk, obviating invasive bone biopsies. Here we examine this hypothesis in a cohort of postmenopausal women with the MRI-based virtual bone biopsy (VBB) (*4*).

Methods

Postmenopausal women, ages 60-80 years, were screened by DXA, and those with T-scores at either the hip or spine -2.5 ± 1.0 were studied with the MRI-based VBB. The data from 79 subjects meeting the enrollment criteria were subjected to micro MRI at the distal tibia and radius, and measures of topology and scale of the TB network computed as described in (*5*). In brief, 3D FLASE spin-echo images acquired with custom-built RF coils at 1.5T at the distal tibial and radial metaphysis at 137x137x410 μm^3 voxel size 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. Vertebral deformities were assessed from mid-line sagittal MRIs (wedge, biconcavity and compression deformity) and a spinal deformity index (*SDI*) determined as the weighted sum of the three types of deformity. Digital topological analysis (*DTA*) was conducted on the skeletonized TB images (in which plates and rods are converted to surfaces and curves) and the voxel type (curve *C*, surface *S*, junction *J* between fundamental types) determined. DTA voxel densities, TB volume fraction (*TB/TV*) and TB thickness (*Tb.Th*) were determined as described previously (*5*) and associations examined between these structural measures and *SDI* using single and multi-parameter regression models.

Results

SDI values of T6-L5 were available in 67 subjects. Virtual cores and cross-sectional images from three subjects are shown in Fig. 1 to illustrate the wide range of TB architecture and structural indices in these subjects. The strongest correlations between *SDI* and structural parameters were those at the distal radius involving the topological parameters, but highly significant relationships were also found for *Tb.Th* and *TB/TV*. In contrast, the correlation with vertebral BMD measured by DXA did not reach significance. Fig. 2 shows an inverse correlation between total surface density (*S*) and *SDI,* suggesting that less plate-like bone is more susceptible to fracture. The data are summarized in Fig. 3 comparing correlation coefficients for various associations between structural parameters and *SDI*. Among the two-parameter correlations, the combination of *PE* (profile edges, essentially free ends) with *EI* (topological erosion index, a composite topological parameter expressing the degree of TB network erosion (*5*)) as independent variables was more strongly associated with the *SDI* than any single parameter (r = 0.56, P<0.0001). This observation suggests that > 30% (r^2 = 0.31) of the variation in vertebral deformity in this group of patients can be explained in terms of variations in structural make-up at the distal radius.

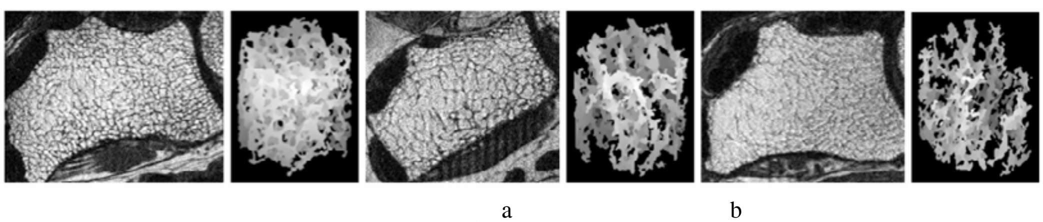


Fig. 1 Micro-MR images of the distal radius and virtual cores from three women: a) 68 y/o; b) 69 y/o; c) 87 y/o. Erosion indices are 0.66, 0.87 and 7.26 whereas TB/TV is less than 40% lower in subject c compared to a.

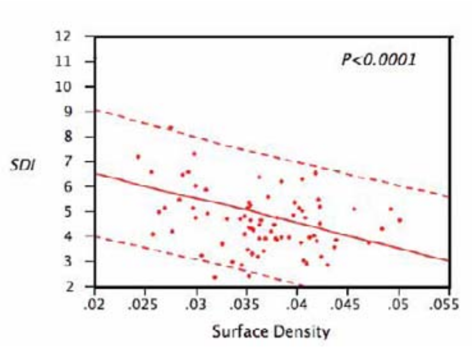
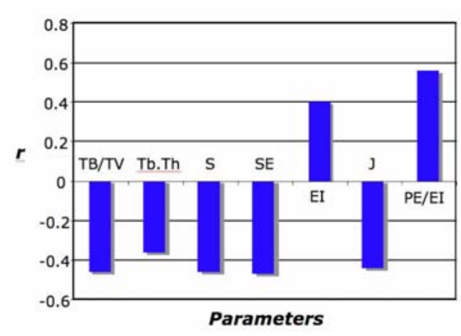


Fig. 2 (left) Correlation between surface voxel density and SDI (r=-0.46).

Fig. 3 (right) Correlation coefficients (r) between SDI and structural parameters (all p<0.001).



Conclusions

This work provides in vivo evidence for a contribution of trabecular topology and scale to vertebral fracture load that is independent of integral spinal BMD.

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