Citation: BoneKEy Reports **3**, Article number: 601 (2014) | doi:10.1038/bonekey.2014.96

www.nature.com/bonekey

COMMENTARY

Where does hip fracture initiate?

Philippe K Zysset

Institute for Surgical Technology and Biomechanics, University of Bern, Bern, Switzerland.

BoneKEy Reports **3**, Article number: 601 (2014) | doi:10.1038/bonekey.2014.96; published online 3 December 2014

Commentary on: Nawathe S, Akhlaghpour H, Bouxsein ML, Keaveny TM. Microstructural failure mechanisms in the human proximal femur for sideways fall loading. *J Bone Miner Res* 2014;**29**:507–515.

The aim of this study was to elucidate the microstructural failure mechanisms in the elderly human proximal femur for sideways fall loading by performing biomechanical testing and nonlinear, micro-finite element (microFE) analysis. The authors should first be acknowledged for taking the initiative of this computation-intensive work that addresses for the first time two important questions in fragility of the proximal femur: where does fracture initiate and what are the major determinants of femoral strength?

In summary, the investigators tested biomechanically eight female and four male fresh-frozen cadaver femurs aged 62–93 in a sideways fall configuration after scanning them with high-resolution peripheral quantitative computed tomography (HRpQCT). The tests were then reproduced with implicit, nonlinear microFE analysis using voxels of 82 μm and a ductile elastic–plastic model for bone tissue. Femoral strength was defined by a 0.2% apparent strain offset criterion, and the relative volumes of yielded bone were tracked distinctively in the trabecular and cortical compartments for both compression and tension. Supplemental videos available at the journal website illustrate the progression of bone tissue yielding in the course of loading.[1]

As expected, a high correlation ($R^2 = 0.92$) was achieved between the ultimate experimental strength and the numerical yield strength. However, the tissue elastic modulus was scaled down to 7.3 GPa to come up with a 1:1 relationship for yield strength. When confronted to micro-tensile test or indentation results, this value is too low for wet femoral tissue but compares favorably with the one retrieved from linear microFE of distal radius sections using similar voxel size (6.8 GPa).[2] Segmentation of the trabecular microstructure at HRpQCT resolution is known to produce substantial geometrical errors, especially at low bone volume fraction,[3] and the errors may even become larger with the stated use of a global threshold. The resulting bone beams and plates become more bulky, exhibit less bending and make the microstructure stiffer.

Interestingly, the ratio of trabecular to cortical bone volume in the neck that is not captured by areal bone mineral density (aBMD) was positively correlated to ultimate strength. Similarly, the concept of structural redundancy defined by the authors as a minimal change in secant stiffness was positively correlated to ultimate strength and not associated with aBMD. The dual-energy X-ray absorptiometry (DXA) parameters neck aBMD, total hip aBMD and BMC delivered only moderate correlations with experimental ultimate strength ($0.64 < R^2 < 0.76$).

A good prediction of structural variables such as yield strength does not necessarily imply a good prediction of the local strain and stress variables, and further validation work is needed to determine how reliable the yield results of microFE analyses with this voxel size really are. This limitation is confirmed by the 33% misclassification of the neck versus trochanteric failure locations by the yield variables of the microFE analyses.

Tissue yielding was highly localized, started in the trabecular compartment but reached and progressed in the cortex as loading increased. Surprisingly, the overall proportion of yielded tissue and the relative importance of cortex to trabecular yielded bone volume increased with femoral strength. This finding sharply contrasts with the hasty claim of a comparative biomechanical study in stance loading that trabecular bone has little or no role in femoral fragility.[4] Although femoral strengths along different loading modes are expected to remain reasonably well correlated,[5,6] the actual distribution of yielded tissue depends crucially on the loading configuration. The sideways fall is an odd load case for which the proximal femur is not adapted, with tensile trabeculae loaded in compression and the medial cortex loaded in bending. It will therefore be important to explore the sensitivity of the reported results with respect to more realistic boundary conditions.

The authors emphasized rightly some further limitations. Given the required computational resources, the number of samples is limited to 12, but the range of femoral morphology is broad with a sevenfold range in femoral neck aBMD and a fivefold range in femoral strength. The tissue material properties are rate independent, fully ductile and homogeneous within and across the trabecular and cortical compartments. On the one hand, tissue elastic properties in the cortex are superior to the ones of single trabeculae.[7] Previous FE analyses of trabecular biopsies suggested that the influence of heterogeneous mineralization is indeed very limited in the physiological linear elastic regime,[8] and it may be speculated that this finding holds for the post-yield regime. However, the presence of *in vivo* microdamage in the form of linear micro-cracks or arrays of nano-cracks described as diffuse damage,[9] which may specifically alter the post-yield properties, is not accounted for in the microFE approach. The same remark holds for residual stresses that are generated during bone growth and remodeling. The influence of tissue ductility was investigated in detail by the authors and is not expected to introduce a bias with respect to volume fraction.[10]

Despite the discussed limitations, this microFE investigation suggests that under sideways loading of the proximal femur, failure initiation occurs in the trabecular compartment and progresses then toward the cortex. Fragility of the proximal femur is related not only to bone loss and the corresponding reduction in aBMD, but also to an alteration of femoral morphology induced by a specific resorption history that cannot be captured by DXA. It should be recalled here that the mechanical properties of the proximal femur emerge from the synergistic adaptation of trabecular and cortical bone under physiological loading. Even though tissue yielding originates in the trabecular compartment in the considered load case, the stress distribution and the propagation to failure cannot be attributed to a specific compartment. The biomechanical objective of treatment against osteoporosis should not only be the maintenance or restoration of bone mass, but also of a trabecular and cortical morphology able to withstand a fall.

Finally, the study illustrates the unique insight gained by FE analysis that relies on the first principles of mechanics and integrates all morphological and material properties of the proximal femur in the evaluation of a specific load case. Although microFE is not applicable to *in vivo* patient data, the gained knowledge contributes to the improvement of homogenized FE analyses based on clinical CT reconstructions toward a better monitoring of bone strength and more importantly of bone fracture risk.

Conflict of Interest

The author declares no conflict of interest.

References

1. Nawathe S, Akhlaghpour H, Bouxsein ML, Keaveny TM. Microstructural failure mechanisms in the human proximal femur for sideways fall loading. *J Bone Miner Res* 2014;**29**:507–515.
2. Macneil JA, Boyd SK. Bone strength at the distal radius can be estimated from high-resolution peripheral quantitative computed tomography and the finite element method. *Bone* 2008;**42**:1203–1213.
3. MacNeil JA, Boyd SK. Accuracy of high-resolution peripheral quantitative computed tomography for measurement of bone quality. *Med Eng Phys* 2007;**29**:1096–1105.
4. Holzer G, von Skrbensky G, Holzer LA, Pichl W. Hip fractures and the contribution of cortical versus trabecular bone to femoral neck strength. *J Bone Miner Res* 2009;**24**:468–474.
5. Keyak JH, Sigurdsson S, Karlsdottir GS, Oskarsdottir D, Sigmarsdottir A, Kornak J *et al.* Effect of finite element model loading condition on fracture risk assessment in men and women: the AGES-Reykjavik study. *Bone* 2013;**57**:18–29.
6. Dall'Ara E, Luisier B, Schmidt R, Pretterklieber M, Kainberger F, Zysset P *et al.* DXA predictions of human femoral mechanical properties depend on the load configuration. *Med Eng Phys* 2013;**35**:1564–1572.
7. Zysset PK, Guo XE, Hoffler CE, Moore KE, Goldstein SA. Elastic modulus and hardness of cortical and trabecular bone lamellae measured by nanoindentation in the human femur. *J Biomech* 1999;**32**:1005–1012.
8. Gross T, Pahr DH, Peyrin F, Zysset PK. Mineral heterogeneity has a minor influence on the apparent elastic properties of human cancellous bone: a SRμCT-based finite element study. *Comput Methods Biomech Biomed Engin* 2012;**15**:1137–1144.
9. Burr DB. Microdamage and bone strength. *Osteoporos Int* 2003;**14**:S67–S72.
10. Nawathe S, Juillard F, Keaveny TM. Theoretical bounds for the influence of tissue-level ductility on the apparent-level strength of human trabecular bone. *J Biomech* 2013;**46**:1293–1299.