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PERSPECTIVES

Use of Finite Element Analysis to Assess Bone Strength

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Introduction

Assessment of areal bone mineral density (BMD) by dual-energy X-ray absorptiometry (DXA) is widely used to diagnose osteoporosis and assess fracture risk. However, clinical observations have highlighted the limitations of DXA with respect to both sensitivity and specificity in fracture risk predictions. From a biomechanics viewpoint, an approach that accurately represents the three-dimensional geometry and heterogeneous distribution of material properties of bone may provide improved estimates of bone strength. In this regard, there is increasing interest in the use of finite element analysis (FEA) to assess bone biomechanical behavior. In this *Perspective*, we describe the finite element method and review its application in bone research. We discuss the strengths and limitations of the approach, evaluate its potential for clinical assessment of fracture risk, and suggest areas of future research. Rather than provide a comprehensive review on this topic, we highlight current trends in the field and important areas of future inquiry.

Description of the Finite Element Method

The finite element (FE) method was first applied to structural analysis in the 1950s (1), and since then has been widely used in nearly every engineering and engineering-related field. In solid and structural mechanics (bone mechanics included), it is the method of choice with respect to computational modeling tools, as it can provide the ability to estimate with good accuracy how an object with a complex geometrical shape (*e.g.*, a whole bone or trabecular network) behaves when it is subjected to external loads.

Conceptually, the FE approach to solid and structural mechanics problems begins by representing the object as a collection of a finite number of building blocks, or elements, each of which is defined by a small number of reference points, or nodes (Fig. 1). This discretization gives the finite element method its name. The deformation of each element that occurs in response to the applied loads is represented by simple yet versatile functions, known as shape functions, in which the only unknowns are the displacements of the nodes. Therefore, once the nodal displacements are computed, the strain distribution throughout each element, and hence the entire object, can be easily obtained.

To compute these displacements, the investigator must specify two additional types of information: 1) the boundary conditions, which are the applied loads and/or applied displacements; and 2) the material properties, such as elastic modulus and Poisson's ratio, for each element. The analysis then seeks the set of nodal displacements that satisfies mechanical equilibrium given the geometry of the object, the boundary conditions, and the material properties. The nodal displacements and material properties are then used to compute the stress distribution throughout the entire object.

In addition to obtaining stress and strain distributions, the nodal displacements can also be used to compute other quantities such as the overall stiffness of the object and the distribution of strain energy density. If the investigator-specified material properties include failure properties, this

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method can also be used to compute when, how, and where the object will fail, although this often requires the use of non-linear modeling approaches and therefore can

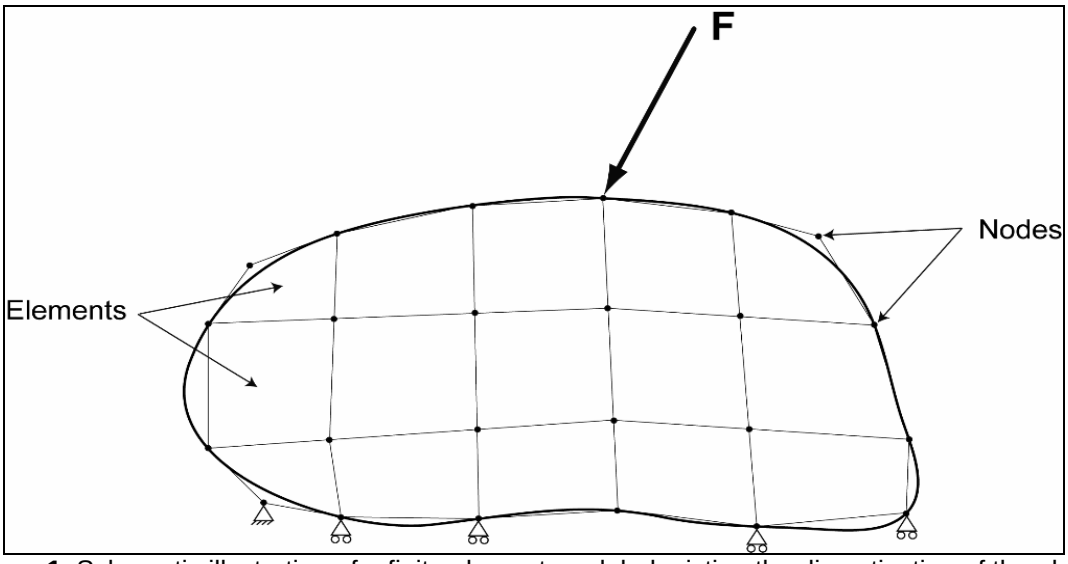

Figure 1. Schematic illustration of a finite element model, depicting the discretization of the object into a collection of elements and nodes, along with the associated boundary conditions.

be computationally intensive. Thus, the FE method can provide *estimates* of quantities that are commonly obtained through mechanical testing (*e.g.*, whole bone stiffness), as well as quantities that are difficult, if not impossible, to measure experimentally (*e.g.*, strain energy density distribution).

However, some cautionary notes are in order. As with any computational tool, the principle of "garbage in, garbage out" invariably applies in FEA. How well the finite element solution approximates the exact solution and the actual biomechanical phenomenon under investigation depends strongly on the quality of the input. Errors resulting from discretization of the object into elements are inherent in any FE analysis. The appropriate type of element for a given analysis must also be chosen carefully, as it can have a significant impact on the results. A discussion of different element types is beyond the scope of this overview but is presented in many dedicated references (2;3). Finally, errors in the choice of material properties and boundary conditions can severely limit the accuracy of the results. This is significant, because biological variation and other challenges associated with measuring joint contact forces, muscle forces, and material properties of biological tissues often prevent an accurate determination of the *actual* properties and applied loads.

Given these sources of error, obtaining meaningful data through use of the FE method requires extensive experience and good judgment on the part of the investigator. Fortunately, many studies to date in bone mechanics have shown that, with appropriate attention to the technical process, it is possible to obtain sound estimates of tissue- and organ-level properties using FEA. In the following sections, we review several studies that have used FEA to investigate the mechanical behavior of trabecular bone and whole bones.

Application of the Finite Element Method to Bone

Due to its ability to handle complex geometries and distributions of material properties, the FE method has been used frequently to estimate the strength and stiffness of whole bones and of trabecular bone, as well as to compute the distributions

of stress and strain within the tissue. In addition to predicting bone strength, FE analyses have been used to test theories of mechano-biological regulation of bone mass and structure (4;5) and to explore the pathophysiology of skeletal diseases and skeletal fragility (6-8). In these studies, one clear, though not unique, advantage of FEA is that it allows one to isolate the effect of a particular characteristic (*e.g.,* tissue modulus or cortical shell thickness) on the mechanical behavior. This is accomplished by varying the parameter of interest while holding all others constant. Such an approach is generally not possible with experiments, and it provides a highly controlled study design with which to test a given hypothesis.

Trabecular Bone

Early FE studies of trabecular bone idealized the trabecular architecture in order to obtain models that were computationally tractable. These idealized models, which consist of regular, randomly seeded, or distorted lattices, are extremely valuable in providing a mechanistic understanding of how changes in trabecular architecture (*e.g.,* trabecular thinning and loss of individual trabeculae) and damage accumulation affect the mechanical behavior of trabecular bone (6;9-14). However, the inherent drawback to these models is that they cannot capture the effects of actual biological variation in trabecular architecture.

High-resolution digital imaging, including micro-computed tomography (μCT) and high-resolution magnetic resonance imaging (HR-MRI), have enabled the creation of finite element models of trabecular bone that possess an exquisite level of anatomical detail. These “high-resolution FE” or “micro-FE” models are created by converting each image voxel occupied by bone tissue directly into a cubic finite element (15;16). Thus, these models capture the complexity of the trabecular architecture implicitly. A micro-FE model of a 5 x 5 x 5 mm^3 cube of trabecular bone will contain up to several hundred thousand elements. Because of the large number of elements, the computational resources and time required to analyze these models can be enormous. To address this issue, custom FE codes that perform these analyses using efficient solution methods and multiple computer processors working in parallel have been developed (16;17). Recently, however, moderately sized micro-FE analyses have been performed using widely available, commercial FE software and high-performance computers (18).

A main advantage of this highly automated, voxel-based approach is that it is relatively quick to create an FE model of a specimen. However, with the exclusive use of cube-shaped elements, the models have irregular surfaces that can cause large errors in the local surface stresses and strains. These errors can be reduced substantially by averaging the FE-computed stresses and strains over a small neighborhood of surface elements (19-21).

To date, micro-FE analyses of trabecular bone have been used in two general areas of study. The first is in examining relationships among the apparent mechanical properties of trabecular bone, trabecular architecture, and the mechanical properties of trabecular tissue. For example, investigators have used experimentally measured apparent moduli and apparent yield properties together with the FE-computed values of these quantities to determine effective elastic and yield properties of trabecular tissue (16;22-25). The effect of specific changes in architecture, such as the introduction of resorption pits and remodeling-induced perforation of trabeculae (26;27) on the apparent mechanical properties has also been explored.

The second area in which micro-FE analysis has become common is in estimating distributions of stress and strain within trabecular tissue in response to loads applied at the apparent level. Studies in this area have demonstrated that, as a consequence of the porous nature of the trabecular structure, a wide range of tissue-level stress and strain magnitudes develop in trabecular tissue under a given applied load (18;22;28;29) (Fig. 2). The implications of this spatial heterogeneity in stresses and strains for damage accumulation, bone

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adaptation, and bone failure are the subjects of ongoing investigation.

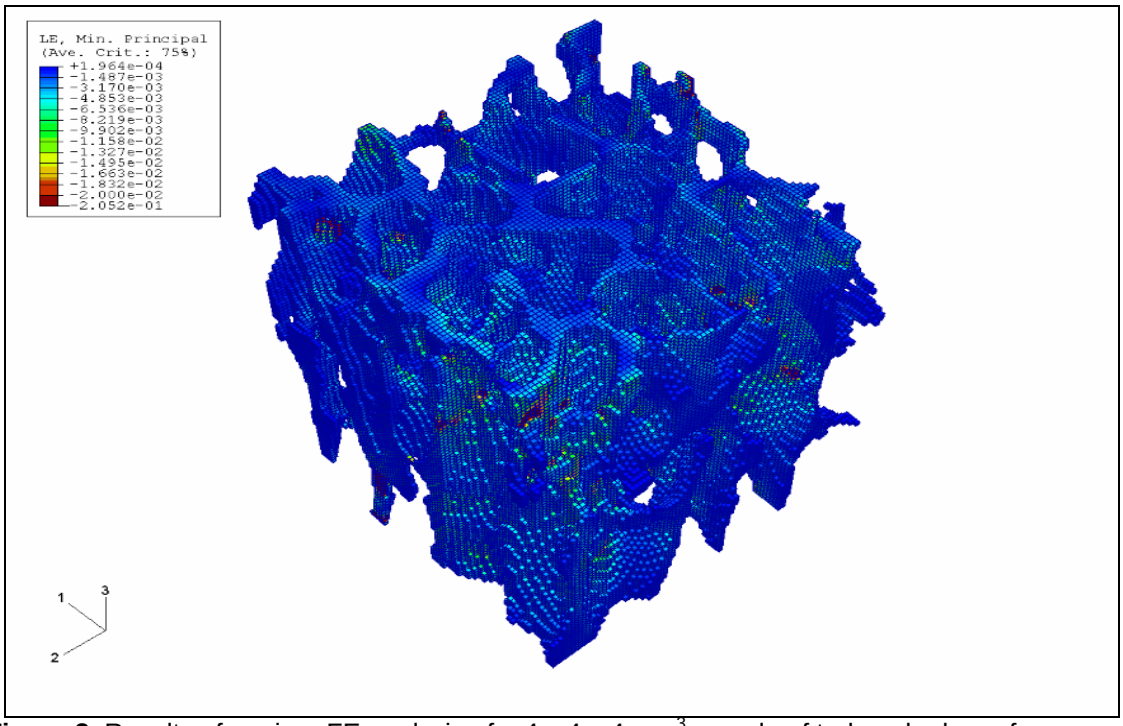

Figure 2. Results of a micro-FE analysis of a 4 x 4 x 4 mm^3 sample of trabecular bone from a human proximal tibia. The color distribution represents values for minimum principal strain throughout the specimen, which is loaded in uniaxial compression along the 3-direction. The results indicate that even simple loading conditions at the apparent level induce a wide variety of tissue-level strains. The apparent level strain is -0.73% (the apparent compressive yield strain). Whereas some regions of tissue experience negligible minimum principal strains (dark blue regions), other regions experience minimum principal strains that are more than 25 times greater in magnitude than the apparent level strain (red regions).

Whole Bones

The stresses and strains in bones cannot be measured in living subjects non-invasively. Thus, in the early 1990s, investigators began to employ “subject-specific” FE modeling, whereby each voxel from a 3D quantitative computed tomography (QCT) scan was converted directly to a cubic finite element (30-32). This approach parallels that used in micro-FE modeling of trabecular bone, although given the standard resolution of QCT scans (slice thickness of 1 to 3 mm), the models created from QCT scans do not resolve individual trabeculae (Fig. 3). Instead, the trabecular bone is treated as a continuum, and the material properties of the elements representing trabecular bone are typically assigned using regressions between a given mechanical property and QCT density (33;34). If the imaging resolution is high enough, however, as with high-resolution MRI or peripheral QCT (pQCT), then micro-FE models of whole bones can be created in which the trabecular structure itself is accounted for (35-37).

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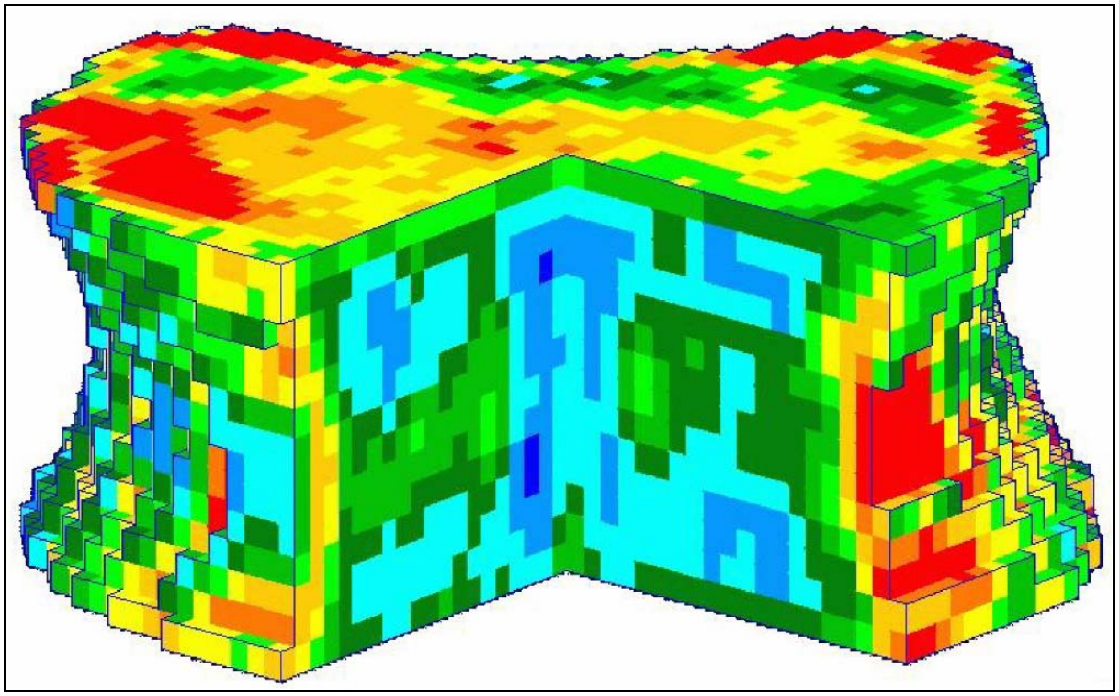

Figure 3. Example of a QCT-based finite element model of a lumbar vertebral body from a human cadaver. Each voxel from the QCT scan is converted to a cubic finite element, where the color represents the element's axial elastic modulus, with red being the highest, green being intermediate, and dark blue being the lowest. Note that adjacent elements can be assigned different material properties, thereby capturing both the geometric and material heterogeneity of the structure (Reprinted from *Bone*, volume 33, RP Crawford, CE Cann and TM Keaveny, Finite element models predict in vitro vertebral body compressive strength better than quantitative computed tomography, pp. 744-750, 2003, with permission from Elsevier).

As with micro-FE modeling of trabecular bone, the ease of creating a voxel-based FE model of an entire bone that is anatomically accurate and incorporates heterogeneous material properties comes with the drawback of errors in the computed stress and strains at the bone surface (38). An alternative approach that reduces these surface irregularities is more labor intensive, as it requires several steps. The QCT data are first used to extract the smooth, 3D geometry of the bone surface, and the whole bone is then automatically meshed using commercially available algorithms. Finally, the material properties (derived from the spatial distribution of QCT density values) are mapped onto the finite element mesh (39). Although no direct comparisons have been made, a recent study suggests that this alternative approach provides more accurate bone surface strains than does the voxel-based approach (32;40). However, it is not known to what extent the accuracy of estimates of whole bone stiffness and strength is affected by the surface irregularity.

Proximal Femur

Finite element analyses of the femur have been used to assess load-sharing characteristics and distributions of stress and strain within the proximal femur during activities of daily living, such as walking and stair climbing (41;42), and following a sideways fall (33;42;43). These FE analyses suggest that the proportions of load carried by the cortical shell and trabecular compartment vary with the loading condition (*i.e.*, stance versus fall), the location in the proximal femur (*i.e.*, neck versus trochanter) and with age (44). In addition, many FE studies have investigated how the presence of a femoral implant alters the usual stress and strain distributions within the bone and may lead to failure of the bone-implant system (45-47).

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With respect to the prediction of bone strength, two studies have compared FE-predicted and experimentally measured failure loads. Keyak, *et al.* (48) reported that QCT-based linear FE analyses explained 76% and 90% of the variance in experimentally measured failure loads from stance and fall loading, respectively, but were not significantly better than those from QCT-derived bone density. In contrast, Cody and colleagues (49) reported that QCT-based FEA explained about 20% more of the variance in experimentally measured femoral strength than did QCT- and DXA-derived BMD measurements. Both of these studies utilized linear FE analyses and isotropic material properties for both cortical and trabecular bone, and it is likely that results could be improved by incorporation of non-linear modeling techniques and anisotropic material properties (50).

Several studies have also assessed the ability of QCT-based FE models of the proximal femur to predict the location and/or type of fracture associated with stance and sideways fall loading (51;42). The FE analyses predict fracture location correctly in about 60-70% of cases. Clearly, however, the fracture location, as well as failure load, are highly sensitive to the choice of failure criterion for the bone tissue and the analytical definition of whole bone failure load (50;52;53). There are currently no standardized algorithms for these estimates.

Finally, the FE method has been used to show that small increases in bone density in critical areas improve the predicted femoral failure load in a sideways fall configuration to a similar extent as do larger, non-specific increases in density (53). van Rietbergen and colleagues (54) evaluated the stress and strain distributions in a normal and an osteoporotic femur using micro-FE models with 96 and 71 million elements, respectively. During gait, strain magnitudes in the osteoporotic femur were higher and less uniformly distributed than those in the normal femur (Fig. 4). Therefore, a greater proportion of the bone tissue is at risk for failure in the osteoporotic femur. As these two studies illustrate, the FE method can be extremely useful in studying the mechanisms underlying bone fracture and, consequently, in identifying treatment options with great promise in increasing bone strength.

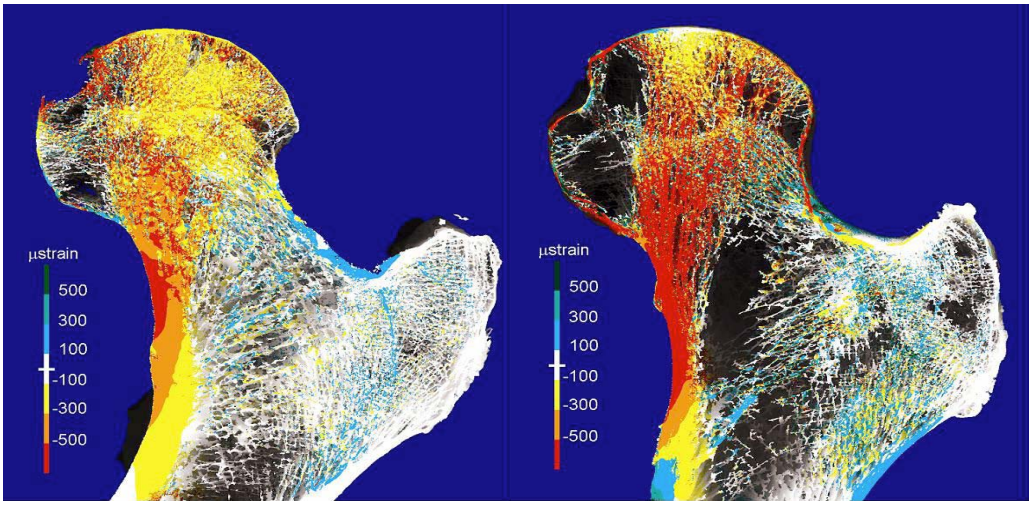

Figure 4. Distribution of minimum principal strains occurring in trabecular tissue during gait in a micro-FE model of a normal (left) and osteoporotic femur (right). (Reproduced from *J Bone Miner Res.* 2003;18:1781-88 with permission of the American Society for Bone and Mineral Research).

Distal Radius

Finite element models of the distal radius derived from high-resolution pQCT (HR-pQCT) have been used to assess load transfer characteristics, to predict whole bone strength, and to assess the biomechanical effects of bone loss and restoration (55-58). For example, Pistoia, *et al.*, (56) acquired HR-pQCT images of the distal radius in human cadavers at 165 µm isotropic voxel size, which is approximately the thickness of a human trabecula, and generated voxel-based FE models. They found strong correlations between the FE-derived and experimentally measured failure loads for a forwards fall, and the correlations between predicted and measured failure loads were higher than those provided by forearm BMD or microstructural parameters alone.

Vertebra

Beginning in the mid-1980s (59), FE analyses of the vertebra focused largely on the contributions of the various components—trabecular centrum, cortical shell, posterior elements—to the stiffness and strength of the whole bone (60-62). Recent FE investigations of load sharing in the vertebra indicate that the proportion of the load borne by the cortical shell varies within a single vertebra along the supero-inferior direction (60;62;63), and that this load sharing is strongly affected by age-related changes in trabecular bone density and by the geometry of the vertebra (62;64).

Overall, efforts to validate the results of FE analyses of the vertebra have indicated that this technique can indeed be a useful and reliable tool. FE-derived estimates of axial stiffness are well correlated with experimentally measured values of stiffness and strength (65), and FE-computed strain distributions in mid-sagittal vertebral sections loaded in axial compression show a high degree of correspondence with experimentally measured strain fields (66). Further, one study reported that FE predictions of vertebral stiffness and strength are more accurate than predictions made using volumetric bone mineral density alone (34). Thus, there is strong interest in incorporating FE modeling into clinical predictions of vertebral fracture risk and in monitoring the effects of osteoporosis therapies on vertebral fracture risk. Analyzing and optimizing vertebroplasty procedures represents another clinical arena in which FEA holds tremendous potential for improving the management of spine fractures (65;67-71).

***In Vivo* Studies**

Improved imaging and computational methods have made subject-specific finite element analyses more feasible than before, and it is inevitable that further technological advances will continue to enhance this capability. Despite the theoretical advantages of FEA for fracture risk prediction *in vivo*, its use to date has been limited to only a few published studies.

In a seminal study of vertebral strength in 43 postmenopausal women, Faulkner and colleagues reported that QCT-based FE analysis discriminated between women with and without a history of vertebral fracture, with less overlap between the two groups than was observed using QCT-based bone density measurements (30). More recently, QCT-based FE analyses were used to explore the mechanisms underlying increased vertebral strength following PTH(1-84) therapy (72). This pilot study reported that vertebral strength increased 20%, whereas BMD increased only 6%, after 1 year of intermittent PTH treatment. The strength gains predicted by the FE analyses were largely due to changes in the vertebral centrum, and did not depend heavily on the heterogeneous distribution of trabecular bone density throughout the vertebral body.

The effects of glucocorticoid treatment on femoral strength were recently explored by QCT-based FE analyses (73). FE analyses of postmenopausal women matched for age, weight, and history of hormone therapy showed that in women with a history of glucocorticoid use, femoral strength was approximately 15% lower than in controls for both fall-loading and stance configurations. Yet, differences in femoral failure load were comparable to deficits in BMD by DXA and

QCT, and consequently, the advantage of FEA over bone densitometry was not clearly defined.

Micro-FE models created from HR-MRI scans have been used recently for *in vivo* estimates of the elastic moduli of trabecular bone from the distal radius (35) and calcaneus (36). In the distal radius, the FE-computed orthotropic elastic moduli were consistently lower, and the degree of elastic anisotropy higher, in postmenopausal women who were classified as osteopenic by hip or spine DXA, than in those with normal BMD (35). In the calcaneus, micro-FE analyses showed that 12 months of idoxifene treatment (5 mg or 10 mg per day) resulted in significant increases in the orthotropic elastic moduli, but not in BMD (36). Although these studies are just two of the many that have used micro-FEA, they are notable in that they demonstrate the feasibility of applying this computational technique for *in vivo*, serial estimates of mechanical properties and for correlating the differences in these mechanical properties to clinical measures of BMD.

Summary

Finite element analysis provides not only estimates of the strength and stiffness of whole bones and bone specimens, but also facilitates exploration of the mechanisms underlying the mechanical behavior of bone and the mechano-biologic regulation of bone adaptation. When the models are created from CT or MR scans of an individual bone, FE analysis affords subject-specific estimates of bone strength and bone-implant interactions. Thus, there is great interest in this computational technique for improving fracture risk predictions and also for pre-operative planning for procedures such as vertebroplasty. Continued advances in computing power and imaging techniques are certain to provide increased fidelity in these predictions, and these advances will concomitantly heighten the need for better estimates of the boundary conditions and bone tissue material properties. In addition, the computational definitions of “failure load” and “bone strength” for a whole bone remain controversial, and require further validation.

Whereas in theory the FE method can provide better *a priori* predictions of bone biomechanical behavior than does DXA, this has not been shown consistently either *in vivo* or *in vitro*. It remains to be seen whether the performance of FE-derived estimates of bone strength can be improved through more accurate input or more sophisticated modeling techniques. Considering the challenges that biological heterogeneity and tissue availability present, it is likely that advances in the clinical use of FEA will occur through integration of ongoing research efforts at various levels (*e.g.,* bone tissue and whole bones), as well as through the application of FE analyses to large clinical datasets. Overall, there is a strong rationale to conduct more studies to determine the accuracy, reproducibility, and clinical utility of this promising technique.

Conflict of Interest: The authors have declared that no conflicts of interest exist.

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