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# Forward: Calcified Tissue International and Musculoskeletal Research Special Issue:

## Bone Material Properties and Skeletal Fragility

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Skeletal fragility, and to a large extent the risk of fracture, is dependent on three general properties of a bone: the amount of bone (mass), the way the mass is distributed (architecture/geometry), and the material properties (characteristics of the mineral, collagen, non-collagenous proteins, skeletal hydration, and interaction among these constituents) of the tissue that compose the bone (Figure 1). Of these three broad characteristics, bone mass has received the greatest attention as a predictor of fracture in large part because it is the easiest to measure in a clinical setting. DEXA measurements of bone mineral density (BMD) have become the standard measure of skeletal health, and alone is used as the definition for pathology: one is diagnosed with osteoporosis if the BMD is greater than 2.5 standard deviations below the young adult mean for a Caucasian woman, regardless of other compensatory characteristics of the bone that may offset the lower BMD. Even so, most scientists who study bone understand the importance of architecture, both the connectivity of the trabecular lattice, as well as the importance of cortical width, thickness, and porosity to bone's rigidity. Architectural features are not completely independent of bone mass (eg loss of bone will affect trabecular connectivity), but can be (section modulus can increase even as bone mass declines). Thus, BMD does not provide a complete picture of fracture risk. Moreover, architectural features are more difficult to measure in a clinical setting and only recently have they been utilized, in combination with BMD, to try to assess fracture risk. One example of this is the recent use of the trabecular bone score (TBS), which integrates trabecular texture analysis with BMD values.

The role that the properties of the bone material itself play, independent of how much bone one has or how it is distributed, has received little attention. There are multiple reasons for this. One is the inherent difficulty of measuring material changes clinically without a biopsy. Another is the historic limitations of our measurement techniques to assess the microstructural and nano-structural changes that occur to the various mineral, collagen and water compartments in bone. However, the development of new technologies that allow measurement of bone material mechanical properties *in vivo* may be leading us to a time when measurements of these properties can contribute to clinical decisions. Also, improvements in imaging and measurement technologies that characterize individual components of the bone matrix, such as atomic force microscopy, wide- and small angle X-ray scattering, ultrashort echo time MRI and others, are contributing to a better understanding of the nanostructural morphology and physiology of bone. These technologies have opened the door to improved hierarchical computational models that can predict mechanical behavior given some knowledge of the material itself.

We are still in the exploratory phases of understanding whether and how the material properties of bone really can impart significant resilience or fragility to the skeleton, and how to use this information for clinical benefit. The time seems appropriate to review what we know of bone tissue properties, how they are measured, and why they may be important to skeletal integrity. This special issue of *Calcified Tissue International and Musculoskeletal Research* begins with an overview of the molecular and tissue level structure of bone, and a description of how one can measure the mechanical properties of bone tissue. This is followed by articles describing the role and importance of each of the individual components of the tissue itself –mineral, collagen, and the interface between these components of the skeletal composite; collagen crosslinking and noncollagenous proteins (which may exert a more significant effect on the bone than their miniscule volumes might predict); and the role of water, which composes 10-15% of the bone by volume, but has been largely ignored by the field. The issue concludes with a paper assessing the clinical importance of changes to the bone material in skeletal disease, independent from mass and architectural effects.

Each author has included a discussion of key questions that remain to be addressed, which we anticipate will stimulate further work in the area to understand both the hierarchical structure of bone, and its importance to overall bone health. We hope that you will find this set of articles gives you a new appreciation and a new understanding of the role of bone as a tissue, and how it contributes to skeletal integrity.

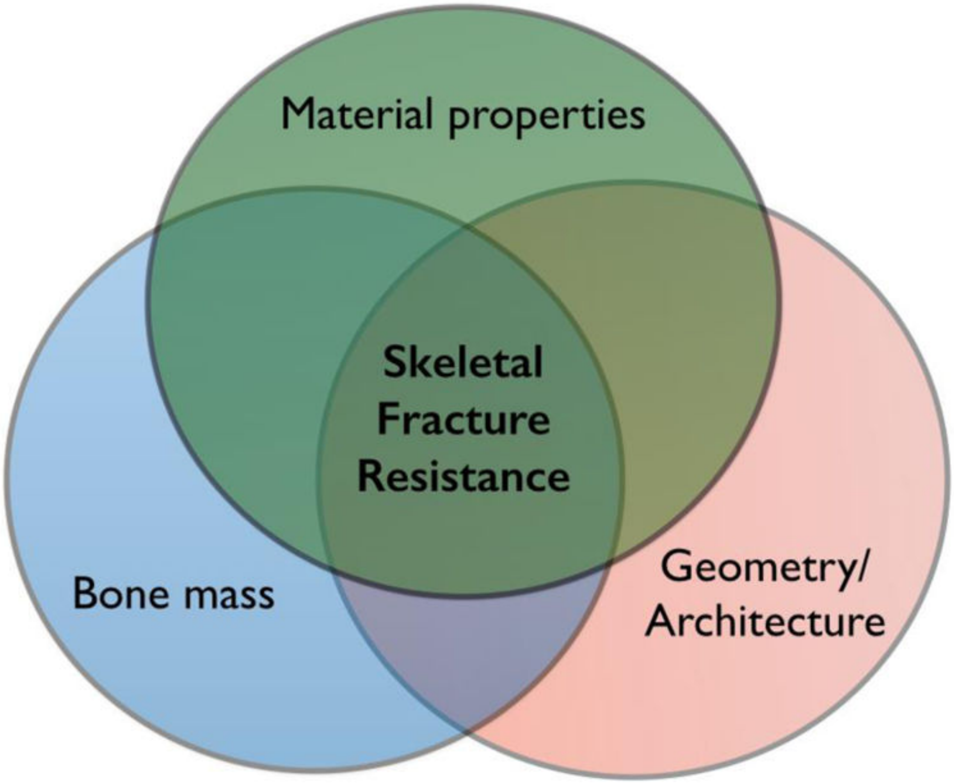


**Figure 1.**

Skeletal properties responsible for determining fracture resistance.