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The role of cortical bone and its microstructure in bone strength

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Abstract

Bone's mechanical competence and its fragility in particular depend to a certain extent on the structure and microstructure of the cortical bone compartment. Beyond bone mineral density (BMD) and bone mineral content, a variety of other features of cortical bone contribute to whole bone's resistance to fracture. Structural properties of cortical bone most commonly employed as surrogate for its mechanical competence include thickness of the cortex, cortical cross-sectional area and area moment of inertia. But microstructural properties such as cortical porosity, crystallinity or the presence of microcracks also contribute to bone's mechanical competence. Microcracks in particular not only weaken the cortical bone tissue but also provide an effective mechanism for energy dissipation. Bone is a damageable, viscoelastic composite and most of all a living material capable of self-repair and thus exhibits a complex repertoire of mechanical properties. This review provides an overview of a variety of features of cortical bone known to provide mechanical competence and how these features may be applied for fracture risk prediction.

Keywords: *cortical bone, osteoporosis, microcracks, remodelling, biomechanics*

Introduction

Age-related osteopenia results in a steep increase in fracture risk particularly at the wrist, the spine and the hip. For instance, the risk for fractures of the femoral neck increases 13-fold from ages 60 to 80 [1]. This dramatic increase in fracture risk is strongly related to a deterioration of bone's mechanical competence, which itself is determined by whole bone structural properties and intrinsic material properties. Structural properties include features such as bone size, bone geometry and also microstructural properties such as trabecular orientation and cortical porosity. Intrinsic material properties include features such as bone mineral density (BMD), chemical composition and size of hydroxyapatite (HA) crystals.

BMD serves as a surrogate measure for the mechanical competence of bones and is used as a direct measure of an individual's fracture risk. Risk assessment is focused on sites rich in trabecular bone, such as the spine, the intertrochanteric region of the femur or the distal radius. Numerous cross-sectional studies have documented that low bone density at these sites is significantly associated with the risk of osteoporotic fractures [2]. The absolute level of bone density and the magnitude of subsequent bone loss are important indicators for risk assessment.

Fracture risk assessment based on the diagnosis of trabecular BMD, however, disregards a wide variety of other features of bone's mechanical competence. Consideration of these features might provide substantial improvement for fracture risk assessment in individuals. Furthermore, several areas in the diagnosis of bone could potentially benefit from the consideration of additional measures of bone's mechanical competence. Measurements at different anatomical locations may considerably disagree with respect to the classification of the degree of osteoporosis, thus posing a therapeutic dilemma in clinical practice. Although there is a strong association between reduced BMD and increased fracture risk, there is still considerable overlap of BMD in patients with and without fractures [3]. Furthermore, there is strong disagreement between changes in bone density and in fracture risk after the therapeutic intervention with anti-resorptive agents. While bone density stabilises or mildly increases, the rate of fracture appears to be considerably diminished [4]. Thus, bone's mechanical competence may be largely explained by trabecular bone density but other factors clearly play an important role and provide space for improvement.

One feature largely disregarded in the diagnosis of bone diseases and fracture risk assessment is the contribution of cortical bone quantity and quality. Cortical bone carries a considerable share of the total load of the skeleton. Biomechanical studies clearly demonstrated that the structural behaviour of whole bone specimens is highly determined by the contribution of cortical bone. In biomechanics, a distinction is usually made between the mechanical behaviour of bone tissue as a material and the mechanical behaviour of a whole bone as a structure. Bone's mechanical competence

reflects both the geometry (size and shape) and the intrinsic material properties (elasticity, strength and toughness). Because of the complexity of the bone failure mechanism, it is not completely clear which properties are actually accountable for bone fragility. Toughness or energy to failure, a tissue property pertaining to the capability of bone tissue to absorb energy during the failure process, is likely to be a dominant determinant of fracture risk. However, bone is a damageable, viscoelastic composite and most of all a living material capable of self-repair and thus exhibits a complex repertoire of mechanical properties.

Structural properties

From a mechanical perspective, it is quite obvious that the rigidity and strength of a structure is determined not only by the amount of material but even more importantly by the arrangement of the material in space. Geometrical measures such as bone size, cross-sectional area or area moment of inertia have frequently shown to predict up to 70–80% of whole bone strength. Biomechanical studies have evaluated the relative contributions of the different bone compartments and the geometric features to the mechanical strength of whole bone specimens. For the distal radius, the best predictors of fracture load are measures of cortical bone mass, cortical area and cortical width [5]. For the proximal femur cortical area, size of the femoral neck and area moment of inertia have been shown to be the strongest predictors of fracture load beyond BMD measurements [5, 6]. The combination of individual parameters in multiple regression models has provided further evidence that geometrical measurements considerably improve the prediction of bone strength [7]. Finally, computational models (finite element models) considering the entire arrangement of bone material in space, the local material properties and the anticipated direction of loading have provided the most accurate prediction of bone strength [8].

Retrospective studies confirmed the association of geometrical properties with the occurrence of fractures, mostly of fractures of the femoral neck [9]. Another predominant geometrical feature observed in femoral neck fractures is local thinning of cortical bone by endocortical resorption [10]. Bone geometry changes with age, adapting to a modified mechanical environment. Bone loss in the femoral neck is therefore lowest in those regions that bear the largest loads during normal gait, whereas cortical thickness is reduced in regions that are primarily loaded during falling. In the femoral shaft, a similar mechanism has been reported long ago [11]. In the distal forearm, the age-related adaptation is reflected in endosteal absorption together with periosteal apposition, increasing the area moment of inertia and thus preserving bone rigidity and strength [12]. Although this adaptive response has been observed in both women and men, it appears to be more effective in men.

Material properties

Bone is a composite material containing about 70% mineral (hydroxyapatite), 22% proteins (type I collagen) and 8% water by weight. The material properties of cortical bone are determined by the quality and the spatial arrangement of these bone constituents. During everyday activity, bone has to withstand both compressive and tensile stresses and bending and torsional moments. Although the mineral constituent resists compression forces very effectively, it has a relatively poor ability to withstand tensile loads. In contrast, the tensile strength of bone results from the collagen fibrils arranged in lamellae. As forces and moments act not only from one direction, the orientation of the collagen fibrils varies between adjacent lamellae. Cortical bone is loaded mostly by bending moments, resulting in a high percentage of tensile strain. The structural quality therefore depends highly on the quality and orientation of its collagen fibrils. Furthermore, stiffness of cortical bone is predominantly associated with mineral content and bone density, whereas its toughness is strongly associated with the quality of the collagen matrix [13]. Although the mineral phase imparts strength and stiffness to bone tissue, with increasing mineralisation, bone becomes brittle and requires less energy to fail. The collagen phase on the other hand provides toughness for cortical bone. If collagen denatures or its composition is altered, cortical bone toughness is reduced [14].

Crystals

Besides structural properties and BMD, the mechanical properties of cortical bone depend on the size and distribution of mineral crystals [15]. Bone mineralisation starts with multiple nucleations of crystals within the collagen fibrils. Crystal size increases by the addition of ions and by the aggregation of crystals, called 'secondary nucleation'. Factors affecting mineral crystal size are the collagen fibrils and other matrix proteins, as well as bone diseases, drugs, diet and age [16]. In young bone, a composition of recently formed small crystals and mature large crystals can be found. This mixture of small and large crystals may represent the optimal situation for good resistance to load. In ageing bone, the average crystal size increases. Bone becomes more brittle because of the greater number of large crystals and tends to fracture more easily. Deviation from the ideal composition is therefore considered to be associated with the deterioration of mechanical properties.

Porosity

Haversian canals and resorption cavities in cortical bone produce a porous bone tissue with pore diameters ranging from a few up to several hundred micrometres (Figure 1). Morphometry and biomechanical testing have perceived strong correlations between intracortical porosity and cortical bone material properties. The number and size of the pores determine intracortical porosity, which accounts for about 70% of elastic modulus and 55% of yield stress (Figure 2) [17]. Local BMD measurements in cortical bone specimens have corroborated these findings [18]. Fracture toughness also decreases significantly with increasing porosity possibly by reducing the available area for the propagation of microcracks [19].

Microcracks

Cortical bone is a composite material in which microcracks accumulate as a consequence of prolonged loading and

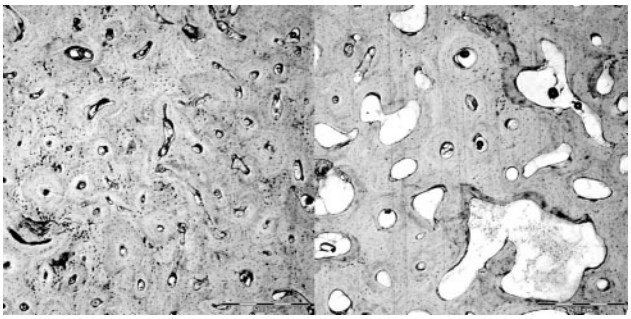

Figure 1. Areas of dense (left) and porous (right) cortical bone from the femoral shaft of a 78-year-old woman. Light microscopic image at 25-fold magnification, Paragon staining.

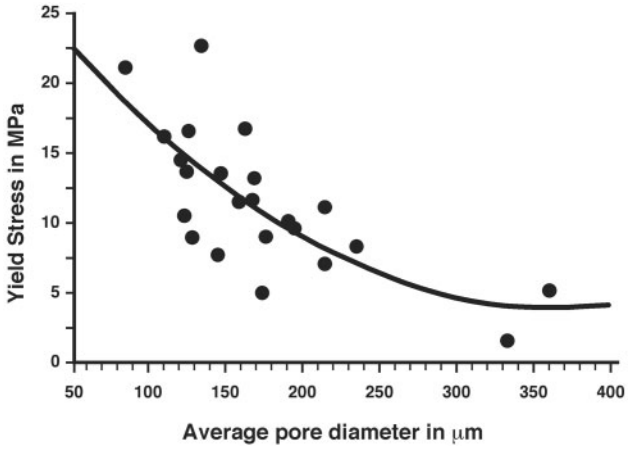

Figure 2. Porosity of human cortical bone measured as average pore diameter is clearly related with decreasing material properties ($n = 23$, $R^2 = 0.54$, $P<0.001$ [18]).

result in bone fatigue. Microcracks are short splits in cortical bone tissue typically in the order of 30–100 μm in length with a 'linear' morphology and result from the disruption of intermolecular bonds (Figure 3) [20]. There may additionally be more diffuse matrix damages at various levels of the hierarchical sublamellar architecture contributing to cortical bone's mechanical behaviour [21]. The propagation of microcracks is frequently observed along cement lines because the osteonal cement lines have a lower resistance to crack propagation. Thus, the majority of microcracks is found between cement lines and the surrounding interstitial tissue. Microcracks occur during fatigue loading of cortical bone and are associated with a significant degradation of bone stiffness. Diffuse damage in particular coincides with yielding of bone. Microcracks occur through everyday activities, accumulate with age and are regularly found throughout the skeleton at load-bearing sites. Microcracks can also be induced during the loading event in a failure process of bone [22]. The generation of new microcracks is a way of dissipating energy during a loading event by local formation of diffuse microdamage. The suppression of crack growth appears to be more important in preventing failure than the

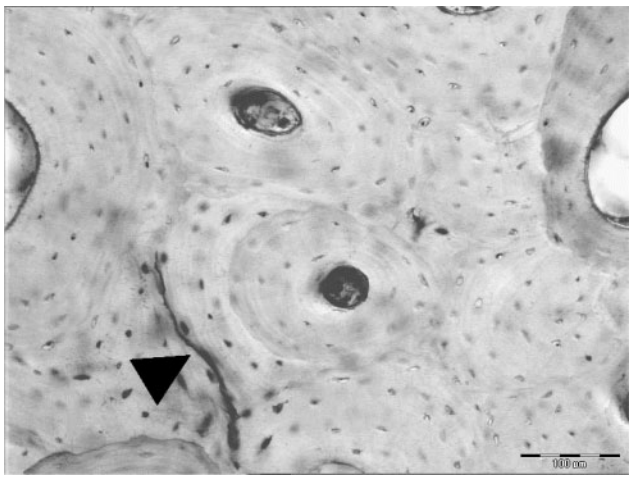

Figure 3. Microcrack (black arrow) in human cortical bone propagating partly along a cement line. Light microscopic image at 100-fold magnification, Paragon staining.

suppression of crack initiation [23]. Although microcrack formation is thought to be an effective way of energy dissipation, microcracks also impose adverse effects on the mechanical competence of bone. Stiffness and strength have been shown to decrease as the number of microdamages in bone increases [24]. It remains unclear, however, to what extent microdamage accumulation contributes to an increase in fracture risk.

Changes with age

From a mechanical perspective, age-related degradation appears to be more pronounced for mechanical properties associated with tissue failure than for those associated with tissue stiffness [25]. Although energy absorption, fracture toughness and ultimate tensile strain show age-related changes of about 5–10% per decade, elastic moduli in tension or compression degrade by only about 2% per decade [26]. It appears, therefore, that the relationship between stiffness properties and failure properties changes with increasing tissue maturity. This is especially problematic because non-invasive image assessment measures mineral density, which is more closely related to stiffness properties than to failure strength or toughness.

Changes in bone's mechanical competence are explained by functional adaptation of bone structure and age-related deterioration of intrinsic mechanical properties. This deterioration is directly related to the bone remodelling process. Each osteonal remodelling event fails to replace all the bone previously removed and results in an increase in cortical bone porosity. The ratio of highly mineralised to new, less mineralised bone tissue is increased when bone remodelling is suppressed, resulting in an increase in the homogeneity of cortical bone tissue. A more homogenous tissue allows cracks to grow more easily and thus reduces the toughness of the composite material. An increased number of cement line interfaces may slow down crack propagation but may also serve as additional sources of crack initiation and may

thus weaken cortical bone tissue. Furthermore, remodelling reduces the regional variability of collagen fibre orientation, leading to changes in mechanical properties. It has been shown that the collagen network itself experiences up to 50% loss in its capability to absorb energy during ageing probably because of an increase in the percentage of denatured collagen [27]. With increasing age, the degree of mineralisation increases, which is reflected in an increase in mineral content of cortical bone tissue [28]. As microdamage in cortical bone accumulates with increasing age, there is a concomitant progressive increase in microcrack density [29]. After the age of 50, microcracks accumulate much more quickly in women than in men.

Clinical application of cortical bone assessment

The direct utilisation of structural properties of cortical bone for the improvement of bone assessment in clinical practice has resulted in only minor improvements in fracture risk prediction [9, 30]. More sophisticated methods combining bone density, geometric properties and engineering principles through finite element analysis are more likely to enhance the predictability of osteoporotic fractures [7, 8]. The inclusion of microstructural properties of cortical bone for bone assessment in patients is very restricted in principle, as well as by technical limitations. Bone biopsies taken from the iliac crest and used for the analysis of histomorphometric properties of trabecular bone are of questionable use for cortical bone analysis. The iliac crest cortical bone is very thin and is also a non-load-bearing bone. Microdamage accumulation, however, occurs predominantly in load-bearing bones. Radiographic approaches for the assessment of microstructural properties are constrained by the limited resolution of non-invasive imaging systems. The development of future imaging techniques will have to concentrate on functional–biological imaging of bone at high enough spatial resolution to estimate microstructural properties.

Key points

- Cortical structure and microstructure contribute to whole bone mechanical competence and fragility.
- Cortical thickness, cortical area and area moment of inertia are strong predictors of bone strength and resistance to fracture.
- Whereas the crystalline structure provides compressive strength and brittleness, collagen fibrils provide tensile strength and toughness.
- Microcracks are an effective mechanism for energy dissipation during catastrophic loading events.
- Age-related accumulation of microdamage weakens cortical bone tissue and possibly contributes to increased susceptibility to fracture.

Conflicts of interest

There are no conflicts of interest to declare.

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