Bone Microdamage

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Significance

Recent interest in the pathogenesis of atypical femoral fractures has highlighted the importance of tissue level ductility in the etiology of clinical fractures [1]. Ductility is a mechanical property different from strength and is associated with the degree to which a material can deform without breaking. Bone tissue with low ductility is quite brittle, and cracks can readily form and propagate in the tissue, often along a relatively linear path such as the transverse fracture plane seen in atypical femoral fractures.

Impaired tissue level ductility may play a role in typical age-related fractures. Vertebral fractures and other insufficiency fractures common in the elderly are often not the result of a single fall or other discrete overload and are instead associated with damage accumulated during multiple loading events. Bone tissue with reduced ductility is more likely to accumulate microscopic cracks and other tissue damage, known collectively as "microdamage". Microscopic tissue damage formed in bone in vivo has been observed in humans and is more prevalent in older patients [2]. While microdamage generated in vivo has been observed in many independent studies, the importance of microdamage to clinical fracture remains poorly understood. Microdamage may weaken bone tissue to the point where failure occurs during activities of daily living or mild trauma such as a fall from standing height. Additionally, microdamage may contribute to bone loss by stimulating bone resorption and remodeling.

The discussion has two parts: a tutorial meant to introduce participants to the concept of tissue ductility and how it differs from strength and stiffness. The tutorial session ends with a review of recent studies examining the mechanical consequences of pre-existing microdamage on bone mechanical performance as well as the response of the body to microdamage, when present.

Learning Objectives: At the completion of the session attendees will be able to:

- Specify the differences between strength, toughness, fracture toughness and fatigue life.
- Associate a material property with different failure modes in bone.
- Learn the challenges associated with measuring microscopic tissue damage in bone tissue.
- Be familiar with the state of the art regarding mechanical consequences of microdamage in bone

Outline:

- Tutorial: What is Mechanical Failure of Bone and Why are There Measures Other Than "Strength"?
- What is Microdamage in Bone?
- What Does Microdamage Do To Bone Mechanical Performance?
- How Does the Body Respond to Microdamage?

Basic Questions:

Question: Is "Strength" the Bottom Line?
Answer:
In the bone research community, mechanical failure of bone is commonly attributed to insufficient "bone strength," but in engineering and materials science, the parameter "strength" is just one of many mechanical properties used to describe mechanical failure (see table below and Figure 1,2). Failure from cyclic loading is characterized by the "fatigue life" of a material, while the ability of the material to resist fracture in the presences of a flaw or crack is referred to as "fracture toughness." Fracture toughness should not to be confused with the term "toughness," a different parameter that expresses the energy absorbed while a specimen is deformed.

Mechanical Property Describing "Failure"	Definition
Yield Strength	The stress at which plastic deformation begins
Ultimate Strength	The maximum stress carried by the material
Toughness	Energy absorbed by material to specified deflection
Fracture Toughness	Resistance to crack extension
Fatigue Life	Number of cycles of loading that may be applied prior to failure (requires applied load magnitude)

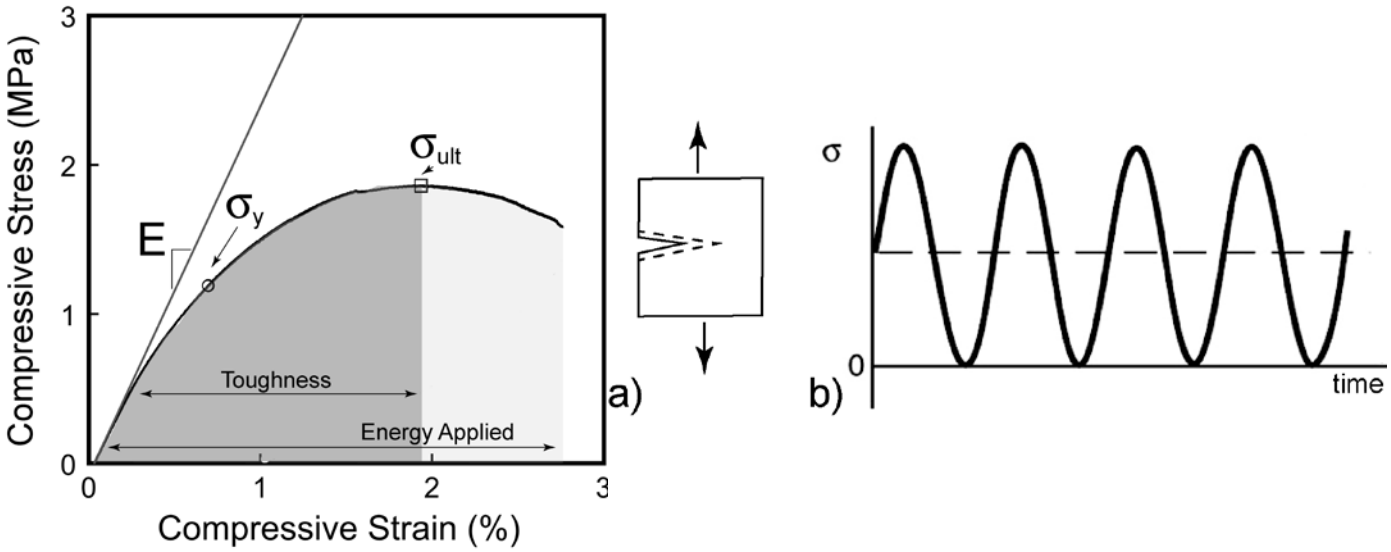

Figure 1. (Left) An example stress-strain curve generated during a compression test of cancellous bone is shown. Definitions of mechanical properties including Young's modulus (E), yield strength (σ_y), ultimate strength (σ_{ult}), toughess (darker shaded region) and energy applied during loading (lighter shaded region). (Right) Illustrations of measurement of a) fracture toughness and b) fatigue life are shown.

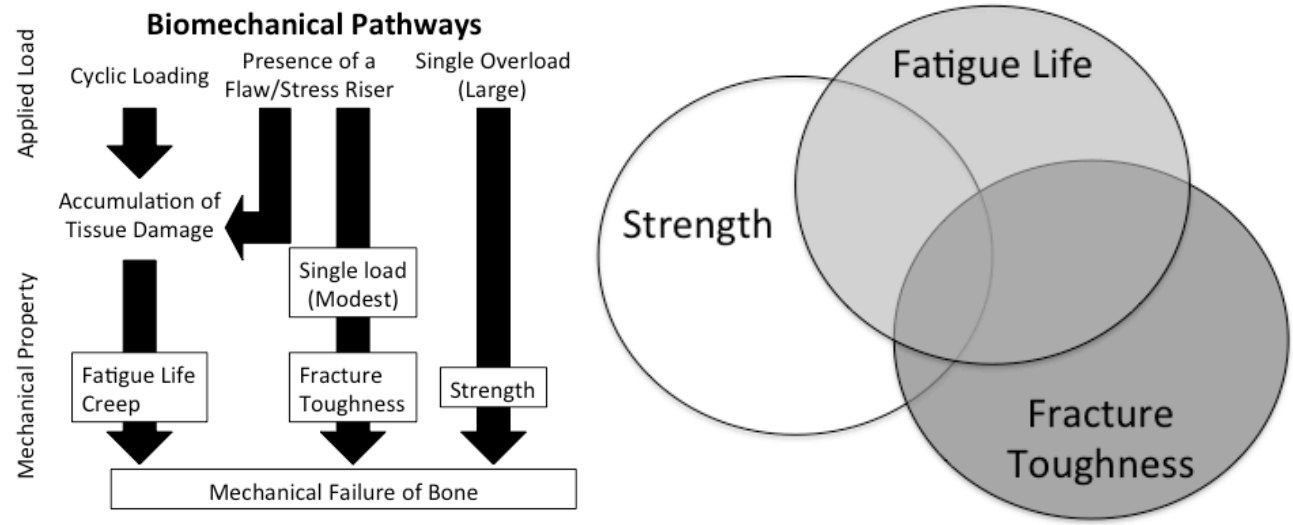

Figure 2. (Left) Mechanical failure of bone is not always due to a single overload such as a fall. Failure may also occur from excessive cyclic loading and/or the presence of a natural stress riser (Haversian canal, resorption cavity or other morphological characteristic). Each biomechanical pathway is related to a different mechanical property (Fatigue life, Fracture Toughness, Strength). (Right) Each mechanical property that describes failure of bone is evaluated with a distinct measurement, yet there is overlap among them. For example, resistance to crack growth is most directly assessed by fracture toughness, but can also influence measures of strength and fatigue life.

Question: What Is Microdamage?
Answer:
Microdamage is a term that refers to cracks and other tissue damage that are smaller than 1mm in size. Microdamage is most commonly observed in histology slides and has been reported to appear in the form of microcracks, cross-hatching microcracks, diffuse damage (a region in which microdamage stain is taken up and consists of a mix of sub-microscopic cracks) and trabecular microfracture [2]. More recently non-light microscopy approaches have been used to characterize diffuse damage at a the nanoscale [3].

Question: How Do We Measure Damage in Bone?
Answer:
There are two methods of assessing damage in bone: Microscopic Examination and Mechanical Examination. Microscopic examination requires directly visualizing the presence of microcracks and other forms of tissue damage, often performed using cut sections and stains used to identify microdamage (and differentiate it from damage caused during cutting). Mechanical examination of damage involves loading the material and determining the degree to which mechanical properties are impaired.

Microscopic Examination of microdamage is traditionally done by hand counts on two-dimensional sections and is therefore subjective in nature. Recently three-dimensional methods of visualizing stained microdamage have been presented. In our experience, measures of microdamage using three-dimensional techniques are systematically larger than those determined using two-dimensional methods and somewhat less subjective since microdamage is assessed with image thresholding rather than direct observation by a histologist.

Question: Does Microdamage Make Bone Weaker?
Answer:
Yes. There have been many studies demonstrating that cortical and cancellous bone submitted to cyclic loading experienced reductions in Young's modulus that were correlated with the amount of microdamage generated by the loading. More recently, microdamage stained with fluorochromes has been used to determine how the amount of microdamage in bone tissue alters bone tissue strength. Modest amounts of microdamage (damage volume fraction DV/BV = 1.5%) were associated with 50-60% reductions in cancellous bone strength [4].

Question: How Does Bone Respond to Microdamage?
Answer:
The generation of microcracks in cortical bone has been shown to be a strong stimulus for the initiation of new bone resorption and remodeling. The effect has been shown to be so strong that it can initiate Haversian remodeling in rodents that don't typically display Haversian remodeling [5] and has been shown to be regulated by osteocytes [6]. Diffuse damage in cortical bone has not been associated with such a strong response and may be repaired through passive mechanisms [7]. Little is known regarding the response to microdamage in cancellous bone. Presumably, microdamage in cancellous bone will trigger bone resorption and remodeling in cancellous bone (using the same mechanisms as in cortical bone) but there is also evidence that microdamage (trabecular microfractures) in cancellous bone can trigger new bone formation in the form of a microcallus (a small callus like structure on a trabecula).

References:

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[5] Bentolila V, Boyce TM, Fyhrie DP, Drumb R, Skerry TM, Schaffler MB. Intracortical remodeling in adult rat long bones after fatigue loading. Bone 1998;23: 275-81.
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Recommended reviews of mechanical failure processes in materials:

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