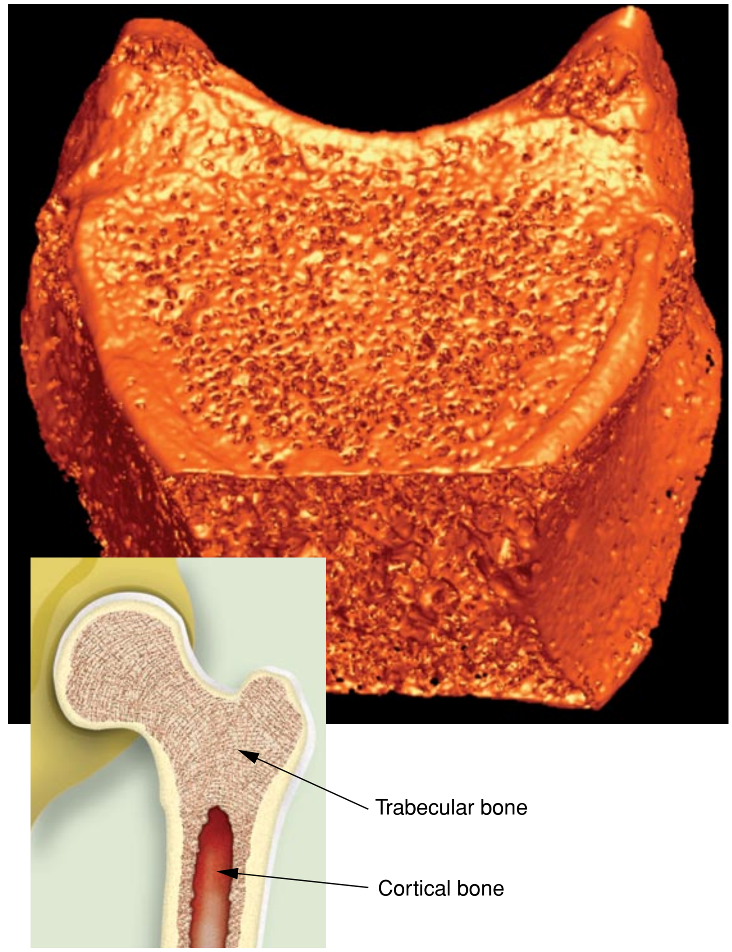
A New Look at How Aging Bones Fracture

A curse of aging bones is the increased possibility of fractures, even with small amounts of stress. A bump or fall that would only bruise a younger person can mean a broken hip or a fractured vertebra for an older person who has developed osteoporosis, a disease attributed to the loss of bone. In fact, spinal fractures are the most common injury associated with the disease.

In most medical circles, this decrease in bone density is believed to be the direct cause of osteoporotic fracture. However, a team of scientists from Lawrence Livermore, the University of California (UC) at Berkeley, and UC Davis has been exploring another possible cause for increased fractures in aging bones. "Our research suggests that a change in the bone's physical structure causes it to fail," says Livermore's John Kinney, the physicist who heads up the project. "In a young vertebra, fracture is governed by the strength of the hard tissue that makes up the bone. We have discovered that, in osteoporotic bone, fracture is controlled not by the strength of the bone tissue but by the manner in which it fails." Kinney obtained funding from Livermore's Laboratory Directed Research and Development Program to examine the biomechanics of spinal fracture.



In adult humans, cortical and trabecular are the two main forms of bone. The spongelike trabecular bone is found nearest the joints in the femur (inset), tibia, humerus, and iliac crest bones as well as in vertebrae. The human vertebra shown above was imaged using a charge-coupled-device camera operating on a beamline at Lawrence Berkeley National Laboratory's Advanced Light Source.

Building Blocks of the Spine

In an effort to explore the mechanisms by which fracture occurs in aging bone, Kinney's team studied the bone structure of individual vertebra in the spine. The human vertebra is composed of an open-celled lattice material called trabecular bone. This bone's cellular foam structure makes it look like sponge. Trabecular bone is also found nearest the joints in large bones, such as the femur (the long bone that joins knee to hip), the tibia (the larger of two bones connecting ankle to knee), the humerus (the long bone connecting shoulder to elbow), and the iliac crest (the upper and widest part of the hip bone). The spongelike trabeculae absorb loads from the joints, similar to how Styrofoam (another open-celled lattice material) used in packaging absorbs impacts.

All living bone "turns over" regularly. That is, old bone is absorbed back into the body (resorption process) and is replaced by new bone (formation process). The average turnover rate for bone is about six years, with that rate being faster for sites close to a blood supply such as at the hip and in vertebrae. However, this turnover process changes as a person ages, particularly in menopausal women.

"At menopause, women experience an acceleration in bone turnover," explains Kinney. "Because an imbalance exists between resorption and formation, with more bone resorbed than formed, an accelerated loss of bone mass occurs during this stage in life." Medical treatments for osteoporosis focus on retarding bone loss by inhibiting this turnover process. "The thought is," says Kinney, "that by stopping the reabsorption of old bone while new bone continues to fill in, albeit slowly, the bone mass will stabilize, resulting in fewer fractures."

Buckling Backbone Up Close

Kinney and his team departed from the usual assumption that the increase of fractures in aging bone is due entirely to lower bone density. Instead, they focused on the possibility that aging bone fractures result from a loss of stability, or buckling, in the structure of the bone lattice. Kinney, along with metallurgist James Stolken from the New Technologies Engineering Division and Nancy Lane from UC Davis, tested this hypothesis using advanced imaging and computational methods.

Vertebrae were obtained from the skeletal archives of the Smithsonian Institution and imaged in three dimensions (3D) using a beamline at Lawrence Berkeley National Laboratory's Advanced Light Source. "We could see from the 3D images that the number and thicknesses of the trabeculae forming the bone were different in young and old bone," says Kinney. In young bone, the trabeculae form a web of short, stubby struts. However, in older bone, these trabeculae are long and slender, and fewer of them exist.

Kinney says, "We wondered if buckling—a mechanical failure of the bone structure itself—could be to blame for some of the fractures that clinicians see. Although a few other researchers had hypothesized that this might be the case, the possibility that trabeculae could buckle had largely been ignored." To explore how vertebrae fail, Kinney and his colleagues combined the detailed structural information gained from the images with finite-element simulations using a parallel version of NIKE3D, which had been developed by Robert Ferencz at Livermore.

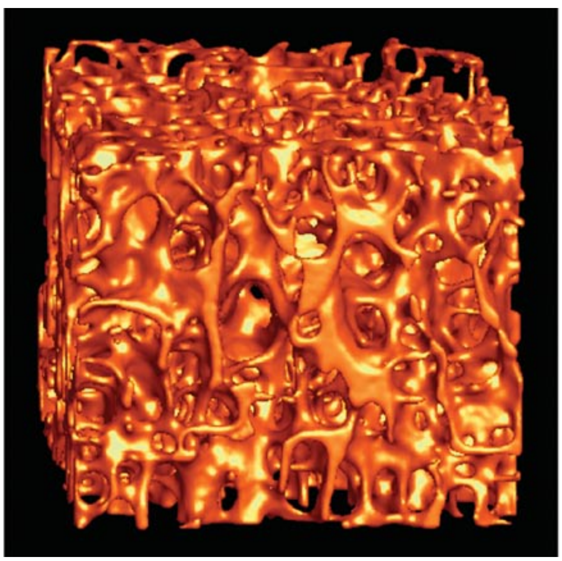
The simulations, which were performed on Livermore's MCR Linux-cluster supercomputer, revealed that a new failure mode occurs in older bone consisting of longer, more slender trabeculae. In younger trabecular bone, strength-initiated failure dominates, in which the stress overcomes the strength of the bone tissue. In older bone, stability-initiated failure dominates because of the instability of the individual trabeculae. That is, older bone is prone to inelastic buckling at stresses far less than expected for strength-based failure.

Buckling is characterized by a sudden failure of a structural member subjected to compressive stress. At failure, these compressive stresses are actually far lower than the compressive stresses that the material itself is able to withstand. The likelihood of a columnlike structure such as bone buckling depends in general on the ratio of the structure's length to its cross section.

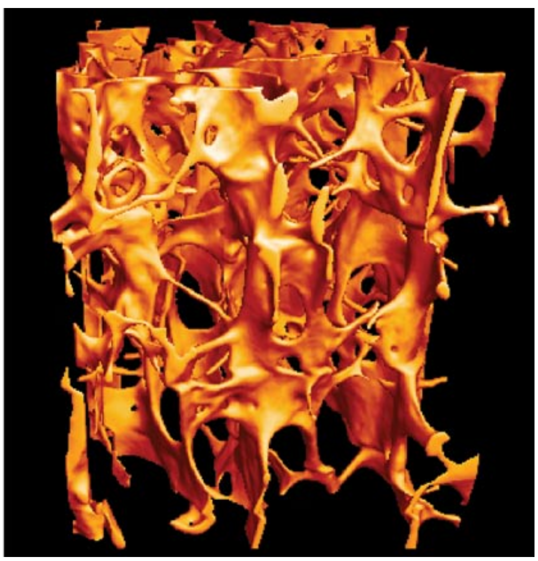
A common example of buckling may be observed when crushing an empty aluminum can. Like a vertebra, the can is loaded axially and when subjected to sufficient loads, it will fail via a buckling instability. Stolken provides a simple example of the sensitivity of buckling to geometric imperfection using two empty aluminum beverage cans. Place the first can, which is undented, on the floor and crush it by stepping on the top, being careful to step as evenly as possible. The can should support a significant fraction of one's body weight before failing. Now repeat the experiment using the second can, which has a small dent in the side wall. The dramatic difference in failure load is due to the initial imperfection (dent).

"Of greater significance, we also found evidence that the osteoporotic vertebrae are hypersensitive to small imperfections," said Kinney. "Small pits on the surfaces of the trabeculae, caused by the cellular process of bone resorption, increase in number as the bone turnover rate accelerates. The pits are enough, in and of

(a)



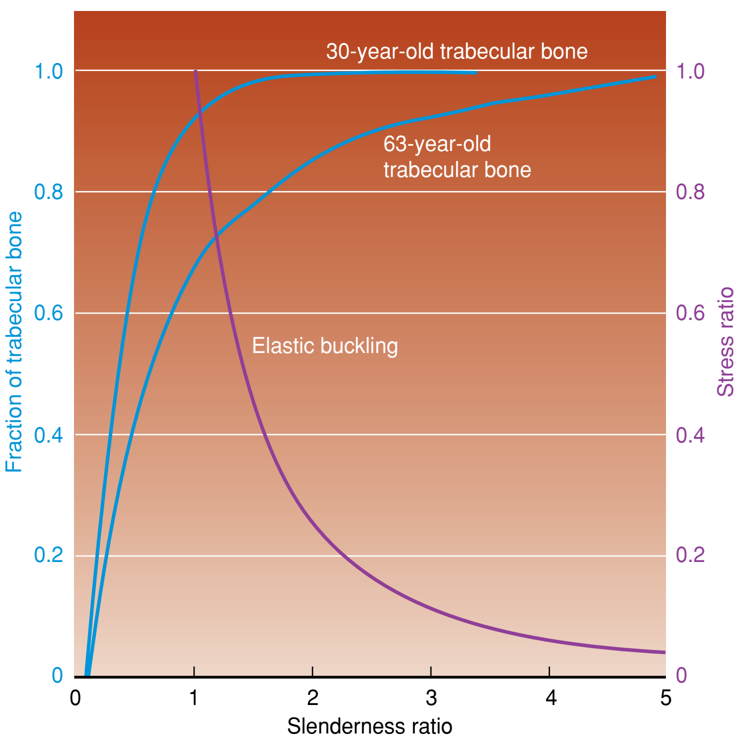
(b)



(a) A three-dimensional synchrotron computed-tomography image of a 4-millimeter-cube of trabecular bone from the vertebra interior of a 30-year-old female shows bone of normal density and architecture. A significant number of trabeculae and platelike structures are aligned in the load-bearing direction. (b) A similar image of a 63-year-old male shows a markedly different bone architecture, with fewer trabeculae and platelike structures. In addition, more of the trabeculae are shaped like slender rods.

themselves, to destabilize the trabecular bone lattice under the right conditions." The team discovered that in aged bone, 60 percent of the trabeculae are subject to inelastic buckling when these pits or flaws are present in the bone.

"Several factors are at work here," says Kinney. "Bone loss makes the trabeculae longer and more slender. In addition, turnover introduces physical defects, in terms of resorption pits." The antiresorptive agents used to combat osteoporosis reduce this pitting and provide extra time to heal these defects. This aspect of bone turnover may be important to the overall understanding of fragile bones.



Comparisons of trabeculae from a 30-year-old woman and a 63-year-old man (blue curves) show that the older bone will break at a lower stress ratio than the younger bone. In this graph, stress is measured as the ratio of elastic buckling stress to tissue yield stress and will always be less than or equal to one. Elastic buckling (purple curve) is shown as a cumulative plot that compares the fraction of trabecular elements having a slenderness ratio that is less than or equal to the slenderness ratio on the horizontal axis.

Improved Understanding of Bone Structure

Kinney and his colleagues in Livermore's Mechanical Engineering Department are examining bone structure and failure from all angles to improve their understanding of osteoporosis and its role in bone fracture. "Once we understand the processes involved, we can better address the problem," says Kinney. "Today, drugs are available to control bone loss and to add bone mass. These drugs reduce fractures, but they also reduce bone turnover. We need to determine if there are negative implications to reducing bone turnover in the long run. Our research in dentin, funded by a grant from the National Institutes of Health, shows that age-related embrittlement can occur in the absence of turnover." Thus, stopping bone turnover may have a downside.

"We've been looking at changes in bone at the macro- and microscales. Now, we must examine the response of bone at the molecular levels. We are piecing it all together, little by little. Someday, I'm confident, we'll have the entire picture before us."

—Ann Parker

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