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Biological Materials Science:

Fracture in Human Bone and the Role of Aging and Disease

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The age-related deterioration of both the fracture properties and the architecture of "hard" mineralized tissue, such as bone, coupled with increased life expectancy, are responsible for increasing incidences of bone fracture in the elderly segment of the population. Indeed, one out of two women and one out of four men over the age of 50 will suffer an osteoporosis-related fracture in their remaining lifetime. In order to facilitate the development of effective treatments that counter this elevation of the fracture risk, an understanding of how the fracture properties of bone degrade with age has become essential. The origins of the fracture toughness of human cortical bone, and dentin (a primary constituent of teeth and simple analog of bone), are examined by considering the salient micro-mechanisms of failure over a broad range of characteristic length-scales from nanoscale to macroscopic dimensions. It is argued that although structure at the nanoscale is important, it is microstructural features at the scale of one to hundreds of microns that are the most important in determining fracture risk. It is

further shown that biological aging (Fig. 1), certain disease states and specific clinical treatments, such as taking steroids (Fig. 2), can cause a significant deterioration in "bone quality" which raises this fracture risk, principally by degrading the bone-matrix structure which in turn critically affects the toughening mechanisms over a broad range of dimensions.

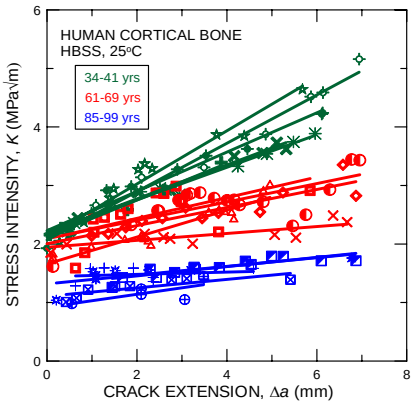

Figure 1: Fracture toughness behavior of aging human bone illustrated in terms of crack-resistance curves (R-curves) for cortical bone tested in a simulated physiological environment. Results show the marked deterioration in both crack-initiation and particularly crack-growth toughness for young (34-41 years), middle-aged (61-69 years) and old (85-99 years) bone. (after Nalla, Kruzic, Kinney, Ritchie, *Bone*, Dec. 2004).

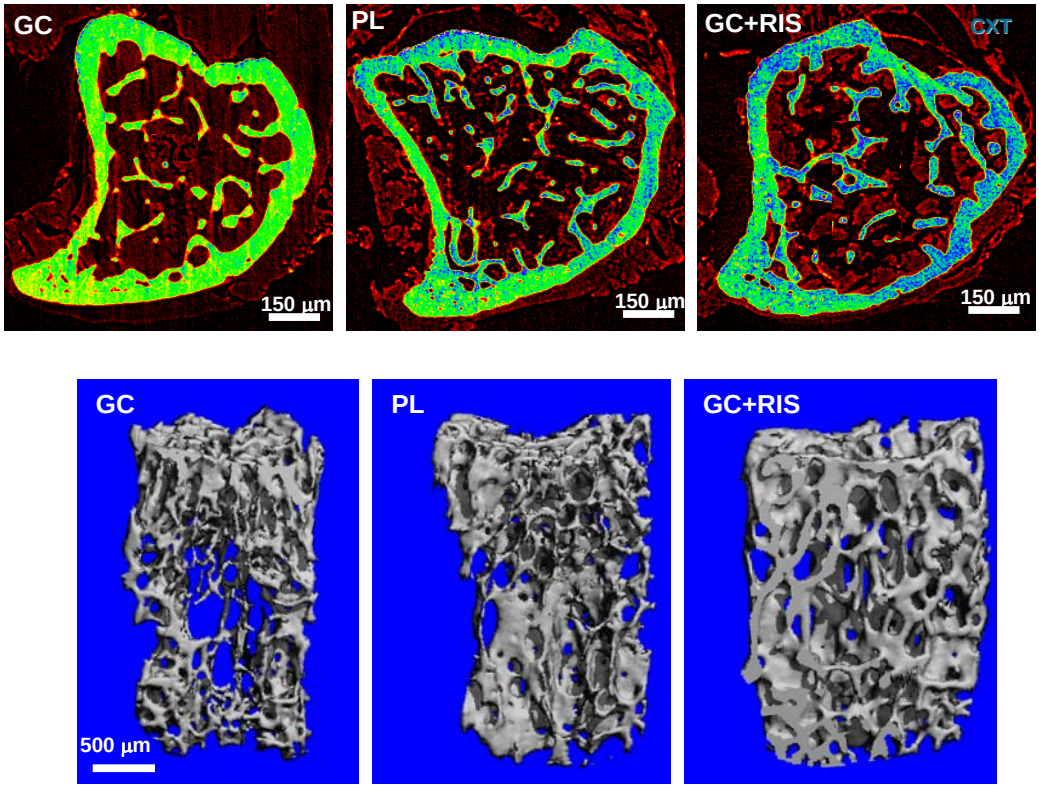

Figure 2: Computed x-ray tomography (XTM) of human trabecular bone showing the marked deterioration in the degree of bone mineralization following steroid (GC: glucocorticord) treatments for 1 year, compared to regular (PL: placebo) bone, whereas concurrent treatment with bisphosphates (RIS: Risedronate) recovers this loss in degree of bone mineralization. Such steroid treatments were found to degrade the fracture toughness of cortical bone by some 20%; however, when taken with bisphonates, the bone-matrix toughness increased by ~24%. Shown in the figure are (upper panel) representative XTM cross-sections and (lower panel) the distribution of 3-D degree of bone mineralization for human iliac crest biopsies treated with baseline (PL), GC+PL for 1 year, and GC+RIS treatment for 1 year. (after Balooch, Yao, Balooch, Nalla, Porter, Lane, and Ritchie, *Nature Medicine*, in review 2006).