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**“Altered Biomechanical and Cellular Properties of
Bisphosphonate-Treated Osteonal Bone Tissue”**

by

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Abstract

The measurement of tissue-level biomechanical properties, including energy-dissipating capacity, may provide information on function and assist in the prediction of tissue failure. In osteoporosis, bone tissue has increased porosity due to rates of bone tissue formation outpaced by resorption. This increase in porosity typically results in fragility fractures of the cancellous spine and femoral neck (hip). Bisphosphonates are the standard pharmaceutical treatment utilized to disrupt bone resorption by killing osteoclasts and reducing this cell's ability to dock, thus preserving bone mass and reducing fracture risk. These drugs are taken by millions.

An undesired side effect of long-term bisphosphonate use is the atypical fracture. Atypical fracture patterns: occur within the cortical shaft of long bones, where porosity is low; increase with duration of treatment; and result from low-energy events (i.e., standing from a seated position). I posit that in the process of reducing osteoclast function, bisphosphonates modify the tissue-level biomechanical quality of bone tissue by reducing turnover, the remodeling process utilized to remove and replace old and damaged tissue with fresh bone. Thus, damage may accumulate and eventually coalesce into a fracture.

My published work demonstrates reduced fatigue life (mechanical cycles to failure), osteon size, and osteocyte cell density, as a result of long-term (3 years) bisphosphonate treatment, in cortical bone of beagles. Further work to be presented explored how two different bisphosphonates administered at clinically-relevant doses for 1 or 3 years affected cortical bone tissue's biomechanical integrity, micro-structural, and cellular properties in terms of osteocyte density. In addition to reduced fracture resistance under cyclic loading, the biomechanical effects included a reduced energy-dissipating capacity at the highest doses. Interestingly, osteocyte density was significantly reduced after 3 versus 1 year of treatment, reinforcing the notion of a duration-dependent effect on cortical tissue. The goal is to detect alterations, prior to adverse fractures, by better monitoring bone's biomechanical quality and predicting the tissues remaining useful life. The results of these studies offer a partial explanation for the association of long-term bisphosphonate treatment with atypical fractures.