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DISSERTATION

"The Role of Osteon Size and Makeup on Cortical Bone Tissue Fatigue Resistance"

by

George Pellegrino

M.D./Ph.D. Program

B.S. 2011, Ursinus College, Collegeville, PA

Thesis Advisor: J. Christopher Fritton, Ph.D.
Assistant Professor
Department of Orthopaedics

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Abstract

Daily mechanical loading induces damage in the form of microcracks throughout the cortical bone tissue. Accumulated damage is removed by the remodeling process and replaced with load-bearing, flexible osteonal columns. With age, remodeling becomes less efficient and more tissue is removed, in extreme cases leading to fragile porous bone. Antiresorptive drugs limit the resorptive phase, and are the current gold standard for slowing bone loss. However, long-term usage has been associated with morbid, low-trauma fracture. A decrease in cortical tissue fatigue life for long-term treatment groups was observed in a recent beagle study. Histological investigation revealed a decrease in the osteon size and osteocyte network density. However, *ex vivo* techniques were not able to definitively connect decreased fatigue life with these changes in the cortical microarchitecture. Thus, finite element models were designed to explore the mechanical influence of osteon size and structural composition on damage nucleation, potential paths of propagation and coalescence.

Our recently published data indicate that at the single osteon level, changes in osteon size are associated with an increased likelihood for damage nucleation within the osteonal features, as opposed to the more brittle interstitium, where damage originates in healthy tissue. Building upon that work, multi-osteon tissue models now indicate that decrease in osteon size is associated with increased volume of brittle, highly stressed interstitial tissue through which damage may nucleate, propagate and coalescence. These tissue models support the use of osteon size to predict changes in bone quality, and may provide a foundation for predicting damage accumulation and subsequent low-trauma fracture risk.

Along with decreases in osteon size, decreasing osteocyte number may indicate a decline in the ability of the tissue to adapt to local loads. Single- and multi-osteon models suggest that the peri-lacunar bone tissue remodeling around the osteocytes, reflected as decreased mechanical properties, can actively alter local tissue fatigue resistance. This result indicates that peri-lacunar remodeling provides a fine-tuning role for load response.

Ultimately, the goal of this body of work was to explore the roles of osteon size and microarchitecture on tissue fatigue resistance to determine if changes to these support structures could be utilized as markers of bone quality. These findings support a connection between osteon size, composition and osteocyte numbers with bone quality and fracture risk. Thus, these factors may provide a foundation in tailoring patient treatment, especially with regard to anti-resorptive drug course.