Determining the impact of osteocyte lacunar-canalicular turnover on bone matrix quality

Doctoral Defense

Ghazal Vahidi

Montana State University
Department of Mechanical and Industrial Engineering
Bozeman, Montana

Tuesday, May 21, 2024, 10:00 AM MDT
Roberts Hall 321
Webex link: https://montana-student.webex.com/meet/ghazal.vahidi

Bone fragility in aging is a major unsolved health problem. Existing treatments for bone fragility are effective for about 50% of the population who suffer from loss of bone mass in aging. However, bone fracture resistance is also determined by the quality of bone tissue, including microarchitecture and matrix properties of the bone. Recently-emerging therapeutics targeting bone matrix quality present new avenues for addressing bone fragility. New data suggests that osteocytes, the most abundant and longest-living bone cells, interact with bone matrix in ways that have been likely overlooked. Osteocytes interact with the bone matrix through resorbing and replacing the bone tissue in their expansive lacunar canalicular system, in a process called LCS turnover. Osteocyte LCS turnover might play an important role in maintaining matrix quality and bone fracture resistance throughout life. However, fundamental knowledge gaps persist regarding this process and its impact on bone matrix properties. In this dissertation, we investigated the impacts of aging on abundance, frequency, and dynamics of osteocyte LCS turnover. We also studied the impacts of osteocyte LCS turnover on the matrix properties of its surrounding tissue. Our findings revealed that osteocyte LCS turnover is a prevalent, frequent, and dynamic process but this process significantly declines with aging. The large decline in LCS turnover in aging can have significant implications for bone quality and fracture resistance. We also demonstrated that osteocyte LCS turnover impacts the matrix quality of its local bone tissue, including modulus and energy dissipation, with nanoscale gradations around lacunae and canaliculi. We adapted contact-resonance atomic force microscopy for mapping the viscoelasticity of hydrated bone at the nanoscale. Findings from this study demonstrate that bone viscoelasticity is highly variable at the nanometer-scale and is higher than bulk bone around some canaliculi. Our data highlights a need to revisit how osteocytes perceive strains, since bone properties differ near lacunae and canaliculi compared with bulk bone tissue. Our findings together demonstrate, for the first time, that the quality of a substantial amount of bone surrounding the LCS is influenced by the frequent and abundant osteocyte LCS turnover, and this process declines with aging. These findings motivate investigating the direct influence of the osteocyte on bone matrix properties in aging and diseases.

Advisor: Dr. Chelsea Heveran