Whole-bone mechanical properties and microstructural features in diabetic rat femurs.

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Type 2 Diabetes Mellitus (T2DM) is one of the fastest-growing diseases in our society. T2D affects one in eleven adults worldwide. There is evidence that T2DM is an independent risk factor for fracture, even after accounting for traditional risk factors, such as neuropathy, decreased visual acuity, and falls. For adults who experience bone fractures, survival probability decreases drastically. Currently, the clinical indicator for bone fragility is bone mineral density (BMD). This indicator is effective in the case of osteoporosis, since osteoporosis induces loss of bone mass or BMD, but not in the case of T2DM, where BMD is mostly unchanged.

This study aimed to determine effective indicators related to bone quality, such as collagen quality, microstructural changes, or cellular activity, to assess the effect of T2DM on the fracture resistance of cortical bone.

The central hypothesis of this project is that changes in bone quality (microstructure, mineral and collagen properties, remodeling) play an essential role in the loss of diabetic bone resistance and increased fracture.

We focused our work on quantifying how changes at the microscale level, such as microstructure, degree of mineralization, canals and lacunar size and density, can impact the whole-bone mechanical properties. We used femurs of 4-month-old Zucker diabetic Sprague Dawley (ZDSD) rats and age-matched control Sprague Dawley (SD). Microscale imaging was performed at the synchrotron microtomography beamline at the Advanced Light Source in Berkeley. Mechanical properties are obtained from flexural strength tests and *in situ* SEM toughness tests.

Microstructural differences between ZDSD and control rats, such as lacunae and canal volume, could be related to whole bone mechanical properties. Diabetes tends to increase lacunae volume and decrease canal volume in ZDSD rat femurs. Yield stress and work to fracture obtained from strength tests showed a decrease in the ZDSD rat's femur compared to the control rat femur. The bending modulus was not affected by the microscale level changes. (Fig.1) Biological and biomechanical changes in diabetic rat bone could be related through osteocyte activity such as local remodeling.

Toughness mechanical properties obtained from *in situ* SEM toughness tests provide insight into the relationship between fracture toughness parameters, such as Kc, and microstructure parameters.

Understanding fundamental bone failure mechanisms and associated risk factors is a crucial first step toward preventing fragility fractures. This is particularly important in the context of increased fracture risk associated with T2DM, which is such a major health issue today.

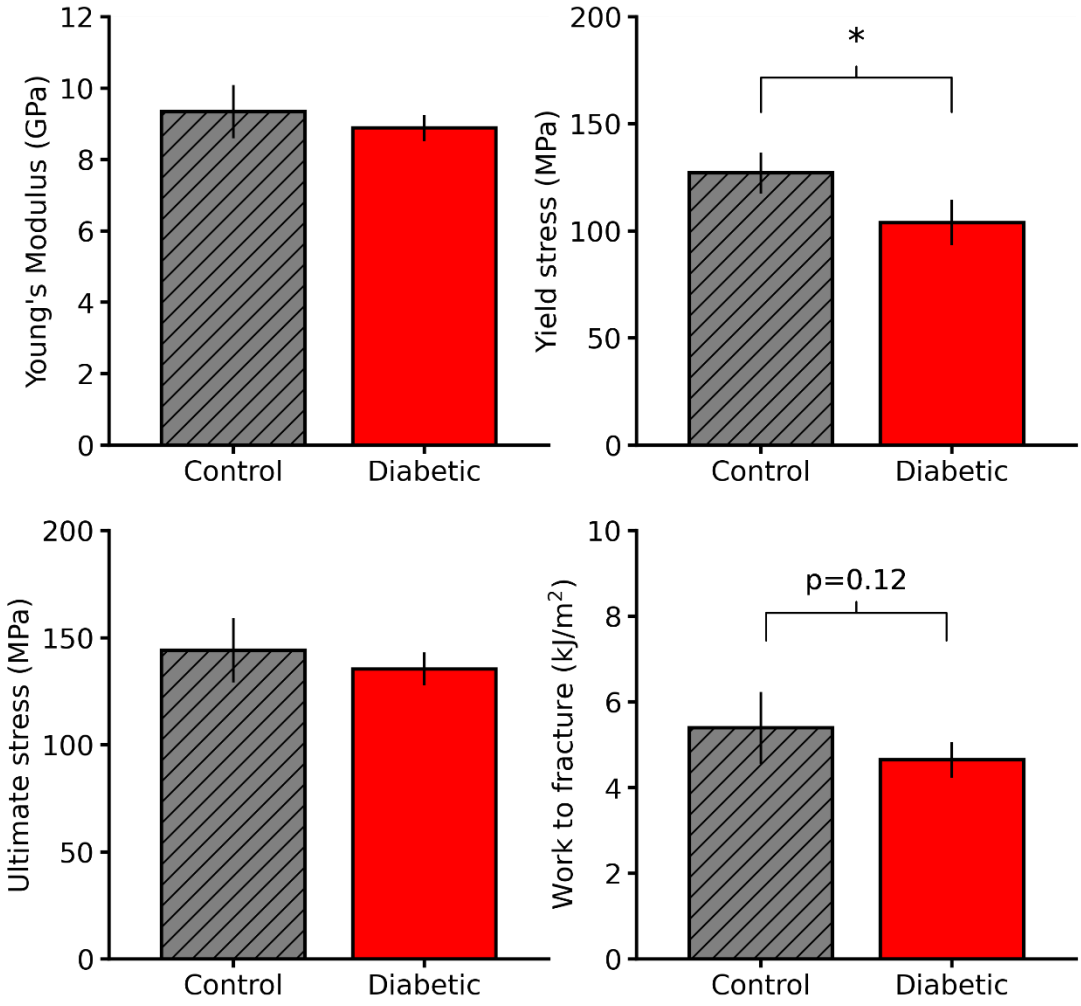

Fig.1: Control (Sprague-Dawley) and diabetic (ZDSD) rat femur mechanical properties obtained from a flexural strength test. * shows statistical differences ($p<0.05$)