Novel Biomechanical Indentation Test Demonstrates Joint Surface Weakening in Mice Lacking Fibroblast Growth Factor Receptor 3 (FGFR3)

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Recent advances in murine molecular genetics have enabled the production of mice with targeted disruption of genes that regulate cartilage and bone metabolism. These mice represent excellent models to study the etiology and progression of complex diseases, including arthritis. Mice lacking FGFR3-/- exhibit defects in cartilage and bone metabolism by 4 months of age. FGFR3-/- mice were used as a prototype to develop a biomechanical indentation method to quantify changes in the surface load bearing properties of articular cartilage overlying subchondral bone. Right and left humeri were harvested from FGFR3+/+ and FGFR3-/- mice (n=4 each) and the distal metaphysis fixed with cement in a small plastic container before dissection of the joint capsule to expose the articular surface. The immobilized humerus was then immersed in PBS for 30 minutes for equilibrium. Controlled compression was applied by an actuator with 0.1 μm displacement precision moving a flat tip indentor of 60 μm diameter positioned perpendicular to the articular surface. A ramp compression at 5 μm/s was applied at two different positions on each humeral head and the force response captured by a load cell with 7 mg precision. Force displacement curves were analyzed to obtain stiffness parameters. Using this technology, it was determined that the load bearing surface of the left humeral head of FGFR3-/- mice was significantly less stiff ($p<0.005$) than that of wild type littermates when measured at 5 μm/s velocity. The lack of difference seen in the right joint is intriguing. Given the progressive degenerative changes that occur in the articular joints of FGFR3-/- mice, starting at 4 months of age, it is predicted that the biomechanical indices of joint degeneration will be more apparent in 6-8 month old mice. This novel method appears to be generally capable of quantitative assessment of joint surface biomechanics in genetically modified mice.