Mapping Articular Cartilage Biomechanical Properties of Normal and Osteoarthritis Mice Using Indentation

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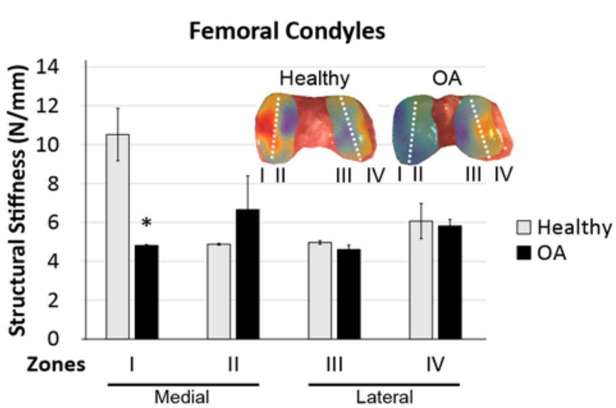
Purpose: Due to their size (~1mm), mouse models pose significant challenges to map biomechanical properties over their articular surfaces. The purpose of this study was to determine if an automated indentation technique could be used to map the biomechanical properties of the articular surfaces in murine knees and to identify early alterations of the articular cartilage of a mouse strain (STR/ort) that spontaneously develops osteoarthritis (OA) on the medial side of their knees.

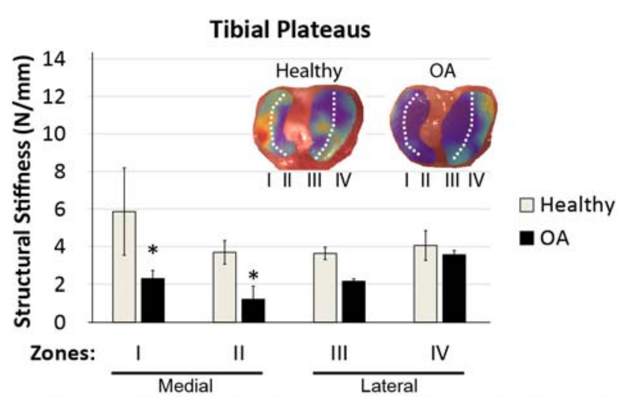
Materials and Methods: The biomechanical measurements were performed *ex vivo,* on the left femoral condyles and tibial plateaus of five healthy Balb/c males (age of 12-15 weeks) and five age- and sex-matched STR/ort mice, using a 3-axis mechanical tester equipped with a multiple-axis load cell. Indentation measurements (30-42/cartilage surfaces) were performed using a 0.35 mm diameter spherical indenter (30 µm indentation in 1 second with 20 second relaxation). Following biomechanical testing, the articular surfaces were fixed in 4% paraformaldehyde for histological assessment. Data reported is the structural stiffness at indentation death of 10µm. To compare the structural stiffness between healthy and OA-developing animals each articular surface were divided into 4 regions, outer medial half (I), inner medial half (II), inner lateral half (III) and outside lateral half (IV). Data is reported as the mean ± SE for each of these regions. Statistical analysis performed by ANOVA.

Results: In healthy animals, mapping of the structural stiffness at an indentation depth of 10 µm showed a spatial distribution similar to that of larger animals (Fig 1 insert). The mean structural stiffness on the lateral condyle (zone III: 5.1±0.3 N/mm, in four regions of the condyles and tibial plateaus (Fig 1 and 2), (mean ±SE, n=2 animals) was similar on the lateral condyles and plateaus of the healthy and OA mice. In contrast, in OA mice the stiffness for the medial condyles (Fig.1) and plateaus (Fig.2) was significantly lower than that of the healthy mice (ANOVA, $p<0.05$).

Conclusions: This study shows that this automated indentation technique can map the biomechanical properties of murine knee joints. The identification of cartilage regions with lower structural stiffness, at sites known to develop OA in the STR/ort strain, suggests this method can be used to identify and characterize OA affected articular surfaces. Studies are ongoing to validate, by histology, the cartilage quality of the affected areas.



Graphic 1: Quantification of the structural stiffness at 10 µm indentation for the left femoral condyles. Inserted images show mapping of the mean structural stiffness for healthy (n = 2) and OA (n = 2) mice with the white dashed lines separating the 4 zones used for quantitation. The graphic represent the mean (±SE) structural stiffness for each of these four zones. Pale gray bars represent healthy (Balb/c, n = 2) 15 weeks old males and black bars represent age- and sex-matched OA (STR/ort, n = 2) mice. Asterisk indicates p<0.05, ANOVA.



Graphic 2: Quantification of the structural stiffness at 10 µm indentation for the left tibial plateaus. Inserted images show mapping of the mean structural stiffness for healthy (n = 2) and OA (n = 2) mice with the white dashed lines separating the 4 zones used for quantitation. The graphic represent the mean (±SE) structural stiffness for each of these four zones. Pale gray bars represent healthy (Balb/c, n = 2) 15 weeks old males and black bars represent age- and sex-matched OA (STR/ort, n = 2) mice. Asterisk indicates p<0.05, ANOVA.