Load-Induced Alteration of Bone and Cartilage Properties in the Rat Tibia Plateau

INTRODUCTION:
Aberrant mechanical loads play a role in the development and progression of osteoarthritis (OA); however, in vivo quantitative assessments of the mechanisms by which articular cartilage responds to sustained compressive loads are limited. Malalignment of the knee and increased body mass index are associated with development of primary OA and increased articular contact stresses are predictive of incident symptomatic knee OA development. Articular chondrocytes respond to mechanical stimuli with baseline levels of load required to maintain cartilage homeostasis and higher levels of load producing dysregulated metabolic processes, cell death and matrix degradation.

A varus loading device (VLD) applied to the hind limb has been described to study the effects of altered loading across the tibiofemoral joint in small animals. The VLD model allows application of controlled levels of altered loading without disruption of the joint capsule while maintaining full range of motion of the knee and normal use of the hind limb. This work investigates load-induced alteration of articular cartilage and subchondral bone following in vivo chronic loading of the rat tibiofemoral joint. We hypothesized that altered compressive loading would induce time-dependent changes to the biomechanical properties of the articular cartilage and subchondral bone.

METHODS:
Animal model: Twenty-five male, Sprague-Dawley rats, 9 months of age, were randomized into one of five treatment groups: 0% body weight (BW) at 0, 6 and 20 weeks and 100% BW at 6 and 20 weeks. NIH guidelines for the care and use of animals were observed. Animals underwent surgery to implant transcutaneous bone plates. Following a 2-week recovery period, animals were fit with a VLD which applied a compressive overload of 0 or 100% BW to the medial compartment of the knee and an equivalent decrease in load to the lateral compartment (Fig.1-A,B). Altered loading was applied continuously (24 hr/day) for 6 or 20 weeks. At completion of the loading protocol, animals were euthanized and tibia plateau from the experimental and contralateral legs were excised, photographed, and stored at -80 °C until biomechanical evaluation.

Biomechanical evaluation: The material properties of the articular cartilage were evaluated in central sites of the medial and lateral compartments of the tibial plateau using a biphasic creep-indentation test (Fig.1-C). Indentation testing used a cylindrical, plane-ended, 0.5 mm-diameter indenter tip, a custom materials testing device (tare load = 0.026 MPa; test load = 0.125 MPa), and a saline bath with protease inhibitors. Following a recovery period, the thickness of the articular cartilage at the testing site was determined using a needle probe test. Material properties (aggregate modulus (HA), permeability (k), and Poisson’s ratio) were determined by curve-fitting the load-displacement response with the biphasic indentation creep solution via a nonlinear regression procedure. A microindentation test was used to determine the modulus of subchondral bone at the articular cartilage test location. Three cycles of repeated loading were applied via a parabolic indenter tip (2.452 N, 30 s). The slope of the load-displacement response during the unloading portion of the third cycle was used to determine the modulus of the subchondral bone.

Statistical analysis: Analysis of variance was used to evaluate differences in means across groups and the Fisher’s LSD procedure to perform pair-wise comparisons between groups.

RESULTS:
Fibrillation of the articular surface in the medial compartment of the experimental limb was observed following increased loading of 100% BW and increased in severity with time (Fig. 2). Changes to the biomechanical properties of the articular cartilage and subchondral bone were observed following chronic loading (Table 1). The mean aggregate modulus of the articular cartilage decreased 57% with loading at 6 weeks and 87% at 20 weeks as compared to 0% BW group at 0 weeks values (p=0.008 and <0.001, respectively). The Poisson’s ratio of the 100% BW group at 20 weeks was reduced as compared to all other groups (p<0.01). The subchondral bone modulus was increased >91% in the 100% BW group at 20 weeks as compared to all other groups (p<0.01).

DISCUSSION:
Application of controlled chronic loads to the tibiofemoral joint initiated degenerative changes analogous to those observed clinically with OA including softening of the articular cartilage and stiffening of the subchondral bone. The VLD applies quantifiable loads and does not disturb the joint capsule eliminating confounding effects from unknown altered loads as in transaction models of OA. The dramatic decrease in aggregate modulus was the first observed change in the degenerative process and preceded significant thinning of the articular cartilage and changes to the subchondral bone.

SIGNIFICANCE:
This work investigates the role of altered mechanical loads, a main risk factor for OA, in the development of degenerative changes in the joint by applying a quantitative load aberration and evaluating the resulting properties of the articular cartilage and underlying subchondral bone. Current findings indicate that altered chronic loads modify the functional properties of both cartilage and bone in a time dependent manner as gross degenerative changes develop.

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REFERENCES: