INTRODUCTION Chondrocytes and their nuclei deform when articular cartilage is compressed (1). Furthermore chondrocytes deform throughout the depth of the tissue in proportion to the magnitude of the applied load (2). Chondrocyte deformation has been shown to influence, either directly or indirectly, the biosynthetic activity, and thus the health, of articular cartilage (1). Furthermore, the heterogeneous structure of normal articular cartilage and the influence this has on the mechanical and biological responses of this tissue to external loading is widely accepted (2, 7). Many of the studies to date have used in-vitro explant loading conditions. Furthermore, little is known about the structural and functional inhomogeneities of osteoarthritic (OA) articular cartilage. The purpose of this study was to apply a uniform static load to early (4 months post anterior cruciate ligament transection (ACL-T)) and endstage (60 months post ACL-T) OA articular cartilage in-situ and to compare the resulting changes to chondrocyte shape and volume.

METHODS Six skeletally mature male cats (mass 5.8±1.7kg) were studied. ACL-T was carried out unilaterally (4) and the animals were allowed free movement until sacrifice either 4 (n=3) or 60 (n=3) months post surgery. Hindlimbs were removed immediately after sacrifice and inspected for degeneration before the experimental femur and patella were prepared for loading. A cylindrical, 1mm diameter, flat, non-porous indenter was used to apply a local surface pressure of 9MPa (value typical of cat gait) to the middle of the specimen at a rate of 4m/s. The indenter was allowed to relax between being immersed in ruthenium hexammine trichloride fixative solution (5) for 2 hours. Full thickness osteochondral blocks (3mm x 1mm) were harvested from the same anatomical sites in experimental specimens. These samples were then embedded and 0.6μm thick sections were cut and stained with toluidine blue for light microscopy. One section from the center of each indented (indent) and a further section 1mm away in the posterior/anterior direction (control) was photographed and the resulting images analyzed using computer software. Cell aspect ratio (height/width) and volumetric fraction (using point counting) were evaluated.

RESULTS The results from this experiment are compared to results obtained from an identical experiment (n=6) using healthy articular cartilage (2). Macroscopic inspection of the hindlimbs revealed a normal contralateral knee and a degenerated experimental joint (4, 3). Figures 1 and 2 show that control chondrocytes maintain their shape and volumetric fraction with disease progression in femoral cartilage though change with OA in patella cartilage (Figs. 1b & 2b arrows). Static compression decreases the aspect ratio of chondrocytes throughout the depth of all tissues (Fig. 1). This decrease is similar for early and endstage OA femoral articular cartilage (Fig. 1a), however differs particularly in the superficial and middle layers of the OA patellar articular cartilage (Fig. 1b). The magnitude of the chondrocyte shape change in endstage OA patella cartilage being larger than that observed in early OA tissue (Fig. 1b brackets). Inspection of Figure 2a reveals that static compression decreases chondrocyte volumetric fraction in the surface and middle layers of both OA and healthy femoral cartilage. In the patella (Fig. 2b) however, the magnitude of the decrease in volumetric fraction is larger in the superficial and middle layers of early OA compared to endstage OA cartilage.

DISCUSSION The results of this study indicate that in endstage OA patella cartilage, chondrocytes in the surface and middle layers are flattened more but lose less volume than chondrocytes in early OA patellae. It has been shown that the elastic modulus of isolated human chondrocytes is not altered with endstage OA disease (6) which would suggest that it is a change in the matrix properties in feline OA patella tissue that is responsible for this altered chondrocyte response to load. Structural changes such as collagen fiber orientation and/or compositional changes such as collagen and proteoglycan density may affect the local articular cartilage strain response to load. The results of this study indicate that significant morphological changes are apparent in early and endstage OA patella that are not apparent in femoral groove articular cartilage. This differential response underlines the need to conduct site-specific comparisons within OA joints. This study demonstrates that early and endstage OA introduces significant changes to the mechanical response of articular cartilage to static compression which could, in turn, influence the biological response of the tissue.

Figure 1: Graphs of cell volumetric fraction as a function of cartilage depth for (a) femoral groove and (b) patella. Each graph compares healthy and OA tissues in control and indented state. Values of CAR have been averaged ±SD within 5 or 10% bins throughout the tissue depth so that n=10 cells for each bin.

Figure 2: Graphs of cell volumetric fraction as a function of cartilage layer for (a) femoral groove and (b) patella. Each graph compares healthy and OA tissues in control and indented state.

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