A New Large Animal Model of Cartilage Repair Using Osteochondral Autograft and Microfracture
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Introduction: Resurfacing chondral defects remains a difficult clinical problem due to the irregular shapes of the defects and the lack of abundant replacement tissue which can be used to resurface these areas. Osteochondral autografts remain a viable treatment option using a mosaicplasty model, but donor site morbidity remains a major limiting factor. Both autograft and allograft replacement remain problematic, due incomplete filling of the defect site, and lack of incorporation between the implanted and host articular cartilage. The objective of this study was to develop a clinically relevant large animal model of articular cartilage repair using osteochondral grafts. The hypothesis was that partial filling of a chondral defect with an osteochondral autograft, augmented by microfracture in an attempt to decrease the amount of donor articular cartilage needed for resurfacing, restores the articular surface.

Materials and Methods: An osteochondral defect (4.5 mm diameter) was made in the medial femoral condyle of the right knee of goats (n=6), and a curette was used to enlarge the chondral defect to approximately 7.5 – 8 mm diameter. An osteochondral core (4.5 mm diameter) was harvested from the trochlea, placed into the defect site, therefore leaving an approximately 3 mm wide gap between the host and implanted cartilages. Six microfracture holes were made within the gap around the core. The animals were allowed normal activity up to termination of the experiment at 6 months. At harvest all animals were assessed grossly, and then the knees (experimental and contralateral control) were assessed by histology and histomorphometry (n = 2), biochemistry (n = 2), and biomechanics (n = 2).

Tissue was fixed and sections stained with toluidine blue or McNeal's tetrazochrome stain and histomorphometry was performed [1]. HPLC was performed to determine collagen I:II ratio in the cartilage. Samples were tested biomechanically by indentation at multiple (19) locations across the repair site and including the surrounding native cartilage [2], followed by cartilage thickness measurement by microscope and digital imaging. The indentation load and thickness data were combined to obtain structural tissue stiffness (N/mm) and material indentation stiffness (MPa). The data were analyzed by considering samples as groups in three different regions, adjacent host cartilage (AHC), microfracture (μfx), and osteochondral core (OC), and four aspects, the intercondylar notch (ICN), medial aspect of the femoral condyle (MC), proximal medial femoral condyle (PC), and distal medial femoral condyle (DC).

Results: Gross visualization of six animals at 6 months after surgery showed most had only a limited and partial repair (Figure 1a). Histology showed regions of fibrous repair, as well as regions devoid of repair tissue surrounded by accompanied by cartilage apparently collapsed or flowed into the unfilled region between the cartilage of the condyl and implanted plug (Figure 1b). The gap between the host articular cartilage and implanted osteochondral core cartilage was reduced from 3 mm to ≤0.1 mm. Histomorphometry showed a reduction of idealize cartilage volume by 15% and 25%, and histology showed loss of proteoglycan in the implanted cartilage and surrounding articular cartilage. Biochemical analysis of cartilage associated with the repair site showed the majority of sites contained >90% collagen type II, although the repair junction of one animal contained 20% collagen type I.

The thickness of samples varied with region. Thickness of articular cartilage in the mosaicplasty core averaged 0.44mm, substantially less than the 1.18 mm of native tissue in that region. The thickness of the cartilaginous tissue where microfracture was performed also was thinner than normal, also there was considerable variability between samples and region within a sample.

The overall structural stiffness of the AHC in the experimental knees (0.83±0.57 N/mm) was similar to that in control knees at the same location (0.77±37 N/mm) as well as the tissue from the μfx and OC regions of the control knees (0.93±0.34 and 0.97±0.22 N/mm)(Figure 1c). The structural stiffness of the cartilage in the transplanted OC region (1.80±0.88 N/mm) was higher than that in the AHC and the control OC. The structural stiffness of the tissue in the μfx region was highly variable. The overall material stiffness of the AHC in the experimental knees (5±3 MPa) was similar to that in control knees at the same location (8±3 MPa), comparable to the tissue from the μfx and OC regions of the control knees (9±3 MPa and 9±2 MPa). The material stiffness of the transplanted OC (9±4 MPa) was higher than the adjacent host cartilage, and similar to the μfx region. The material stiffness of the tissue in the μfx region was relatively soft (3±2 kPa) when compared to the tissue from other regions. The structural and material stiffness of the adjacent host cartilage, microfracture, and osteochondral core had regional differences.

Discussion: A new large animal model has been developed for study of cartilage repair using autologous osteochondral graft and microfracture (representing clinical treatment), and is also relevant for allograft and tissue engineered construct implantation. The model allows for assessment of the implant, surrounding cartilage and gaps between the implant and host tissue. This study shows that when a gap is allowed between the tissues, microfracture inconsistently fills that defect site, and the surrounding cartilage flows or collapses into the defect to minimize the gap size. An outcome is tissue with inferior mechanical properties at and near the junction, and early signs of potential cartilage degeneration. Future studies will assess methods to enhance and stabilize the implant-host cartilage interface.

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Figure 1. (a) Typical gross image of repair at 6 months. (b) Histology showing filling of gap by surrounding host cartilage and osteochondral plug cartilage. (c) Biochemical results, dark bar = experimental, light bar = control.