INTRODUCTION: Human articular cartilage has limited capacity for self-repair. Animal models for cartilage injury and degeneration are important to the study of methods to enhance repair. While it is accepted clinically that osteochondral defects can be expected to progress to osteoarthritis, there is no defined animal model for this process. It is generally accepted that large animal models may more closely resemble the human condition. High costs of large animal experiments limit their utility. While small animal models have been criticized for cartilage repair because of tissue thickness and potential for intrinsic healing, less expensive small animal models permit a larger spectrum of studies in cartilage restoration. This study was conducted to test the hypothesis that (1) rat osteochondral defects progress rapidly to osteoarthritis, and (2) that the rat osteochondral defect model is a useful small animal model for studying cartilage injury and repair.

MATERIAL & METHODS: After IACUC approval, osteochondral defects were created in both knees of sixteen 12 weeks old male Sprague-Dawley rats (32 knees) using a 1.5 mm diameter drill to a depth of 1 mm. Defects were made to the trochlea or the medial femoral condyle. Rats were sacrificed at 4 weeks (trochlea, n=8; condyle, n=8) and 12 weeks (trochlea, n=8; condyle, n=8). Four 6 months old male Sprague-Dawley rats were used as control (n=8 knees). After sacrifice, the distal femurs were harvested and India Ink applied for gross assessment according to the method of Yoshioka. Yoshioka score grades the cartilage from 1 to 4, (1 = normal and 4 = advanced osteoarthritis with intermediate grades based on the retention of India Ink in surface defects). The samples were then processed for histology (hematoxalin & eosin (H&E) and Safranin O). Histological grading was by the modified Mankin score. Type II collagen and Interleukin-1α (IL-1α) immunofluorescence was performed. Statistical analysis was with the Fisher exact test for gross morphology and one-way ANOVA for histological grading. The level of significance was set at p<0.05.

RESULTS: Osteochondral defects resulted in the development of joint osteophytosis consistent with osteoarthritis by 12 weeks (Figure 1B). At 4 weeks, the trochllear defects were velvety and the retained ink appeared as intense black patches (Yoshioka G III, n=8). The condylar defect group at 4 weeks had similar findings (Yoshioka G III, n=7; and G IV, n=1). At 12 weeks, the trochllear defects were similar to the 4 weeks group (G III, n=7; and G IV, n=1). The condylar defect group at 12 weeks progressed to include complete cartilage loss with exposed bone (G IV, n=8). The control group of age matched 6 month old rats had minimal fibrillation detectable only as minute specks of retained India ink to either the trochllea or the condyle (G II, n=8) (Figure 1A).

Histological assessment at 4 weeks where higher Mankin scores represent increased degeneration showed cartilage degeneration and a fibrous repair in all defects (Figures 2 and 3). All osteochondral groups had higher degeneration than the control group (p<0.05). Condylar defects had more degeneration than trochllear defects (p<0.001). For lesions at the same site, Mankin scores at 12 weeks were similar to 4 weeks scores (p=0.973 for trochea, p=0.647 for condyles).

Immunofluorescence revealed the absence of type II collagen within the repair sites (Figure 2C) and a progressive increase in IL-1α (Figure 4). The control group did not express IL-1α (Figure 4A). The presence of IL-1α expressing cells in both the repairs and the surrounding tissues (Figures 4B and 4C) of the osteochondral defect groups show an underlying inflammatory process. The absence of type II collagen was consistent with histological observations of a poor quality fibrous repair.

DISCUSSION: The results show that rat osteochondral defects progressed rapidly to cartilage degeneration and to osteoarthritis. Defect healing was incomplete and with poor quality fibrous tissue. Unlike the rabbit osteochondral defect model where hyaline repairs can be observed at early time points, the rat osteochondral defect exhibited gross and histological signs of poor healing and degeneration by 4 weeks. Joint changes consisting of osteophytosis were seen at twelve weeks. Condylar defects progressed more rapidly than trochllear defects with higher gross and histological degeneration grades at 12 weeks than at 4 weeks. The data show that this novel small animal model is potentially useful for both osteoarthritis and tissue engineering studies. This model can be used to validate methods of investigations or treatments before application to larger animals. It may also permit molecular biologic investigations, evaluating pro and anti-inflammatory cytokines and mediators due to the better availability of antibodies for rats than for large animals. More importantly, the poor healing rat defects may provide more relevant information about potential cartilage treatments than the larger rabbit or smaller mouse and guine pig models. As such, the rat osteochondral defect model is a suitable, cost-effective model for preliminary studies of cartilage injury, degeneration, and repair.


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