Repair of osteochondral defects in goats is modulated by anatomic site, timepoint, and treatment

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Introduction: The goat model has become an important tool in determining efficacy of products for the treatment of focal defects. Recent publications have included goat studies of 6–12 week duration with defects created in the trochlear groove or the femoral condyle [1-3]. However, the repair of defects in these models has not been fully characterized and the impact of experimental conditions has not been elucidated. This study was designed to determine the effect of anatomic site, timepoint and treatment on early repair of focal cartilage defects in a caprine model.

Materials and Methods: Osteochondral defects (4.5mm diameter, 10mm depth) were created in the right stifle joints of six mature Nubian mix goats. Two defects were created in both the medial femoral condyle and the lateral patellar groove [4], with the edges of the two defects being 5mm apart. Of the two defects, one defect was left empty while the other defect was filled with an autograft plug that was press-fit into the defect such that it was flush with the host cartilage. The knee was wrapped with a modified Thomas splint for 2 weeks. After six weeks, the goats underwent a similar surgery in the left stifle joint. After 12 weeks, the animals were sacrificed and the defects were examined and scored grossly [5]. Afterwards, they were decalcified in an HCl-based solution, paraffin-embedded, stained with H&E or Safranin-O fast green, and scored [6]. The histological scoring system assesses filling of the defect, integration with surround cartilage, Safranin-O staining, cellular morphology, defect architecture, surface architecture, replacement of the subchondral bone, and remodeling of the tidemark. The scoring system was modified so that the highest scores corresponded to native articular cartilage. Data were analyzed using three-way ANOVA to determine the significance of timepoint (6 weeks versus 12 weeks), anatomic site (medial femoral condyle versus lateral trocheal groove), and condition (autograft versus empty defect). Fischer’s LSD was used for post-hoc analysis.

Results: Gross appearance of the defects, based on macroscopic scoring, was modulated by condition and anatomic site. Autografts had higher macroscopic scores than empty defects (p<0.0001) and defects in the trochlear groove scored higher than those in the condyle (p<0.001). Timepoint did not modulate outcome (p=0.10). These findings were supported by the gross appearance of the defects.

Histological scores for autografts were significantly higher than those for empty defects in all categories except integration, where empty defects scored higher than autografts (p<0.001). Fibrous and fibrocartilaginous tissues filled the empty defects while autograft-treated defects were surrounded by clefs (Figure 1). However, it should be noted that integration with the bone was absent in empty defects. The effect of treatment was true for both anatomic sites and both timepoints.

Anatomic site modulated defect filling (p=0.009), integration (p=0.018), defect architecture (p=0.027), surface architecture (p=0.006) and the composite score (0.007). This was true for both treatments and timepoints. In each of these categories, defects in the trochlear groove scored higher than those in the femoral condyle. When the composite score was analyzed further, the interaction between anatomic site and treatment was significant (p<0.001). The composite score for autograft-treated defects did not vary with site (p=0.42). However, the composite score for empty defects was higher in the groove than the condyle (p<0.0001). The same interaction effect modulated defect filling, integration and defect architecture. Anatomic site generally modulated outcomes of empty defects, with the outcome of empty defects being better in the groove than the condyle. The performance of autograft-treated defects was generally independent of site.

Timepoint had an effect on defect filling (p=0.002), defect architecture (p=0.028), replacement of the subchondral bone (p<0.001), and the composite score (p=0.033). The effects of timepoint were true for both treatments and anatomic sites. Defect filling, defect architecture, and the composite score improved with time. However, scores for the replacement of the subchondral bone were higher at 6 weeks than at 12 weeks. When analyzed further, the interaction between condition and timepoint was significant (p<0.0001). Scores for replacement of the bone were statistically similar for empty defects at both timepoints (p=1.00) as there was no subchondral bone present in the empty defects at these timepoints. However, replacement of the subchondral bone in autograft-treated defects was significantly higher at 6-weeks than at 12-weeks (p<0.0001). This was due to the new bone being above the original tidemark at the 12-week timepoint.

Discussion: This study demonstrates the importance of anatomic site, treatment, timepoint and their interactions on the early assessment of cartilage repair. These differences may be related to mechanical loading, vascularization of the subchondral bone, contour or other factors. The effects of anatomic site and timepoint on cartilage repair have not been extensively documented and need to be further evaluated in order to understand their importance in large animal pre-clinical models. Based on our results, great care should be taken when designing preclinical studies of this type so that the effect of the study’s design is anticipated and considered when determining efficacy and experimental outcome.


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Figure 1: Representative Safron-fast green stained sections of autograft-treated defects (A) and empty defects (B) after 12-weeks in the trochlear groove.

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