LOAD-DEPENDENT HEALING OF RABBIT KNEE OSTEOCHONDRAL DEFECTS

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INTRODUCTION
In the human knee joint, early motion and weight-bearing has been advocated advantageous in stimulating regeneration of hyaline cartilage. In experimental studies the natural healing response of an osteochondral defect has been shown to be load-dependent. When under load, a defect is found to be filled with mature hyaline-like cartilage with poor integration to the surrounding cartilage. In contrast, the unloaded defects show more fibrous-like cartilage with good integration.

A large number of studies of cartilage repair are done on rabbits. The caged rabbit spends the major part of the day in a sitting position in which the load is concentrated on the posterior aspect of the femoral condyles while the anterior aspect is unloaded. Studying the natural healing response of an empty defect is believed to reflect the intrinsic repair response to osteochondral injury, and could also be considered as an animal model for the widely used microfracture treatment.

Based on this, we decided to investigate if there was a difference in the healing response of defects created in the anterior aspect of the femoral condyle compared with that of defects in the posterior aspect.

METHODS
Six 4-month-old New Zealand White rabbits were used. All procedures followed an Institutional Animal Care and Use Committee-approved protocol. The rabbits were anesthetized by intra muscular injections of a mixture of ketamine hydrochloride and xylazine. An anterior defect was created by exposing the knee joint through a medial longitudinal parapatellar incision. With the knee maximally flexed, a full-thickness defect (3 mm in diameter by 3 mm deep) through the articular cartilage and into the subchondral bone was prepared on the center of the condyle, 1.5 mm above the medial meniscus. A posterior defect was created in the center of the medial femoral condyles through a longitudinal incision in the semi-flexed knee, anterior to the medial hamstring muscle. Rabbits were killed 12 weeks after surgery. The distal femur was carefully dissected. The specimens were fixed and sections of 6 µm were cut through the entire thickness of the defect. The sections were stained with toluidine blue. Representative sections through the center of the defects were scored blindly and independently by three investigators with a 29-point scale of the 24-point scale of O’Driscoll et al. The histological scores were compared with a Student-Newman-Keuls all pairwise multiple-comparison procedure to identify differences among groups. P-values <0.05 were considered significant.

RESULTS
Twelve weeks after surgery, the typical healing response of an anterior (non weight-bearing) defect presented fibrocartilaginous tissue while in most defects, did not reach the level of the surface of the surrounding tissue. An amorphous tissue containing few cells connected the healing tissue to the adjoining cartilage. The posterior (weight-bearing), defects presented hyaline-like cartilage with a distinct cleft at the edge of the defect, separating it from the surrounding cartilage. The bottom of both anterior and posterior defects presented bone. The presence of hyaline-like cartilage was the most distinct feature of the posterior defects. The scores of this parameter were 8 in five out of six posterior defects compared to a maximum of 6 in two of the anterior defects. Integration in the anterior and posterior margins of the defects was evaluated. Only in one out of twelve margins all three of the observers considered partial integration to be present in the posterior defects, while there were 5 fully integrated and 6 partially integrated among the 12 margins of the anterior defects. Overall, the histological score of the anterior defects was 12.6 ± 1.3 and in the posterior defects 18.7 ± 4.0.

DISCUSSION
The use of posterior osteochondral defects for the study of joint surface repair is not previously reported. Our findings of a consistent difference in the healing response dependent on the location of the defect is in agreement with previous data. The mature hyaline cartilage that was found in the posterior defects provides a platform where emphasis could be put on the integration issue. In our previous experiments we have used anterior defects for the study of osteochondral repair. Only when enhancing repair with hyaluronic acid polymer sponges the results have been comparable to the intrinsic repair of posterior defects. We have not, in this study, tried to establish what factors, apart from load, are responsible for the different repair patterns. The areas of integration in our study showed a low cellularity, which may indicate vulnerability to load, when present. This might explain the differences in integration pattern between loaded and unloaded defects, but does not explain the differences in repair tissue phenotype, structure or proteoglycan content.

CONCLUSION
Based on our results, we consider the study of healing posterior defects should be considered where there is an aim to use rabbit experiments to mimic the weight-bearing situation in human knees. The widely used defect placement in the patellar groove does not provide a situation directly comparable to the convex femoral condyle since even larger defects are contained by the concavity of the groove, thus protecting the defect from load and shear stress. Also, the surgical technique when creating a postero-medial defect provides easy access to the site, without disturbing the extensor apparatus.

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