Introduction: Recently a new canine model of osteoarthritis (OA; the ‘groove’ model), has been described (1,2). In this canine model, damage to articular cartilage of the weight-bearing areas of the femoral condyles in one knee, not damaging the subchondral bone and not causing joint instability, is the trigger for development of OA. To strengthen this trigger for development of OA, loading of the affected joint is intensified temporarily, by fixing the contralateral control limb to the trunk of the dog.

Biochemical and histological evaluation showed osteoarthritic features mimicking human OA. At 10 weeks, collagen was damaged and proteoglycan turnover was disturbed. Histologically, moderate cartilage destruction, fibrillation of the articular surface and chondrocyte clustering was evident. These characteristics of OA were also observed at the tibial plateau, cartilage that was not harmed during surgery. Nevertheless, it could be suggest that the changes observed at 10 weeks in the groove model represent the surgically applied damage, rather than being features of OA.

Therefore, in the present we evaluated cartilage damage in this ‘groove’ model shortly after surgical procedures.

Animals and Methods: In 15 female Beagle dogs, articular cartilage on the weight bearing areas of the femoral condyles in the right knee was damaged by use of a sharp triangular pin. Longitudinal and transversal grooves were made without damaging the subchondral bone. After surgery dogs were exercised 5 days/week for 4 hrs/day. Three days/week, during exercise, the dogs were forced to load the experimental joint by fixing the contra-lateral control limb to the trunk. After 3, 10 and 40 weeks, 5 animals were killed and cartilage matrix turnover determined.

• Proteoglycan (PG) synthesis rate as a measure for matrix synthesis was determined by 35S incorporation.
• Retention of newly formed proteoglycans was determined by the release of radio-labeled glycosaminoglycans (GAGs) during 3 days of culture, normalized to the synthesis of proteoglycans (percentage newly formed proteoglycans).
• Proteoglycan release was determined by Alcian Blue precipitation of the GAGs in the culture medium and normalized to the proteoglycan content (percentage proteoglycan release).
• Proteoglycan content was determined in a papain digest of cartilage by Alcian Blue precipitation of the GAGs.

The Animal Ethical Committee of the University Medical Center Utrecht, The Netherlands, approved the animal experiment.

Results: Chondrocytes attempt to repair the damaged cartilage matrix by increasing proteoglycan synthesis (Figure 1a). At 3 weeks we found a statistically significant increased proteoglycan synthesis (+87% compared to control, p<0.05), which was even further increased at 10 weeks (+105%, p<0.05 compared to control followed-up. At 40 weeks post-surgery, the proteoglycan synthesis was significantly less enhanced (+38%, p<0.05 compared to control).

The repair activity seemed to be effective at 3 weeks, since the release of newly formed proteoglycans (Figure 1b) was not changed (+15%, not significant) in the experimental joint compared to the control joint. This was not the case in both the 10 weeks and 40 weeks follow-up groups, where a statistically significant increase in the percentage release of newly formed proteoglycans was found (+68% and +38% respectively, both p<0.001).

In addition, also the total proteoglycan release (both newly formed and resident proteoglycans, Figure 1c) was statistically significant increased at 10 weeks (+55%, p<0.05). This release was progressively at 40 weeks follow-up (+77%, p<0.001). However, at 3 weeks there was no change in proteoglycan release compared to the control joint (-8%, not significant).

As a result of the increased release of resident and newly formed proteoglycans, the proteoglycan content of the cartilage matrix (Figure 1d) decreased in the experimental joint compared to the control joint.

Ten weeks after OA induction proteoglycan content was decreased by 14%, while at 40 weeks after OA induction proteoglycan content was even decreased by 20% (p<0.009). In contrast, at 3 weeks after OA induction there was a tendency of increased proteoglycan content by 12%, although not statistical significant.

Discussion: The increased synthesis shortly after surgical damage represents an attempt to repair. An enhanced synthesis without additional changes is observed. In time the cartilage fails and a progressive increase in release of resident and newly formed proteoglycans is observed, which leads to a progressive decrease in proteoglycan content. This sequence of events is similar to that described for human OA. The present results clearly show that the changes observed in the groove model of OA at 10 weeks (and also 40 weeks) are not the expression of the surgically applied damage but are the result of progressive features of OA.

In addition, in the canine groove model the degenerative changes in the cartilage matrix integrity are slowly progressive over time in the first year after induction. The slowly progressive phase in the first year after the initial induction phase is expected to proceed to full-blown osteoarthritis in several years, as observed for the ACLT model, although this has to be proven.

These features make the groove model suitable for studying OA in vivo in an early stage of disease. Moreover, assuming cartilage repair upon treatment is possible, the trigger being the cartilage damage itself, could be removed by treatment. Therefore, the model would be suitable for long-term follow-up even after treatment has stopped.

Therefore, the groove model makes a valuable contribution to the search for treatment strategies focused at repair of cartilage in osteoarthritis.