

# Study of the evolution of the osteoarthritis pathology and the mechanical properties of cartilage in a spontaneous osteoarthritis model in the Dunkin-Hartley guinea pigs

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PURPOSE

In animal models, the severity of cartilage damage is assessed by histological scores evaluating the structure, the proteoglycan content, the integrity of the tidemark, the cellularity, and osteophytes. In parallel to these histological analyzes, we studied the mechanical properties of cartilage at different stages of disease progression in the Dunkin-Hartley guinea pigs. We also correlated the severity of histological lesions with the mechanical properties of cartilage.

METHODS

Sixty, male, 3-week-old Dunkin-Hartley guinea pigs from Charles River Laboratories (Paris, France) were used. Guinea pigs were randomized into 5 groups of 12 guinea pigs. At 4-week-old and every 8 weeks until week 36, twelve Hartley guinea pigs were sacrificed. Histological severity of the lesion was evaluated using OARSI score and mechanical properties of cartilage were assessed by the MACH-1 technology (Biomomentum, Canada). To do this, the tibial plateaus and femoral condyles of 60 guinea pigs were taken. An indentation protocol and measurement automated thickness was applied to cover the entire articular surface. The Young modulus (measure of the stiffness of the cartilage) and the thickness were calculated using the Mach-1 Analysis software.

## RESULTS

Histological assessment of cartilage lesions showed that guinea pigs spontaneously developed severe knee osteoarthritis. In all animals, the global histological score increased significantly with age until week 28 ( $p < 0.0001$  between week 4 and 28) and then stabilized (between weeks 28 and 36) (Fig. 1). Significant differences in thickness and young modulus between groups over time were observed (Fig. 2). The cartilage thickness gradually decreased until week 20 and then remained stable between weeks 28 and 36. A significantly positive correlation was observed between the global OARSI histological score and the young modulus (condyle:  $r = 0.566$ ,  $p < 0.0001$ ; tibial plateau:  $r = 0.442$ ,  $p < 0.0012$ , Fig. 3).

When histological items were analyzed individually, it appears that the structure of the cartilage and the proteoglycan content were better correlated with the instantaneous modulus of the femoral condyle ( $r = 0.58$ ,  $p < 0.0001$ ;  $r = 0.517$ ,  $p < 0.0001$ ) than with other items.

At the tibial plateaus, the strongest associations were found between the items cartilage structure and integrity of tidemark and the young modulus ( $r = 0.435$ ,  $p = 0.0014$ ;  $r = 0.433$ ,  $p = 0.0015$ ).

Conversely, a significantly negative correlation was also observed between the global histological score and OA cartilage thickness (condyle:  $r = -0.346$ ,  $p = 0.009$ ; plateau:  $r = -0.273$ ,  $p = 0.045$ ) (Fig. 3).

Fig.1

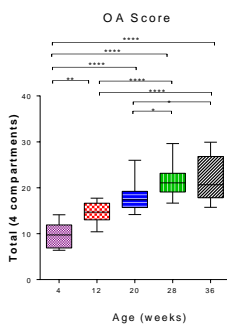


Fig.2

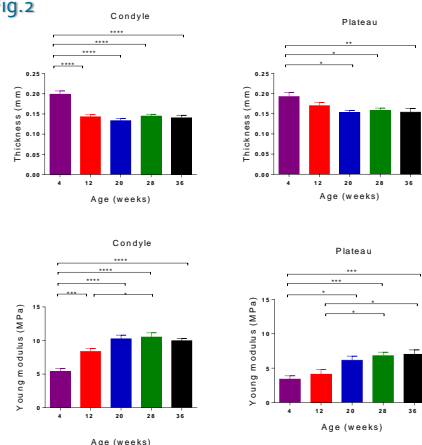
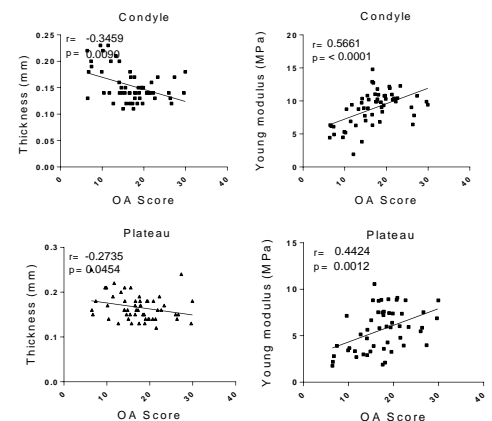


Fig.3



## CONCLUSION

As expected, the global histological score increased significantly with the age of the animals. We also showed a correlation between the instantaneous modulus and the severity of the histological lesions of the cartilage. These observations show the added value of studying the mechanical properties of cartilage in animals. The mechanical parameters give additional information on the articular cartilage quality.

