Title	**Multiscale assessment of the dynamic mechanical properties of articular cartilage**
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Collaborations	**Samuel Buff (Director of ICE laboratory, VetagroSup)** **Sébastien Lustig (Head of orthopedics department, Hôpital de la Croix-Rousse)**

Context:

The articular cartilage is a thin tissue covering the extremities of long bones, transmitting loads between adjacent bones and enabling movement with low friction (Sophia Fox et al., 2009). Lesions of articular cartilage linked to trauma and pathologies, such as arthrosis, represent an increasing public health problem, especially due to the population aging. They could lead to joint disfunction and pain related to articular cartilage degeneration and other consequences on surrounding tissues (Allen et al., 2022).

Before reaching the ultimate stage of the articular cartilage degradation requesting a joint prosthesis, there exist surgical treatments to fill the cartilaginous lesions using neo-tissues obtained from tissue engineering (Du et al., 2020). However, the development and conservation of tissue such as articular cartilage after implantation is still a challenge in particular due to the cells sensitivity to their environment.

The articular cartilage is mainly composed of an extra-cellular matrix and a single cellular type, the chondrocytes. The complex organization of the extra-cellular matrix confers to the cartilage its mechanical properties. In particular, these properties vary along the tissue depth and the distance from the chondrocytes (Petitjean et al., 2023) (Figure 1).

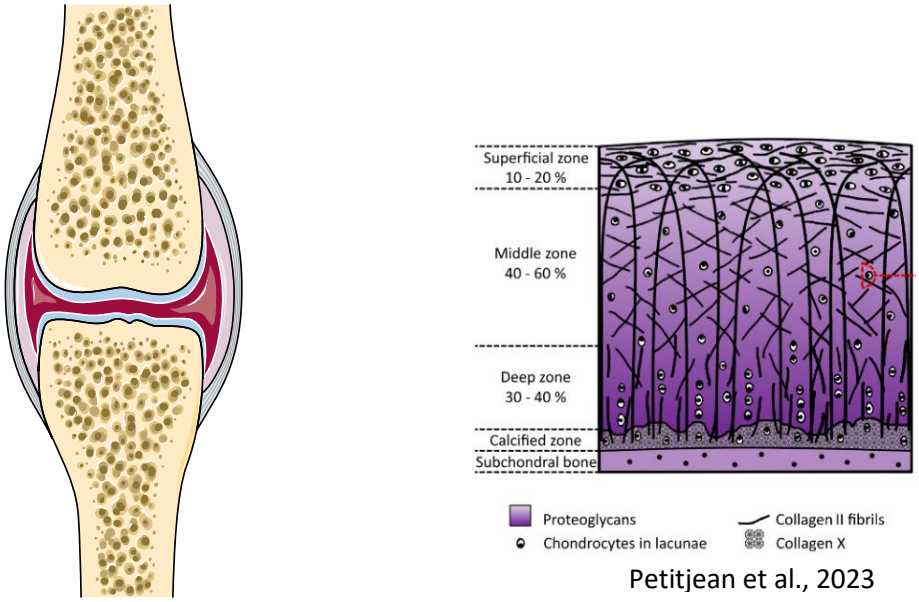

Figure 1: left - diagram of a generic joint with articular cartilage in blue, right – structural organization of the articular cartilage with zonal distribution from the surface to the subchondral bone

Moreover, if the mechanical properties of the articular cartilage offer a certain rigidity at the tissue level, the extra-cellular matrix close to the cells is much more flexible. Thus, it was observed that stiff tissues produced by tissue engineering are adapted to joint mechanical stress, but chondrocytes phenotype tends to hypertrophy. On the contrary, less stiff tissues support the conservation of a chondrocyte phenotype, but are more sensitive to the joint mechanical environment and lead in the long term to a dedifferentiation of the chondrocytes towards fibroblasts. Despite a large body of knowledge on mechanical properties of articular cartilage, to date no tissue engineering products are really effective.

Most data on microstructural strains during tissue loading are obtained once mechanical equilibrium reached, due to the acquisition time needed for the imaging methods considered. Thus, tissue response is assessed in quasi-static. However, joint dynamic loadings induce production of the extra-cellular matrix of the articular cartilage by the chondrocytes. In addition, it seems essential to be able to assess stimuli at the cellular level to better define the specifications of the tissues that could be produced by tissue engineering.

Objectives: In this context, the objective of this project is to develop a protocol to analyze the mechanical properties of the extra-cellular matrix at different scales up to strain around the cells, under dynamic loadings.

Methodology: To achieve this goal, the main steps will be:
- to contribute to the collection of canine articular cartilage specimens. The composition and architecture of canine articular cartilage are similar to those of human cartilages (Arokoski et al., 1999). The additional advantage of this animal model is the possibility to have normal and arthritic cartilages.
- in parallel, to choose the imaging modality to assess the strain of the cartilage at the scale of the tissue and the cellular scale, under dynamic loading.
- to apply the methodology to the canine cartilage specimens and analyze the data
- to apply the methodology to human cartilage specimens (obtained after knee prosthesis surgery) and analyze the data

Collaborations: This project will be performed in close collaboration with VetaAgro Sup (canine specimens) and Croix-Rousse Hospital (human specimens).

Candidate profile: This position is open to international students coming to France for the first time or awardees of the Master grant of the Graduate School Medical Device Engineering of the Université Claude Bernard Lyon 1. Candidates should have academic knowledge in mechanics, tissue biomechanics and imaging. Master degree in mechanics, biomechanics or bioengineering is requested.

Applications: Candidates should send their application by e-mail to the supervisors, which should include a Curriculum Vitae, a letter of motivation, transcripts of Master's grades (M1 and M2) and a letter of recommendation from a previous internship.

Funding: funded by the Graduate School Medical Device Engineering of the Université Claude Bernard Lyon 1 within the program "Graduate +" (21-SFRI-0001) operated by the French National Research Agency (ANR)

References:

Allen KD, Thoma LM, Golightly YM., 2022. Epidemiology of osteoarthritis. Osteoarthritis Cartilage. 2022 Feb;30(2):184-195. doi: 10.1016/j.joca.2021.04.020

Arokoski, J.P.A., Hyttinen, M.M., Helminen, H.J., Jurvelin, J.S., 1999. Biomechanical and structural characteristics of canine femoral and tibial cartilage. J. Biomed. Mater. Res. 48, 99–107. https://doi.org/10.1002/(SICI)1097-4636(1999)48:2<99::AID-JBM1>3.0.CO;2-N

Du, D., Hsu, P., Zhu, Z., Zhang, C., 2020. Current surgical options and innovation for repairing articular cartilage defects in the femoral head. J. Orthop. Transl. 21, 122–128. https://doi.org/10.1016/j.jot.2019.06.002

Petitjean, N., Canadas, P., Royer, P., Noël, D., Le Floc'h, S., 2023. Cartilage biomechanics: From the basic facts to the challenges of tissue engineering. J. Biomed. Mater. Res. A 111, 1067–1089. https://doi.org/10.1002/jbm.a.37478

Sophia Fox, A.J., Bedi, A., Rodeo, S.A., 2009. The Basic Science of Articular Cartilage. Sports Health 1, 461–468. https://doi.org/10.1177/1941738109350438