Morphological assessment of non-human primate models of osteoarthritis using HR-MRI and μCT arthrography

Emmanuel Chereul, Denis Grenier, Anne-Laure Perrier, F. Taborik, L. Mahieu-Williame, Kevin Tse-Ve-Koon, T. Chuzel, S Martin, L Magnier, X. Pesesse, et al.

Morphological assessment of non-human primate models of osteoarthritis using HR-MRI and µCT arthrography

E. Chereul[1], D. Grenier[2], A-L. Perrier[2], F. Taborik[3], L. Mahieu-Williame[2], K. Tse Ve Koon[2], T. Chuzel[1], S. Martin[1], L. Magnier[1], X. Pesesse[4], S. Pietri[5], H. Contamin[3] and O. Beuf[2]

[1]VOXCAN, Marcy l'Etoile, France ; [2]Université de Lyon, CREATIS CNRS UMR 5220; Inserm U1044; INSA-Lyon; Université Lyon 1, Villeurbanne, France ; [3]Cynbiose, Marcy l'Etoile, France ; [4]Bone Therapeuthics, Grosselies, Belgium; [5]Laboratoire de Rhumatologie, Hôpital Erasme, ULB, Bruxelles, Belgium.

olivier.beuf@creatis.insa-lyon.fr

Introduction

- Small animal models of osteoarthritis (OA) do not mimic perfectly the complex conditions occurring in human OA.
- OA that closely resembles the human condition occurs naturally in primate. Non-human primates (NHP) could be a useful model for human OA.
- Non-invasive techniques such as 3D HR-MRI have been validated to directly assess the cartilage thickness on guinea pigs (1) and different cartilage compartment volumes on rat models of OA (2-3).
- Nonetheless, spatial resolution is limited compared to µCT scanner that however needs contrast agent injected in the joint to depict cartilage limits.

Objectives

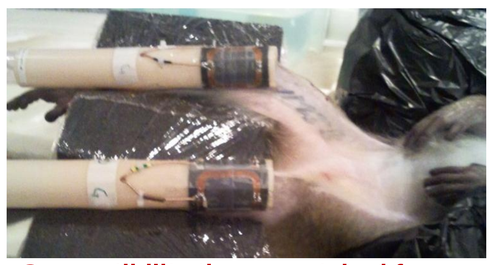
- The aim of this work, based on morphological parameters assessed on MRI and µCT arthrography (µCTA) acquisitions, was:
  - To assess the potential µCTA protocol impact on the model follow-up
  - To compare quantifications results based on both imaging modalities
  - To characterize an induced model of OA by transection of the anterior cruciate ligament (ACL).

Material and method

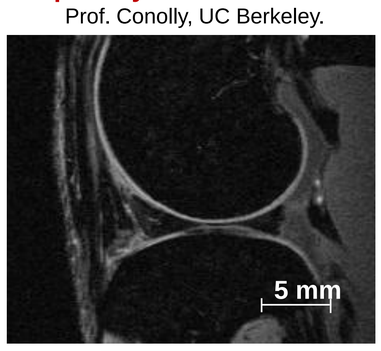
- The ethical guidelines for animal experimental investigations were followed and the experimental protocol was approved by the Animal Ethics Committee from Ecole nationale vétérinaire de Lyon (VetAgro Sup), Marcy l'Etoile.
- Group 1&3 (n=3+3): control animals – only the right knee was injected with HexabrixTM for µCTA imaging. MR imaging of both knees.
- Group 2 (n=6): ACL transection of the right knee only. Multi-modal imaging of both knees.
- Longitudinal follow-up using HR-MRI and µCTA of 4 year old female cynomolgus at baseline, D15 (µCTA only), D30, D60, D90, D180.

MRI acquisition protocol

- 1.5T Siemens Sonata system
- 3D water excitation FLASH sequence: 25° flip angle, 27 ms TR, 11.7 ms TE, 70 Hz/Pixel receiver bandwidth
- A pair of homemade two-channel array coil
- In-plane pixel: 112x131 µm2, partition thickness: 220 µm
- scan time/knee : 20 min
- Total examination time: 90 min



Susceptibility tissue-matched foam
Prof. Conolly, UC Berkeley.



µCTA acquisition protocol

- 2mL HexabrixTM (320mg/mL) with 40/60 dilution in PBS was injected in the synovial capsule with 23G needle.
- GE Locus µ-CT (standard voltage and amperage)
- Isotropic voxel of 90 µm
- Scan time for both knees : 15 min
- Total examination time: 30 min

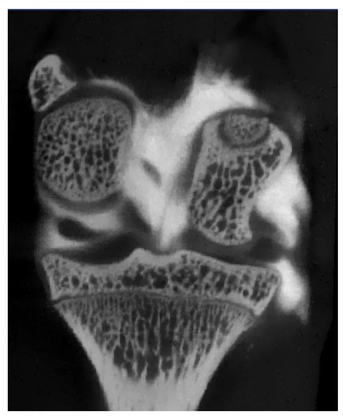
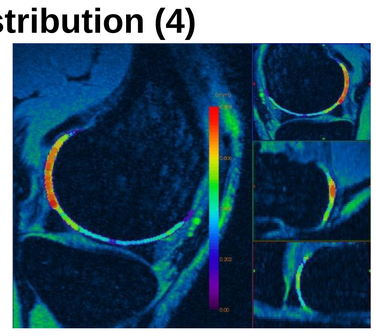
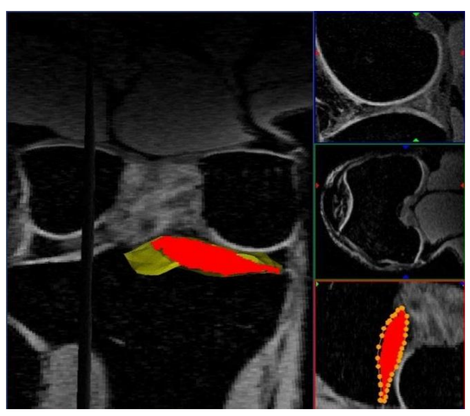


Image processing protocol and cartilage quantification parameters

- Binarization performed in two steps:
  - Manual segmentation
  - Global thresholding
- Thickness distribution (4)

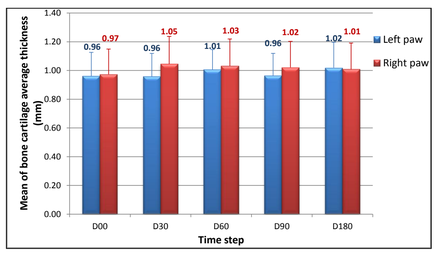




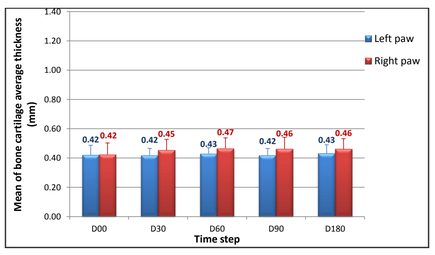
Results

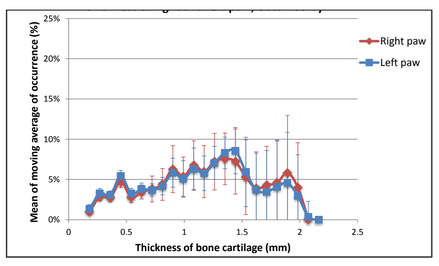
G1 & G3 - MRI-based quantification of left and right tibial plateaus

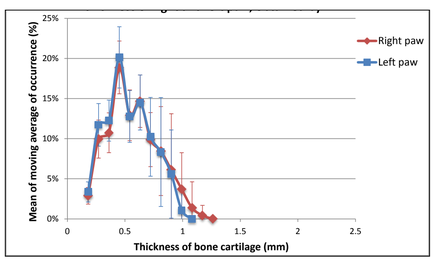
Medial



Lateral







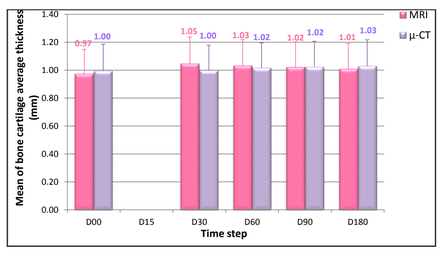
➡ Repeated injections for µCTA have no impact on cartilage quantification

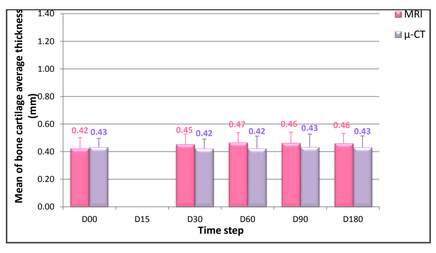
G1&G3 vs G2 - Mean of tibial cartilage average thicknesses of right knee obtained by µCTA and MRI

Medial

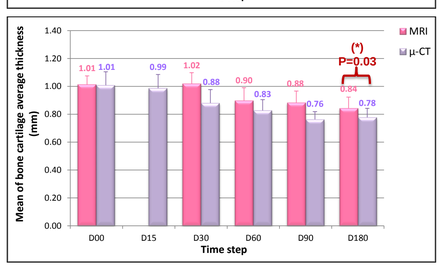
Lateral

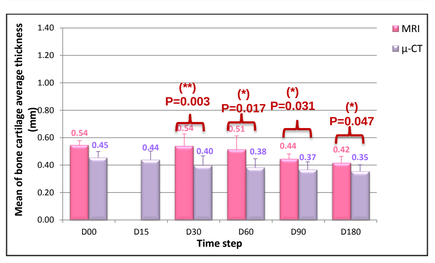
G1&G3 – control group





G2 – ACL transection of right knee

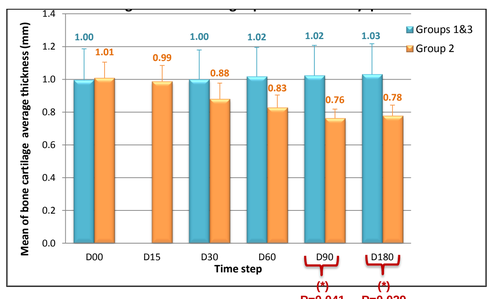




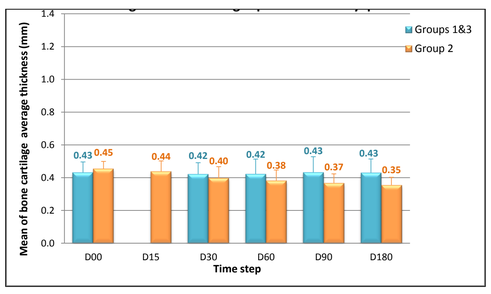
➡ Similar trend between µCTA and MRI with systematic thickness overestimation by MR

G1&G3 vs G2 - Mean of tibial cartilage average thicknesses of right knee obtained by µCTA

Medial



Lateral



➡ Significative decrease of cartilage thickness starting at D90 and D180 on NPH model of OA

Conclusion

- No differences were found with MRI examination between non injected and injected knees (required for the µCTA protocol) over the time.
- No difference was found between µCTA- and MRI-based cartilage thickness methods on control groups (G1&G3) since no residual measurement between both methods were found above the resolution of these techniques. Differences shown with G2 have to be further investigated.
- NHP model of OA was characterized by both imaging methods showing a monotone progression of the cartilage thinning up to -24.6±5.7% on D90 and -27.2%±5.2 on D180.

Perspectives

- MRI and µCTA modalities are valuable to measure cartilage morphology.
- Additional information can be obtained:
  - Indirectly about cartilage structure (T2, T1rho…) with MRI
  - Subchondral bone density with µCTA

References:
1. R. Bolbos et al., Osteoarthritis Cartilage 15:656-65 (2007).
2. A. Rengle et al., IEEE Trans Biomed Eng 56:2891-2897 (2009).
3. JC. Goebel et al., Rheumatology 49:1654-1664 (2010).
4. T. Hildebrand and P. Ruegsegger, J Microsc 185:67–75 (1997).

Acknowledgements: This work was funded by OSEO with grant E! 5671 from the Eurostars European program and performed within the framework of the LABEX PRIMES (ANR-11-LABX-0063) of Université de Lyon, within the program "Investissements d'Avenir" (ANR-11-IDEX-0007) operated by the French National Research Agency (ANR).

ISMRM, Salt Lake City, USA, 2013