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

E. Chereul¹, D. Grenier², A-L. Perrier², F. Taborik³, L. Mahieu-Williame², K. Tse Ve Koon²; T. Chuzel¹, S. Martin¹, L. Magnier¹, X. Pesesse⁴, Sandra Pietri⁵, H. Contamin³ and O. Beuf²

olivier.beuf@creatis.insa-lyon.fr

¹VOXCAN, Marcy l’Etoile, France; ²Université de Lyon, CREATIS CNRS UMR 5220; Inserm U1044; INSA-Lyon; Université Lyon 1, Villeurbanne, France; ³Cynbiose, Marcy l’Etoile, France; ⁴Bone Therapeutics, Grosselies, Belgium; ⁵Laboratoire de Rhumatologie, Hôpital Erasme, ULB, Bruxelles, Belgium.
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).
Materials and Methods

- 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 Hexabrix™ 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.
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
μCTA acquisition protocol

- 2mL Hexabrix™ (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

Two steps

Manual segmentation

Global thresholding

- Thickness distribution (4)

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

Mean of cartilage average thicknesses

Repeated injections for μCTA have no impact on cartilage quantification
Results: G1&G3 with G2 - Mean of tibial cartilage average thicknesses of right knee obtained by µCTA and MRI

G1&G3 – control group

G2 – ACL transection of right knee

Similar trend between µCTA and MRI with systematic overestimate
Results: G1&G3 with G2 - Mean of tibial cartilage average thicknesses of right knee obtained by µCTA

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 $-24.6\pm 5.7\%$ on D90 and $-27.2\%\pm 5.2$ on D180.

Perspectives

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

- Funded by OSEO with grant E! 5671 from the Eurostars European program.

- This work was conducted in the framework of the LabEX PRIMES

Lyon, city of lights