

# Morphological assessment of non-human primate models of osteoarthritis using HR-MRI and $\mu$ CT arthrography

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# 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  $\mu$ CT scanner that however needs contrast agent injected in the joint to depict cartilage limits.

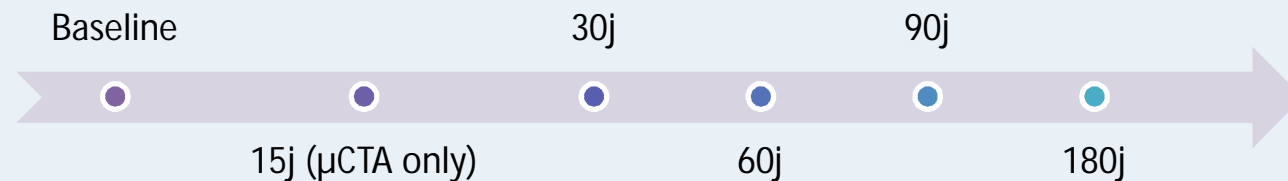
1. R. Bolbos et al., Osteoarthritis Cartilage 15:656-65 (2007).
2. A. Rengle et al., IEEE Trans Biomed Eng 56:2891-2897 (2009).
3. JC. Goebel et al., Rheumatology 49:1654-1664 (2010).

# Objectives

- The aim of this work, based on morphological parameters assessed on MRI and  $\mu$ CT arthrography ( $\mu$ CTA) acquisitions, was:
  - To assess the potential  $\mu$ CTA 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  $\mu$ CTA 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  $\mu$ CTA of 4 year old female cynomolgus.

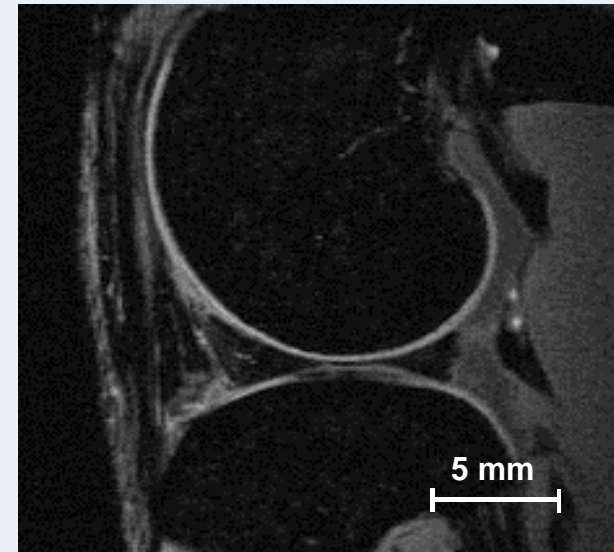


# MRI acquisition protocol

- 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  $\mu\text{m}^2$ , partition  
thickness: 220  $\mu\text{m}$
- scan time/knee : 20 min
- Total examination time: 90 min

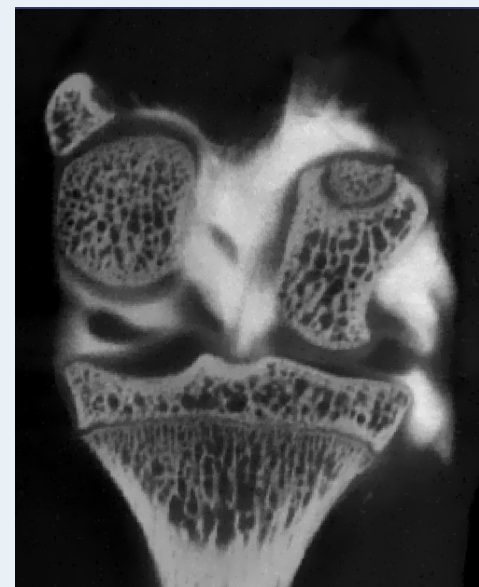
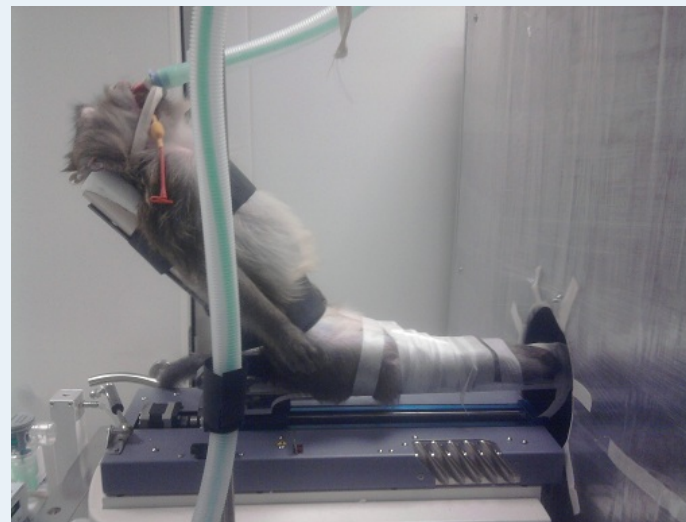


Susceptibility tissue-matched foam



## $\mu$ CTA acquisition protocol

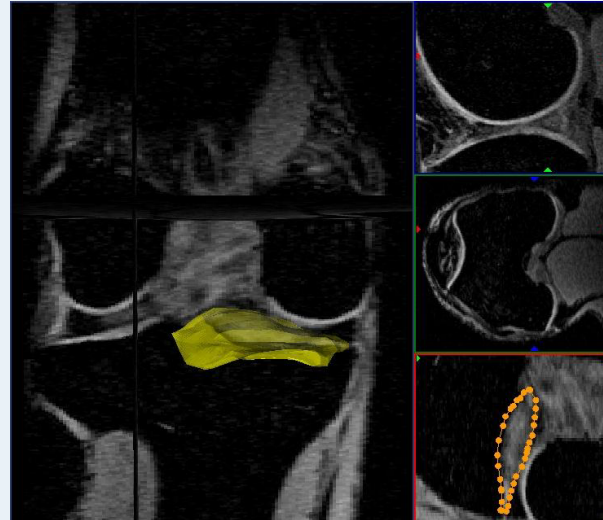
- 2mL Hexabrix™ (320mg/mL) with 40/60 dilution in PBS was injected in the synovial capsule with 23G needle.
- GE Locus  $\mu$ -CT (standard voltage and amperage)
- Isotropic voxel of 90  $\mu$ m
- Scan time for both knees : 15 min
- Total examination time: 30 min



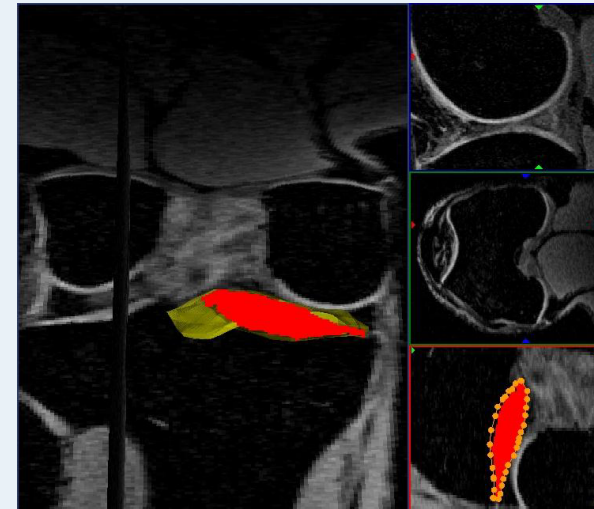
# Image processing protocol and cartilage quantification parameters

- Binarization

Two steps

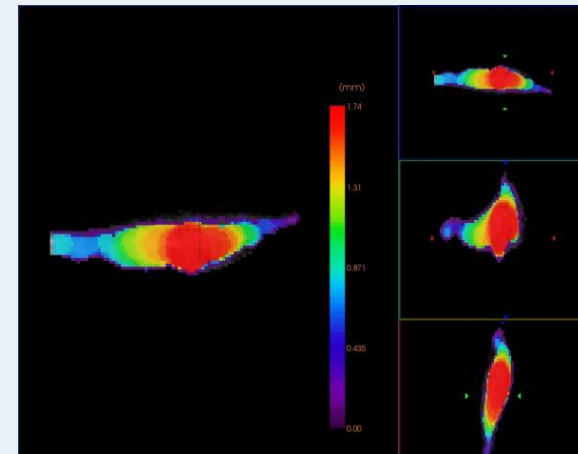
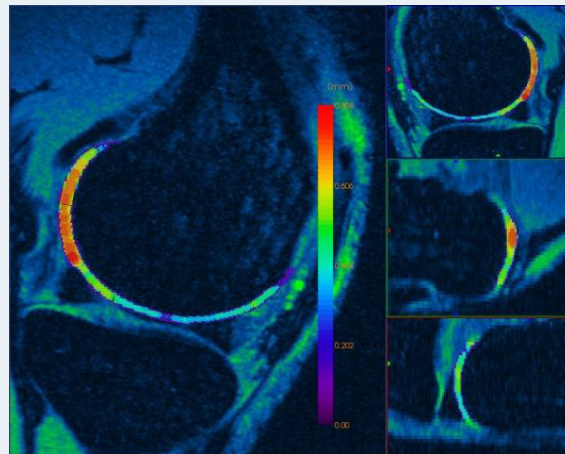


Manual segmentation



Global thresholding

- Thickness distribution (4)

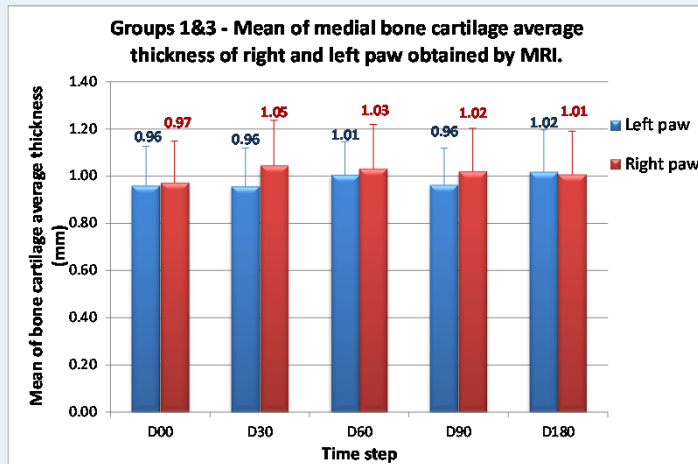


4. T. Hildebrand and P. Ruegsegger, J Microsc 185:67–75 (1997).

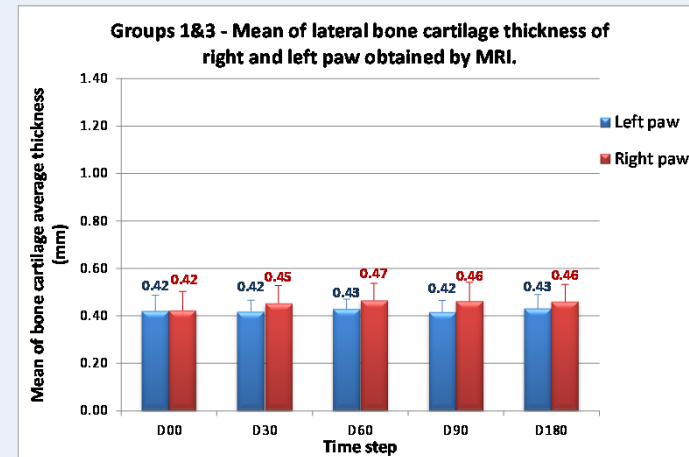
# Results: G1 & G3 - MRI-based quantification of left and right tibial plateaus

## Mean of cartilage average thicknesses

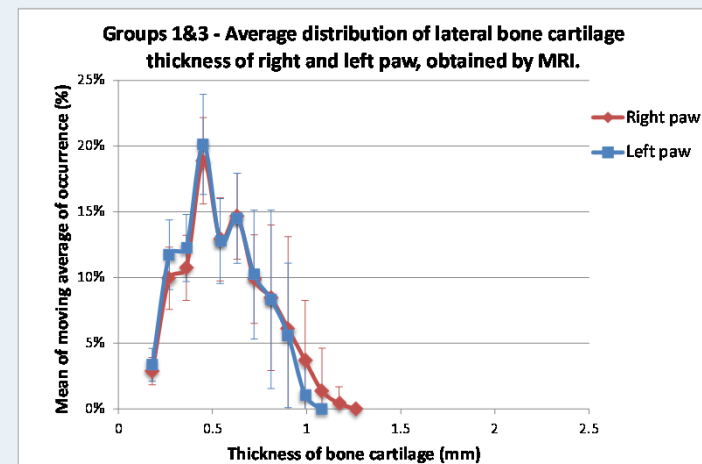
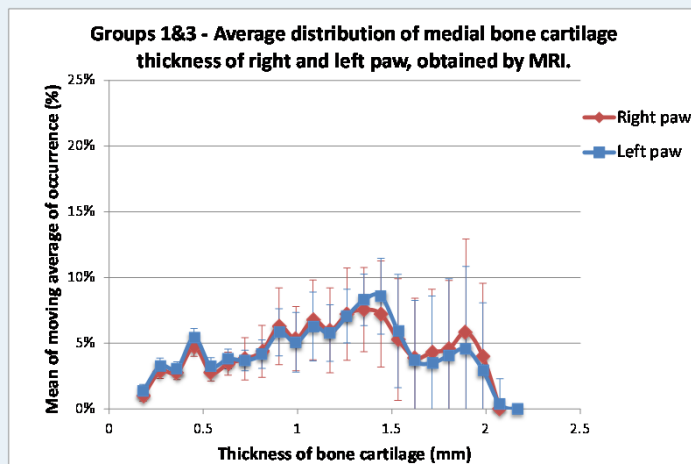
Medial side



Lateral side



## Distribution of thicknesses



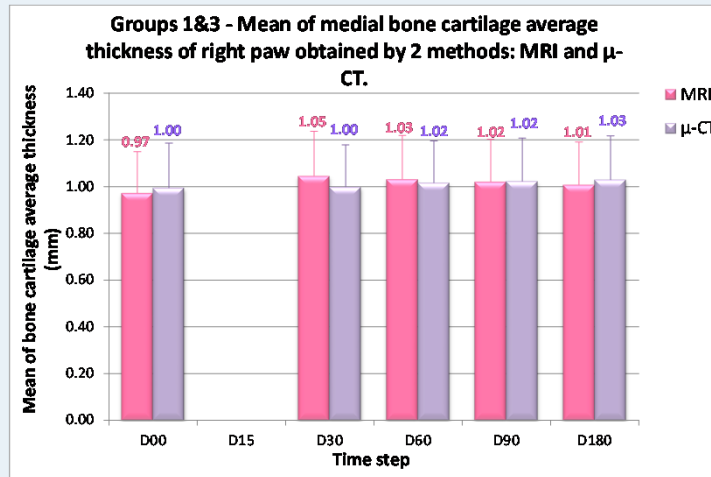
Repeated injections for  $\mu$ CTA have no impact on cartilage quantification



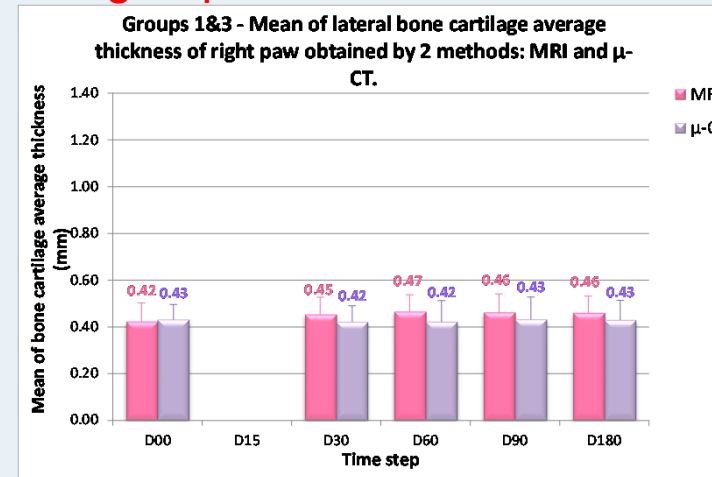
# Results: G1&G3 with G2 - Mean of tibial cartilage average thicknesses of right knee obtained by $\mu$ CTA and MRI

## G1&G3 – control group

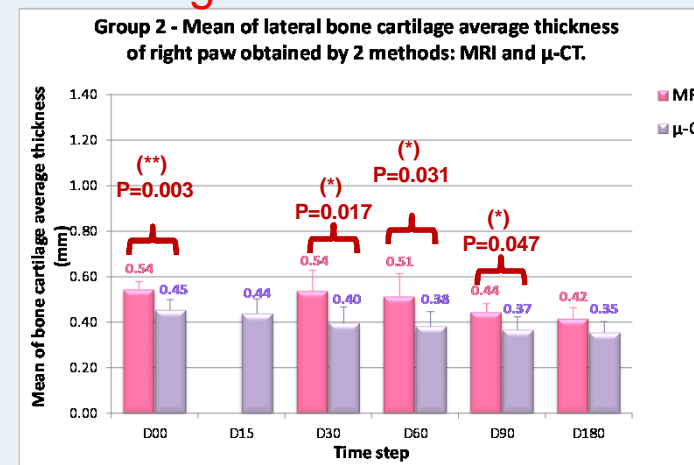
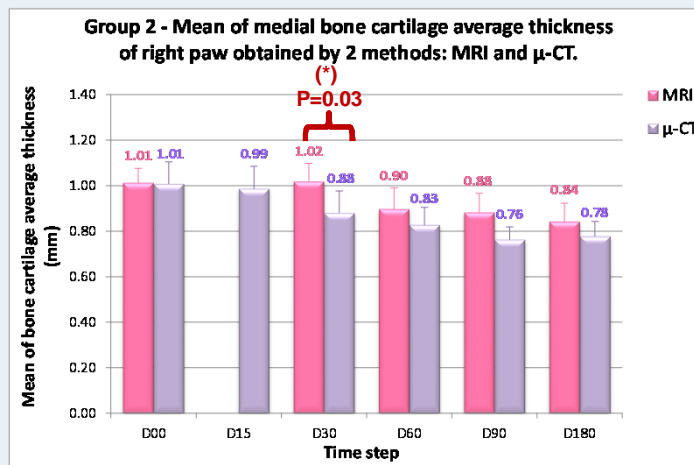
Medial side



Lateral side

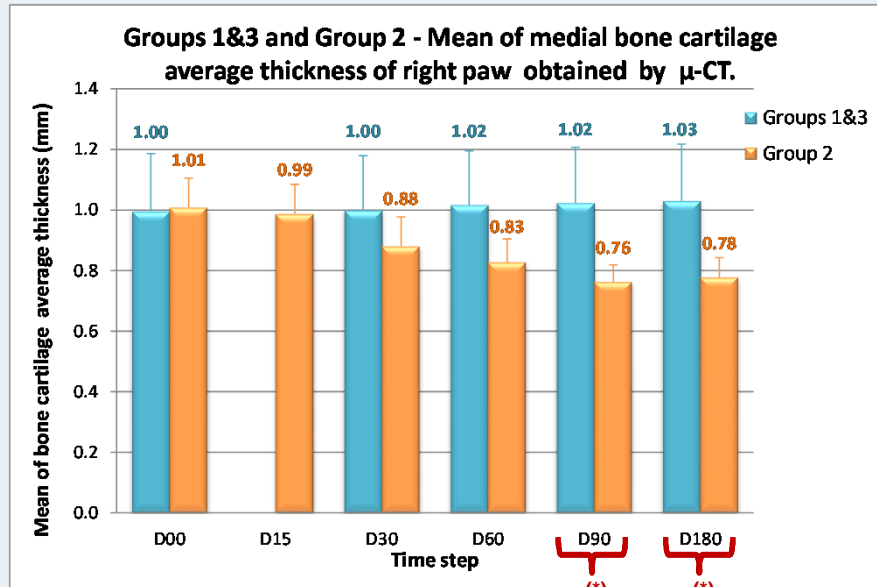


## G2 – ACL transection of right knee

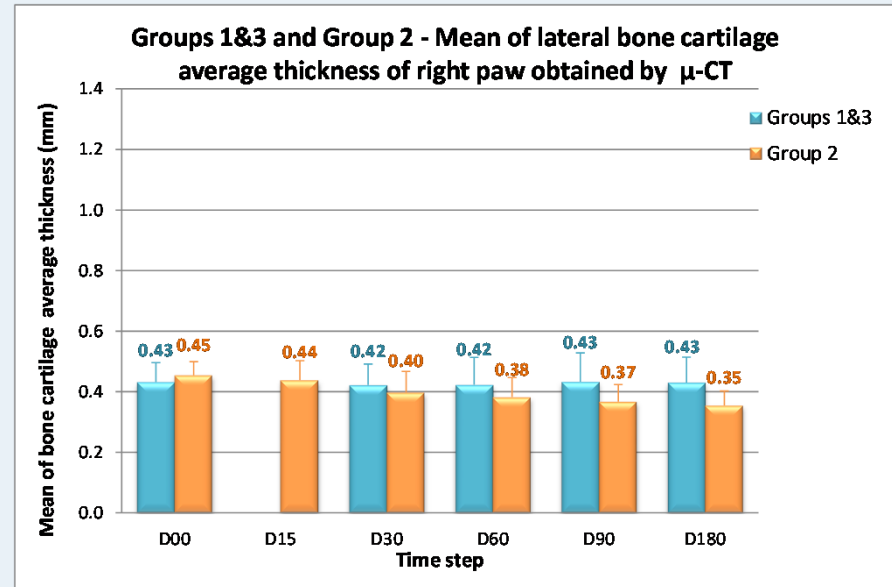


Similar trend between  $\mu$ CTA and MRI with systematic overestimate

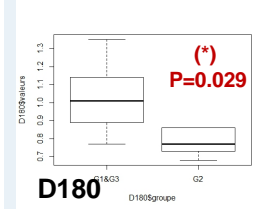
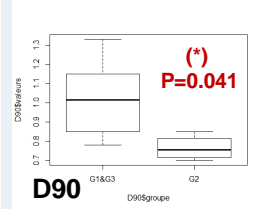
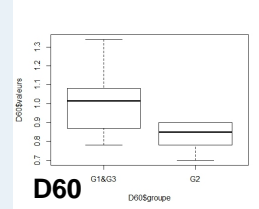
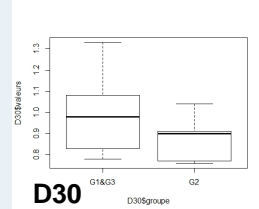
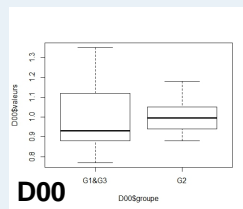
# Results: G1&G3 with G2 - Mean of tibial cartilage average thicknesses of right knee obtained by $\mu$ CTA



Medial side



Lateral side



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  $\mu$ CTA protocol) over the time.
- No difference was found between  $\mu$ CTA- 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  $\mu$ CTA 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  $\mu$ CTA

# Acknowledgments

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Lyon, city of lights

