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Morphological assessment of non-human primate models of osteoarthritis using HR-MRI and μ 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 making non-human primates (NHP) useful to model the human disease. Non-invasive techniques such as 3D HR-MRI have been validated to directly assess the cartilage thickness on guinea pigs (1) and instrumental developments allowed volume quantification in the different compartments of the cartilage can be achieve on rat models of OA (2-3). Nonetheless, spatial resolution is limited compared to CT scanner that however needs contrast agent injected in the joint to depict cartilage limits. The aim of this work was, based on morphological parameters assessed on MRI and μ CT arthrography (CTA) acquisitions, 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 of our institution. Three groups of young four year old female primates were constituted. (i) Group 1 (n=3) and Group 3 (n=3) with control animals where only the right knee was injected with contrast agent (Hexabrix 320mg/ml); (ii) Group 2 (n=6) with ACL transection of the right knee; Group 1 and 3 both allow to assess the potential µCTA protocol impact on the model (comparing right and left knee thicknesses by MRI) and the model characterization (comparing right knee thicknesses of all groups). Primates were examined at baseline, 30, 60, 90 and 180 days after surgery. For μ CTA, an additional measurement point was performed at D15. MRI was performed on a 1.5T Siemens Sonata system using a dedicated home-made pair of two-channel array coil. Each dual-channels array coil was interfaced with a flex interface from Siemens and a coil configuration file was created to drive the interface in array mode. HR-MRI was performed in the sagittal plane using a 3D water excitation FLASH sequence. A total of 120 partitions (220 µm thick) were acquired with an in-plane pixel of 112 x 131 µm2. The scan time was 20 min. µCTAs were performed on a GE Locus µ-CT at standard voltage and amperage parameters with an isotropic resolution of 90µm. The scan time was 15 min. For each animal, both knees were scanned in the same FOV. For both modalities, 3D thicknesses of the lateral and medial cartilage tibial plateaus were assessed using the same image processing protocol. First a double segmentation procedure was achieved with a rough and manually handled contour segmentation to isolate the cartilage regions of interest (ROI) followed by a regional automatic global segmentation procedure extracting medial and lateral cartilage ROIs. Inside the segmented ROIs, the quantification of cartilage thicknesses was performed using the method described by Hildebrand et al. (4).

Results

The μ CTA protocol (repeated injection of contrast agent in the knee) did not interfere with the model development since comparisons of cartilage thickness MRI measurements between injected and non-injected knees in control animals showed a mean residual of R1 = 0.015±0.134 mm, a value well below MRI spatial resolution. Additionally; the cartilage thickness μ CTA measurements (acquisition and processing protocols) did not show any bias with respect to MRI-based cartilage thickness in control animals: the mean residual between both measurements was R2 = 0.036±0.068 mm, a value well below MRI or μ CTA resolution too. Both imaging modalities showed superimpose 3D thickness distributions measurements. Mean cartilage thickness of medial tibia plateaus of the right joint were found constant for G1 but decreased significantly for G2 from D15 (-2.1±5.5 %) to D90 (-25.8±6.1 %) and with intermediate values on D30 (-12.6±8.1 %) and D60 (-20.2±4.8 %).

Conclusion

The cartilage thickness μ -CTA measurement on a NHP model of OA by transection of the ACL was validated with respect to the MRI approach since no residual measurement between both methods were found above the resolution of these techniques. Moreover the NHP model of OA was characterized by both imaging methods showing a monotone progression of the cartilage thinning up to -25.8±6.1% on D90.

References

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