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

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Introduction

Small animal models of osteoarthritis (OA) do not perfectly mimic the complex conditions occurring in human OA. In primates however, naturally occurring OA closely resembles human OA thus making non-human primates (NHP) useful models for 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 on rat models of OA (2-3). Nonetheless, spatial resolution is limited compared to CT scanner but the latter requires injection of contrast agent in the joint so as to depict cartilage limits. The aim of this work was, based on morphological parameters assessed on MRI and µCT arthrography (CTA) acquisitions, to characterize an induced model of OA by transection of the anterior cruciate ligament (ACL).

Material and Methods

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 enabled assessment of 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 µCTA, 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 element consists of a rectangular loop (30 x 35 mm^2 internal dimensions with 5 mm width and 35µm thickness copper track) etched on a flexible 508µm thick substrate. Decoupling between the two channels was achieved with optimal coil overlapping to minimize coupling between the two elements. 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 with 25° flip angle, 27 ms TR, 11.7 ms TE, 70 Hz/Pixel receiver bandwidth. A total of 120 partitions (220 µm thick) were acquired with a FOV of 50 x 50 mm^2 and an acquisition matrix size of 448 x 381 leading to an in-plane pixel of 112 x 131 μm^2. The scan time was 20 min. The primates were placed in supine position with both dual array coils placed on top of patella to encompass the whole knee joint. A minimum distance of 100 mm between both knees was keep to insure a minimum of 20dB decoupling between internal coil elements located at medial sides. 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

In vivo MR images acquired with the array coil associated with the HR-MRI protocol nicely depicted the cartilage. Such acquisitions were suitable to apply the segmentation procedure leading to articular cartilage volumes and thickness distributions. The µCTA protocol (repeated injection of contrast agent in the knee) did not interfere with the model development since comparisons of MRI-measured cartilage thickness between injected and non-injected knees in control animals showed a mean residual of R1 = 0.059±0.132 mm, a value well below MRI spatial resolution. Additionally; the cartilage thickness µCTA 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 = 0.027±0.090 mm, a value well below MRI or µCTA resolution too. Both imaging modalities showed superimposed 3D thickness distributions measurements. Mean cartilage thickness of medial tibia plateaus of the right joint were found constant for group 1 but decreased significantly for group 2 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 developed two-channel phased array coil improved the SNR and has an acceptable signal uniformity allowing a relatively straightforward segmentation process and quantification of cartilage morphology (thickness, volume). 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. Both imaging modalities appear valuable to measure cartilage morphology (volume and thickness). The choice of one on the other could be done based on imaging systems available or on additional information needs such as indirect cartilage structure (T2, T1rho…) for MRI or subchondral bone density for µCTA.

References

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Acknowledgements

This work is funded by OSEO by grant E! 5671 from the Eurostars European program and is conducted in the framework of the LabEX PRIMES.