Morphological assessment of non-human primate model of osteoarthritis: Comparison of HR-MRI with CT arthrography (CTA)

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Introduction

Many models of induced osteoarthritis (OA) are described in the literature, most of them in small animals. The limitations of these models, in adequately mimicking a condition as complex as human OA, need to be fully considered. Indeed, these models are rather ineffective in evaluating new treatments and especially in transposing observations to human disease considering the large genetic, phenotypic and pathophysiological heterogeneity between human and rodent. OA that closely resembles the human condition occurs naturally in primate. The histological lesions of OA in human and monkey knee joints include articular cartilage fibrillation and clefting. These lesions coincide with an increase in the thickness of the subchondral bone plate in both species and it has been suggested that this thickening may precede cartilage breakdown. These similarities make that these animals are useful to model the human disease. Non-invasive techniques to measure and qualify in-vivo the cartilage thickness in animal model of OA has been developed (1) and have greatly improve existing strategy to assess OA treatments and cartilage repair strategies. Established reproducibility confirmed that 3D HR-MRI could directly assess the cartilage thickness on guinea pigs (2) and recent instrumental developments demonstrated that volume quantification in the different compartments of the cartilage can be achieve on rat models of OA (3-4). Nonetheless, spatial resolution is limited compared to CT scanner. The aim of this work was (i) to develop a dedicated protocol for knee joint examination of cynomolgus primates at 1.5T and with µ-CT arthroscanner (µCTA); (ii) to compare morphological parameters assessed based on MRI and µCTA acquisitions on a group of 10 old primates with spontaneous OA.

Material and Methods

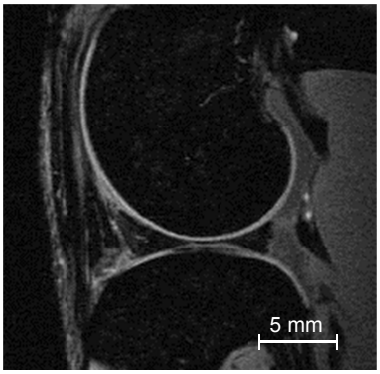
The MRI experiments were performed on a 1.5T Siemens Sonata system. A pair of two-channel array coil was built on a thermoformable plastic support with about 32 mm outer diameter. Each element consists in a rectangular loop (30 x 35 mm^2 internal dimensions with 5 mm width and 35µm thickness copper track) etched on a flexible 508µm thick substrate (Rogers™ RT/Duroid 5880). The decoupling between the two channels was achieved with optimal coil overlapping to minimize coupling between the two elements (minimize $|S_{12}|$ parameter). 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. The designed phased array coil were compared to the Siemens 40mm diameter small loop coil. Experimental characterization (signal uniformity and SNR) was performed on cylindrical phantoms filled with 1,25g/L of $NiSO_4$ with 5g/L of NaCl solution. The ethical guidelines for experimental investigations with animals were followed, and the experimental protocol was approved by the Animal Ethics Committee of our institution. Ten female primates between 12 and 18 years old (mean 13.8±1.8) were examined. The primates were placed in supine position with both dual array coils was placed on top of patella to encompass the whole knee joint. A minimum distance of 100 mm between both knees was keep to insure at least 20dB decoupling between internal coil elements located at medial sides. 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. 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 sequentially scanned. 3D thicknesses of the tibial plateau cartilage layers were assessed both on lateral and medial sides of the knee by using the same image processing protocol for each kind of acquisitions (MRI and µCTA). This protocol consisted in a double segmentation procedure: a first rough and manually handled contour segmentation to isolate the cartilage regions of interest (ROI) and avoid any divergence of the second region automatic global segmentation procedure which accurately extracts the morphology of both medial and lateral cartilage ROIs. Parameters of the second segmentation procedure were adapted for MRI or µCTA acquisitions. Inside the cartilage ROIs, the quantification of cartilage thicknesses was performed following the method previously described (5). Morphological results were compared in terms of distribution of the 3D thickness parameters obtained for each cartilage compartment. This analysis gives access to as many parameters as voxels describing the cartilage tissue. The spread of the thickness distribution with maximum-values at a given thickness characterizes the cartilage compartment.

Results

The SNR gain for the shaped two-channel array coil was 4.4 compared to the 40 mm diameter surface coil with 16% signal uniformity in the region of interest. In vivo images acquired with the array coil associated with the HR-MRI protocol nicely depicted the cartilage (Fig. 1). Such acquisitions were suitable to apply the segmentation procedure leading to articular cartilage volumes and thickness distributions. Simultaneous HR-MRI of both joints could not be reliably performed due to the lack of reproducibility in the magnetic field uniformity with two knees separated with air. In the examined group of old female primates, a coherent description with both imaging modalities was observed with superimpose 3D thickness distributions measured on the same animals. The presence of spontaneous OA was established (narrower thickness distribution) among the animals. For instance, the mean maximum thicknesses in the tibial plateaus without OA lesions were found to be 1.53 mm for the lateral compartment and 1.98 mm for the medial compartment. Furthermore, mean thickness distributions were found different in the lateral and medial compartments with the most common values determined at 0.81 mm and 1.89 mm respectively.

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). Both imaging approaches gave similar normalized cartilage thickness distributions on the same animals. These coherent results showed that both imaging modalities are valuable to measure cartilage morphology (volume and thickness) and could be chosen depending on additional information requested e.g. indirect cartilage structure (T2, T1rho…) for MRI or subchondral bone density for µCTA.



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