Investigation of Subchondral Bone cysts and Cartilage defects using *in vivo* 9.4T MRI in a model of Osteoarthritis

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Motivation: Osteoarthritis (OA) is a widespread degenerative disease affecting the articular cartilage and subchondral bone in synovial joints[1]. The production of new disease modifying OA drugs, that treat bone and cartilage, has been hampered by a lack of reproducible and longitudinal pre-clinical models. Previous work using an *ex vivo* rabbit model of OA demonstrated the ability to monitor changes to all tissue types using dual-modality imaging[2]. However, recent advances in Magnetic Resonance Imaging (MRI) and micro-Computed Tomography (μCT) now allow for *in vivo* imaging of rodent hind limbs, with scan times below 45 minutes for either modality.

Objective: To non-invasively investigate the development of subchondral bone cysts and cartilage degeneration – occurring in an *in vivo*, longitudinal pre-clinical model of OA – using combined, 9.4-Tesla MRI and μCT.

Methods: *In Vivo* MRI images were acquired on 8 healthy, male Sprague-Dawley rats using a Varian 9.4-Tesla scanner, prior to, and every 4 weeks after OA induction for up to 12 weeks. Animals were anesthetized with an injection of a ketamine/xylazine mixture (0.1 mL/100 gm). Volumetric imaging data were collected in the sagittal plane, using a 3D FLASH imaging sequence (TE=3.0 ms; TR=10 ms; FA= 5.5; 12 averages), with a 256 x 256 x 64 matrix size. A 2.0 cm surface coil was placed on the joint line of the right knee, and the animals were scanned in the supine position for 32 minutes. The resulting three-dimensional (3D) data set had 100 x 100 x 150 μm sized voxels. Once MRI imaging was complete, the rodent was scanned in the same position using a bench-top μCT scanner. The μCT scans produced 3D data with isotropic, 45 x 45 x 45 μm sized voxels (80 kVp, 0.45 mA, 400 msec exposure, 5 averages), with a total scan time of 17 minutes. In order to compare the changes to structures containing bone and non-bone elements, such as the menisci, the MRI images were re-sampled to 45 μm isotropic voxels, to allow for a 6-point anatomical, rigid-body registration with the μCT images.

Results: The knee imaging experiments, using a single dose of injected anesthetic, were successfully completed for each rodent in less than one hour. Qualitative observations of the MRI images (Fig. 1) demonstrate the capability to accurately delineated several soft-tissue structures in the knee such as: patellar tendon (PT), cruciate ligaments (CL), articular cartilage (AC), menisci (MN), and synovial fluid. The μCT protocol produced sufficient spatial resolution and signal-to-noise ratio (SNR = 19) to quantify subchondral bone composition, with a low entrance exposure (0.36 Gray). Rigid-body registration between both modalities enabled accurate comparison between images at the same 3D location within the knee. Using information from the MRI and μCT images simultaneously, we were able to distinguish between bone, and non-bone components within pathological structures, such as the formation of subchondral bone cysts that appeared as early as 8 weeks post OA induction.

Conclusions: The preliminary results from this study have shown that *in vivo* MRI and μCT are effective methods for both qualitative, and quantitative monitoring of OA development in the rodent knee longitudinally. A combined, dual-modality approach provides a complete characterization of both soft and mineralized tissues – and the capacity to measure differences non-destructively – within a single animal over time. In the future, this imaging data will be compared with the post-mortem histological investigation of the equivalent rat knees, allowing us to define the tissue and cell types located within the bone and cartilage pathologies associated with OA.

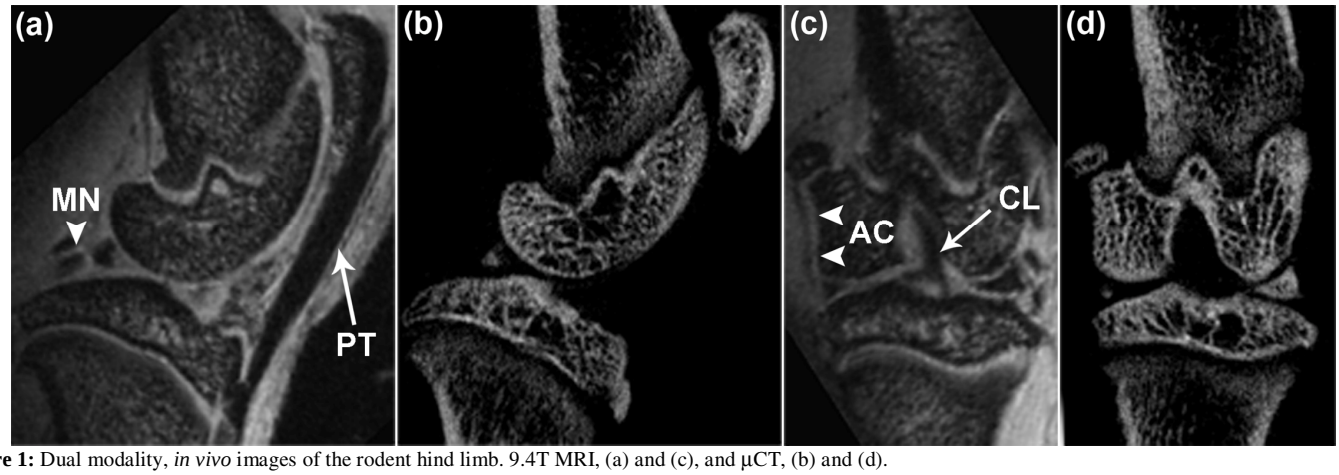

Figure 1: Dual modality, *in vivo* images of the rodent hind limb. 9.4T MRI, (a) and (c), and μCT, (b) and (d).

References:

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