T2 signal and orientation changes are early indicators of cartilage degeneration.

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Introduction The integrity of the collagenous network at the surface of articular cartilage is essential for cartilage health. As the initial histopathological changes of osteoarthritis (OA) occur at the articular surface,[1] an in vivo test of cartilage surface integrity could be an early and sensitive test for diagnosing and for monitoring the pathogenesis of OA. T_2 is related to cartilage collagen organization[2], and the collagenous network of normal articular cartilage has been shown to be dense, highly organized, and anisotropic when studied by high-field MRI[3]. When articular cartilage is imaged with the articular surface parallel to B_0 and the sample is subsequently rotated in a planar fashion, the anisotropy of collagen fibres in the superficial zone (SZ) can be monitored[4]. The aim of this study was to determine if high-field MRI, in particular T_2, can be used as a biomarker of articular cartilage surface degeneration in a canine model of early osteoarthritis.
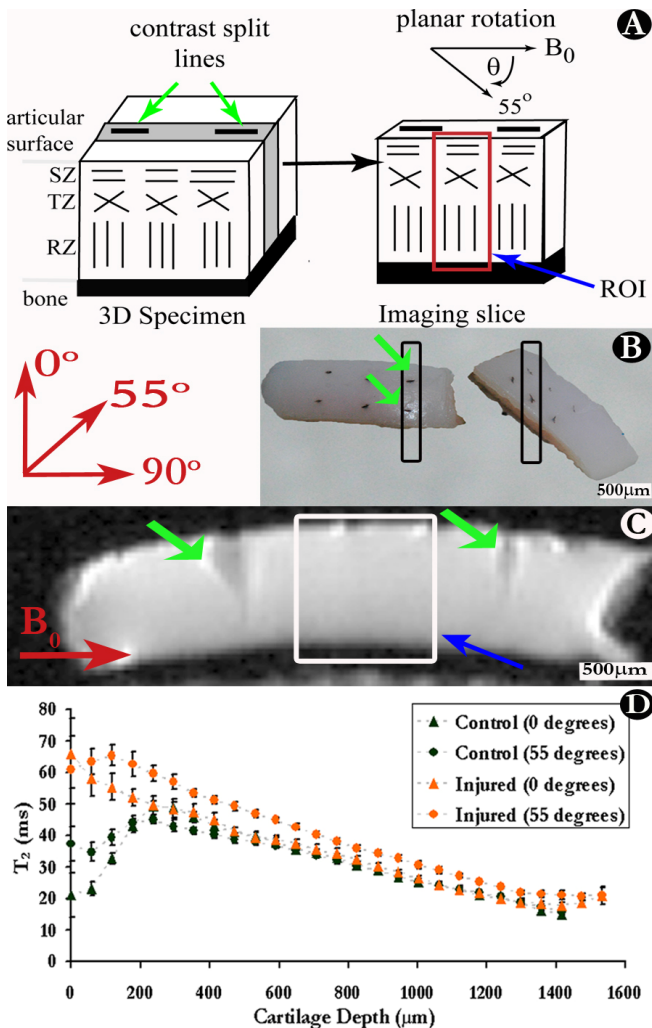

Methods Six skeletally mature canines underwent unilateral cruciate ligament transaction with the contralateral joint serving as the un-operated internal control. Animals were euthanized 12-weeks post-surgery. The medial femoral condyles were probed for surface collagen orientation by creating split lines[5] using a cocktail of 2:1 Higgins Black Magic India Ink and the MR contrast agent Feridex IV (11.2 mg Fe/mL) **(Fig 1A & B)**. Cartilage samples were wrapped in Parafilm, orientated with the articular surface facing up, and imaged in a 9.4T horizontal magnet (Bruker) at various orientations to B_0 using a planar method of rotation **(Fig 1A)**. A spin-echo sequence was used: TE/TR=9/3000, 256x256 matrix, 16 echoes, FOV=15x15mm, voxel: 0.059x0.059x1mm. Regions of interest were defined between adjacent split lines **(Fig 1B & 1C)**, and T_2 maps were calculated using a mono-exponential estimation. T_2 profiles were calculated by averaging 16 voxel rows parallel to the articular surface for each ROI, and presented as mean ± SD. T_2 values were compared using paired t-tests.

Results Figure 1D shows a representative T_2 surface-to-deep profile. T_2 profiles reveal an increase in cartilage thickness with injury in all six animals (**Fig 1D**). T_2 relaxation at the articular surface was short in controls but significantly longer in the injured animals (p<0.05, n=6 animals). Imaging orientation with respect to B_0 influenced T_2 throughout the depth of the cartilage, particularly at the surface. Both treatments (injury and imaging orientation) had the least effect on T_2 near the bone surface (**Fig 1D**). The orientation effect was more obvious in the controls, as the change in T_2 from 0 to 55° was significantly more in the controls than in the injured samples (p<0.05, n=6 animals).

Discussion An increase in cartilage thickness with injury is characteristic of early osteoarthritis (OA) in this model[6]. The change in T_2 with OA at the surface compared to deeper zones suggests that T_2 can be used to distinguish intact from injured cartilage. The change in surface T_2 w.r.t. angle in the control samples is a feature of the magic angle effect[2], as surface collagen fibres were identified with contrast split lines and oriented at 0 and 55 degrees to B_0. The reduction in magic angle effect on T_2 at the articular surface after injury implies that the collagenous network in this region becomes more isotropic, i.e., has become disorganized in this model of early OA. This study demonstrates that T_2 can be used as a sensitive biomarker of cartilage surface injury in this animal model of early osteoarthritis.

Fig 1. **A**: Rotation schematic showing cartilage histological zones, where the cartilage is rotated w.r.t. the surface collagen split line orientation. **B**: Injured (left) and control (right) cartilage surfaces (viewed en face and oriented to have same anatomical position) showing contrast split lines (green arrows) and image slices (black rectangles). **C**: MRI slice showing contrast split lines (green arrows) and region of interest (white rectangle) for calculating T_2 maps. **D**: Representative T_2 surface-to-deep profiles (mean ± SD of voxel rows in ROI, n=16 voxels) for one animal.

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