Longitudinal Evaluation of Cartilage Degeneration in ACL-Injured Knees using MR T1rho Quantification and Laminar Analysis

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INTRODUCTION

Patients with anterior cruciate ligament (ACL) injuries have a high risk of developing osteoarthritis (OA) later in life, despite ACL reconstruction (1,2). However, the mechanism of OA development in ACL-injured knees remains elusive. Recent development of imaging techniques that can detect cartilage matrix changes have the potential to provide information about early cartilage degeneration, and therefore may be valuable in understanding the development of OA in these ACL-injured knees as well as in helping improve patient management. Previously, we have observed significant elevated $T_{1\rho}$ values in cartilage overlying bone marrow edema-like lesions (BMEL) in acute ACL-injured knees (3). In this study, we followed these patients for up to 2 years and have developed techniques to examine the $T_{1\rho}$ values in different layers of cartilage. The goal of this study was to longitudinally evaluate 1) BMEL changes and 2) cartilage degeneration in ACL-injured knees using MR $T_{1\rho}$ relaxation time quantification and laminar analysis, both in lateral compartments where the initial BMELs are typically located and in medial compartments.

METHODS

Nine patients with ACL injuries (5 male, 4 female, mean age at baseline = 34.8 years, age range = 27-45 years) and 7 healthy volunteers (5 male, 2 female, mean age = 33 years, age range = 26-57 years) were scanned with a 3T GE Excite Signa MR scanner using a transmit/receive quadrature knee coil. Patients were initially scanned prior to surgery within 4 weeks of injury (n=9) and subsequently at 2 weeks (n=7), 6 months (n=7), 1 year (n=9), and 2 years (n=4) post surgery. The imaging protocol included sagittal T_2-weighted fast spin-echo (FSE) images (matrix = 512×256, FOV = 16cm, slice thickness = 2mm), sagittal 3D water excitation high-resolution spoiled gradient-echo (SPGR) images (matrix = 512×512, FOV = 16cm, slice thickness = 1mm), and a $T_{1\rho}$ quantification sequence based on 3D SPGR previously developed in our lab (MAPSS [4], FOV = 14cm, slice thickness = 3mm, time of spin-lock = 0/10/40/80 ms, spin lock frequency = 500Hz). BMEL regions were semi-automatically segmented in the FSE images using thresholding, and volumes were calculated. In follow-up exams, BMEL caused by surgical intervention (close to the screw and not present at baseline) were excluded from the analysis. Cartilage of the lateral/medial femoral condyles (LFC/MFC) and the lateral/medial tibia (LT/MT) were segmented semi-automatically in the SPGR images using an in-house developed software, and were further divided into sub-compartments (Fig 1A). Regions of cartilage overlying BMEL (OC) and the surrounding cartilage in the same compartment (SC) were defined at each time point based on the BMEL present at baseline. $T_{1\rho}$ maps were reconstructed by fitting the $T_{1\rho}$-weighted images pixel-by-pixel and were subsequently aligned to their SPGR images. An in-house developed laminar analysis program was used to equally divide cartilage contours into 2 layers: *deep* (closest to the bone) and *superficial*. $T_{1\rho}$ values for the layers of OC, SC, and cartilage sub-compartments were obtained. A Student's t-test that assumes a two-tailed distribution and unequal sample variances was used for statistical analysis ($\alpha = 0.05$).

RESULTS

The initial BMELs were found primarily in LFC and LT (7 in LT, 5 in LFC, 3 in MT and 2 in MFC). The volume of BMEL decreased at each follow-up exam, with significant changes from baseline starting at 6 months (6.4 ± 6.6 cm^3 vs 0.79 ± 1.1 cm^3, $P < 0.05$) and continuing to 1 year (0.49 ± 0.98 cm^3, $P < 0.05$) and 2 years (0.04 ± 0.09 cm^3, $P < 0.05$). By 1 and 2 year follow-up exams, 50% and 78% of lesions were completely resolved, respectively. In the LT, at 1 year follow-up, both deep and superficial layers of OC had significantly elevated $T_{1\rho}$ values compared to corresponding layers of SC (38.2 ± 4.3ms vs 30.1 ± 5.6ms for deep; 46.1 ± 4.4ms vs 37.9 ± 1.1ms for superficial, $P < 0.05$) (Fig 1D). At 2 years, both layers of the overlying cartilage were still elevated, but the difference was at edge significance for this small cohort (39.0 ± 5.6ms vs 30.2 ± 4.1ms, $P = 0.06$ for deep; 45.3 ± 4.7ms vs 37.1 ± 0.5ms, $P = 0.08$ for superficial). Among cartilage sub-compartments, MFC-3 showed a significantly higher $T_{1\rho}$ value in the superficial layer at both 1 year and 2 year follow-up compared to controls (48.3 ± 6.9ms vs 41.0 ± 4.8ms for 1 year follow-up; 52.7 ± 1.0ms for 2 year follow-up, $P < 0.05$) (Fig 1B). At 1year, MT-2 $T_{1\rho}$ times in the superficial layer were elevated significantly compared to controls (45.6 ± 5.9ms vs 39.4 ± 5.8ms, $P = 0.05$) (Fig 1C). For both MFC-3 and MT-2, $T_{1\rho}$ times of the deep layers were not significantly different from controls at any time point.
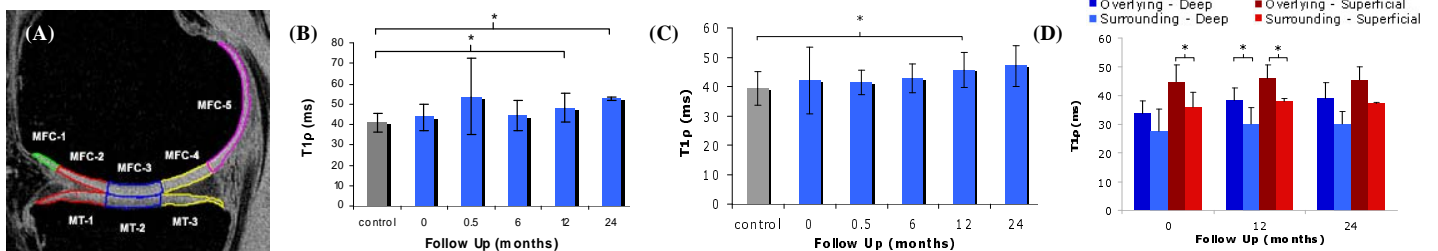
Fig. 1 (A) MFC and MT cartilage sub-compartments. MFC-3 and MT-2 are the weight-bearing sub-compartments and contacting areas of MFC and MT. (B) $T_{1\rho}$ values in superficial layer of cartilage in MFC-3 over time. (C) $T_{1\rho}$ values in superficial layer of cartilage in MT-2 over time. (D) $T_{1\rho}$ values of deep and superficial layers in cartilage overlying and surrounding BMEL in the LT. In graphs (B)-(D), asterisks (*) denote significant differences ($P < 0.05$).

DISCUSSION

$T_{1\rho}$ relaxation time mapping in cartilage provides quantitative assessment of potential early cartilage degeneration in knee injuries. Furthermore, laminar analysis provides us with detailed information in each layer of cartilage, which may be more sensitive than the average relaxation time evaluation in the whole compartment. Previous histological studies have proposed that BMEL-overlying cartilage may have sustained irreversible injury during impact from acute injuries (5). The elevated $T_{1\rho}$ values in cartilage overlying BMEL, at both baseline and follow-ups, suggest irreversible damage in these regions, despite resolution of BMEL at follow-ups. Cartilage $T_{1\rho}$ values were elevated, particularly in the superficial layers, as early as one-year in the medial compartments (MFC-3 and MT-2, the weight-bearing sub-compartments and contacting areas of MFC and MT). These regions are normally the sites for early OA onset, potentially due to change of loading even after ACL reconstruction. Early biochemical changes in these regions as indicated by elevated $T_{1\rho}$ values can be risk factors for OA development in these injured knees. Further investigation with more patients and longer follow-up times is warranted to test the significance.

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