INTRODUCTION:
Anterior cruciate ligament (ACL) injuries place the knee at risk for early osteoarthritis (OA), and there is evidence to suggest that ACL reconstruction, the standard of care for ACL injuries, does not reduce this risk. An in vivo method that can detect early changes in articular cartilage integrity could provide insight into the mechanisms by which post-traumatic OA develops in these patients, which could lead to more effective treatment strategies. Delayed Gadolinium-Enhanced MR Imaging of Cartilage (dGEMRIC) has been used to study changes in articular cartilage glycosaminoglycan (GAG) content following ACL injury [1, 2]. GAG is an important structural molecule of cartilage, and its loss is associated with articular cartilage degeneration [3]. dGEMRIC involves the creation of T1 maps of hyaline cartilage after the administration of an IV dose of an anionic gadolinium [Gd(DTPA)2−] contrast agent. Because cartilage matrix is composed largely of negatively charged GAG molecules, it repels the negatively charged ions of the contrast agent. Subsequently, the Gd(DTPA)2− concentration is higher in cartilage regions with lower GAG concentration; the cartilage T1 relaxation time is thereby reduced [3]. The resulting dGEMRIC index is correlated with cartilage GAG concentration.

For the purpose of this study, both knees of subjects with a unilateral ACL injury were imaged following injury (just before ACL reconstruction), and again 12 months after ACL reconstruction. Our objective was to compare the dGEMRIC indices of the femoral and tibial articular cartilage in the ACL-injured and contralateral uninjured knees before and after reconstruction. We hypothesized that the dGEMRIC indices of the ACL-injured knees would be lower than those of the contralateral knees at both the 0- (before surgery) and 12-month (after surgery) time points.

METHODS:
7 subjects (2 men, 5 women; mean age 39.3 years; range 26-48 years) who satisfied the inclusion criteria (unilateral ACL injury, no prior history of knee injury, less than 1/3 co-involvement of the meniscus, and no predisposing diseases for arthritis) were included in the study. The median time between injury and 0-month imaging was 76 days (range 45-410 days), and the median time between 0-month and 12-month imaging was 416 days (range 372-446 days). 3 subjects received hamstring allografts, 2 received hamstring autografts, and 2 received patellar tendon autografts. Of the 7 subjects, 2 underwent ACL reconstruction with partial meniscectomy; one in the medial, and the other in the lateral compartment. A third subject underwent medial meniscal repair during the reconstruction procedure. Upon arthroscopic inspection, one subject had Grade II chondrosis of the medial cartilage surface. The articular cartilage appeared healthy in all other subjects. All procedures were performed by the same orthopaedic surgeon (PDF).

dGEMRIC was performed on a 1.5T Siemens Symphony magnet. At each time point, each subject received an 0.2mmol/kg IV injection of Gd(DTPA)2− (Magnevist®, Bayer Healthcare) contrast agent, followed by a saline flush. Immediately after contrast injection, each subject walked for 10 minutes to promote contrast diffusion into the synovial fluid and cartilage. After 90 minutes, a series of 5 fast-spin echo inversion recovery sequences (inversion times of 1650, 650, 350, 150, and 28ms; TR=1800ms; TE=19ms; FOV=160mm; matrix=384 x 384; voxel size=0.4 x 0.4 x 3mm; NEX = 1) were acquired in the median plane of the medial femoral condyle for subsequent T1 mapping of the tibial and femoral cartilage. The order in which knees were scanned (injured knee first vs. uninjured knee first) was alternated between subjects, though a previous study found that the dGEMRIC indices were not sensitive to the 15-minute delay between contrast administration and image acquisition of each knee [2]. The MRIMapper software package (rev. 2006a R2; Beth Israel Deaconess Medical Center, Boston, MA) was used to create T1 maps of each knee, and to calculate the dGEMRIC index for the articular cartilage of each femur and tibia at each time point. Statistical comparisons were made between the dGEMRIC indices of the ACL-reconstructed and contralateral uninjured knees at the 0- and 12-month time points using a two-way repeated measures ANOVA.

RESULTS:
The dGEMRIC indices of the femoral and tibial articular cartilage of the injured knees were significantly lower than those of the contralateral uninjured knees following ACL injury, and 12 months after ACL reconstruction (p=0.005 and p=0.041, respectively) [Fig. 1]. At the pre-operative time point, the mean dGEMRIC indices of the ACL-injured knees were lower than those of the contralateral uninjured knees by 7.1% (405ms vs. 436ms) and 10.8% (399ms vs. 448ms) in the femur and tibia, respectively. Similarly, at the 12-month post-operative time point, the mean dGEMRIC indices of the ACL-reconstructed knees were lower than those of the contralateral uninjured knees by 8.1% (397ms vs. 432ms) and 8.4% (413ms vs. 451ms) for the femur and tibia, respectively. There were no significant differences due to time (p=0.442), and no significant interactions between treatment and time for both the femur and tibia (p=0.910).

Fig. 1: Mean dGEMRIC indices of the femoral and tibial articular cartilage in the ACL-reconstructed and contralateral uninjured knees at 0 and 12 months. Error bars represent one standard error.

DISCUSSION:
The lower dGEMRIC indices in the ACL-injured and ACL-reconstructed knees reflect a lower GAG content in the medial compartment of the femoral and tibial articular cartilage when compared to those of the contralateral uninjured knees. The reduced indices did not appear to change with time. It is interesting to note that the dGEMRIC indices for the ACL-injured and ACL-reconstructed knees were within the range of those reported for patients with mild OA [4, 5]. These findings suggest that cartilage integrity may be jeopardized following injury, and that the current standard of care, ACL reconstruction, does not restore cartilage health in a 12-month timeframe. In this study, the dGEMRIC method was able to detect early changes in cartilage metabolism in this patient population; the method could thus be used in future studies to better understand chondropathy following ACL injury, and to compare different treatment options.

REFERENCES:

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