sessions of pre-surgery rehabilitation (post-training/pre-surgery), 6 months post-surgery and 5 years post-surgery. The testing protocol included gait and electromyography (EMG) analysis wherein subjects maintained a self-selected walking speed. An 8-camera video system (Vicon, Oxford Metrics Limited, London, UK) was used to record kinematic parameters. Kinetic parameters were recorded using a force platform (Bertec Corporation, Worthington, OH). Surface-EMG recordings (Motion Lab Systems, Baton Rouge, LA) were collected from 7 muscles crossing the knee joint. The flexor muscles included semimembranosus, long head of biceps femoris and medial/lateral gastrocnemii, while the extensor muscles included rectus femoris and medial/lateral vasti. Peak medial compartment (pMC) load was computed using a validated Hill-type EMG-informed musculoskeletal model, which was anatomically scaled and calibrated for each subject. pMC loads thus obtained were normalized to body weight (BW) for each trial. Similarly, peak knee adduction moment (pKAM) was normalized to % BW height, and knee adduction moment impulse (KAMI) was normalized to % BW height * seconds. 3 trials per subject were averaged for the involved knee. Each of the biomechanical parameters indicative of knee joint loading were reported for the OA vs. non-OA groups using mean and standard error (SE) bars.

Results: For pMC, pKAM and KAMI, the most relevant difference between the OA vs. non-OA groups was evident 6 months post-surgery, signified by non-overlapping SE bars (Figures 1, 2 and 3). Further, there were no differences between the two groups for each of the biomechanical parameters 5 years post-surgery.

Conclusions: For subjects who showed radiographic signs of knee OA as early as 5 years post-surgery, the data demonstrate reduced loading in the involved knee as early as 6 months post-surgery. What followed was a prolonged period of normal loading, starting at 1-2 years, and extending up to 5 years (based on our previous and current results). Comparing the involved knee of OA vs. non-OA groups presented here, the data suggests that premature knee OA after ACLR develops during a period marked by early unloading, followed by an extended period of normal loading. Also, this OA onset period does not appear to be associated with elevated loading.

Figure 1. Peak Medial Compartment (pMC) load in the involved knee.

Figure 2. Peak Knee Adduction Moment (pKAM) in the involved knee.

Figure 3. Knee Adduction Moment Impulse (KAMI) in the involved knee.

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HIGH-RESOLUTION NMR STUDIES OF CARTILAGE MOLECULAR MOTION
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Purpose: Osteoarthritis is a degenerative disease of the joints that affects more than 60 million Americans. Osteoarthritis (OA) is characterized by the deterioration of the articular cartilage which is a soft tissue comprised mainly of water, collagen, and proteoglycan aggregate. One clinical diagnostic method for OA is magnetic resonance imaging (MRI) using T1- and T2- weighted images which describe the loss of cartilage and joint space in 8-bit grayscale. Nuclear magnetic resonance (NMR) is the fundamental physical process used for MRI. NMR can provide information about molecular motion in multi-component systems such as cartilage. The objective of this study was to characterize molecular motion from cartilage samples obtained from Stage IV osteoarthritic female hips to better understand cartilage structure-function relationships. Toward this goal, we quantified molecular motion with T1-T2 correlations and high-resolution NMR diffusion measurements of articular cartilage.

Methods: T1-T2 correlation maps and molecular diffusion coefficients were determined for articular cartilage samples. Cartilage was obtained from human joint replacement patients and separated into superficial-middle and middle-deep samples (n = 4) by shaving sections of cartilage from the femoral head. All donors were classified as KL stage IV. The shaving from the superficial-most ~200-500 microns were classified as surface-middle and the shavings from the bottom ~500 microns and deeper were classified as middle-deep. The T1-T2 correlations were measured with a modified Carr Purcell Meiboom Gill (CPMG) Sequence and analyzed with nonlinear regression analysis. The effective diffusion coefficient was obtained by use of the pulse gradient stimulated echo (PGSE) sequence and analyzing the data with the Stejskal-Tanner relationship. The molecular displacement observation time was varied from 15-600 ms to examine restricted diffusion. To differentiate diffusion between the macromolecular cartilage matrix and water, the gradient magnitude was varied. For macromolecules, the gradient strength varied from 2.05 to 17.81 Tesla/meter, and diffusion coefficients were obtained by fitting linear regions of the multi-exponential data signal decay curve. For water diffusion, the gradient was less than 1 T/m, which is the strength used in clinical MRI.

Results: T1-T2 maps show distinct patterns indicating the presence of two molecular populations (e.g. a solid-like and liquid-like population, Figure 1). The location of maximum T1 and T2 intensity did not vary
greatly between deep-middle and superficial-middle zones (p > 0.13, Figure 1). Using a PGStE sequence and large gradient values, we found two macromolecule populations, one fast moving and one slower moving for both the superficial-middle and middle-deep samples. The relative proportion of these populations and diffusion coefficients was patient-specific (Figure 2). There was no difference in the polymer diffusion between superficial-middle and middle-deep zones (p > 0.17, Figure 2).

There was a difference between the effective self-diffusion coefficient of water in the superficial-middle and middle-deep zones (all p < 0.02, Figure 3A). When utilizing an extended range of displacement observation times (15 - 600 ms), we found water effective diffusion coefficients indicating a pore size of 0.157 nm for the superficial zone and 1.6 nm for the deep zone (Figure 3). **Conclusions:** This study shows multiple populations of macromolecules in human arthritic articular cartilage via distinct populations of NMR-measured effective diffusion coefficients. To our knowledge, this is the first time this approach has been used to study human cartilage tissue. Future research may extend these results to clinical MRI by combined measurements of water diffusion and pore size which, paired with T1 and T2 images, may improve the diagnostic sensitivity for osteoarthritis. Future studies will examine structure-function relationships via combinations of macromolecular NMR and biochemical experiments.