Dynamic Changes in Subchondral Tibiofemoral Joint Space as a Predictor of Early Cartilage Damage

Chelsea Marsh1, Scott Tashman, Ph.D2.
1University of Pittsburgh, Pittsburgh, PA, USA, 2University of Pittsburgh Medical Center, Pittsburgh, PA, USA.

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Introduction: About half of all patients with meniscal tears will develop OA within 10-20 years of injury, while the other half will be symptom-free. Currently the only way to noninvasively detect the presence of knee OA is to use joint space radiographs or MRI. While these tools can reliably distinguish between early and late-stage OA, they are unable to predict OA prior to the development of significant cartilage lesions. Often during arthroscopy, surgeons identify areas of “softened” cartilage, which do not always correlate with visible signs of surface damage or cartilage loss. This softening has been related to changes in the cartilage matrix, which could represent early structural damage that can lead to irreversible cartilage damage and OA. The purpose of this study is to use dynamic stereo radiography to examine the change in tibiofemoral joint space as an indicator of early cartilage damage following meniscal injury and partial meniscectomy. We hypothesize that subjects with softened articular cartilage will have different load-response curves than subjects with healthy cartilage, which could indicate the early presence of OA.

Methods: 19 subjects participated in this IRB-approved study and were separated into 3 groups - partial meniscectomy subjects with softened articular cartilage (n=5, 4M, 1F), partial meniscectomy subjects with healthy articular cartilage (n=4, 2M, 2F), and age/sex matched healthy controls (n=10, 6M, 4F). Articular cartilage status was graded during arthroscopy using the Outerbridge scale, where grade 0 corresponded with healthy cartilage and grade 1 corresponded with softened cartilage. Exclusion criteria for the study included previous injury/surgery to the affected limb, age outside of the 25-55 year range, and a BMI >35. Subjects performed two tasks - a step-loading activity and running on a level treadmill. The step-loading activity utilized a modified leg press machine, and weight equivalent to half of the subject’s body weight was applied to the affected leg, as shown in Figure 1. The step loading activity was performed twice - once at full extension and again at 15° of flexion. Before each test, subjects rested supine for thirty minutes to allow for the articular cartilage to return to its unloaded state. For the step-loading trials, stereo-radiographic images were captured at 50 frames/s from 0.4 seconds before the weight was released until 0.8 second after the weight was released, at 4 frames/s for the next 19 seconds, and then for 10-frame bursts at 150 frames/s in one-minute increments until the subject had held the weight for 5 minutes or was too fatigued to continue. Following the leg press activities, the subject rested for another 30 minutes and then ran on a level treadmill at 2.5 m/s. Images were collected during stance phase at 150 frames/s immediately upon starting to run, and collection repeated at one-minute increments until 5 minutes or subject fatigue.

In addition to kinematic testing, all subjects underwent a unilateral CT scan that was segmented to create patient-specific bone models of the femur and tibia using a previously-described method [1]. The segmented bone models were then matched to the X-ray images gathered during kinematic testing using a computerized, model-based tracking technique [2]. The location and orientation of the femur and tibia were then projected into 3D space, and their motions and positions relative to one another were calculated.

The tibiofemoral subchondral joint space was extracted for each frame from the central subregion of the medial tibial plateau. For the leg-press trials, joint space values for the entire loading phase were plotted against time. These distances are normalized to the unloaded joint space value at the beginning of the trial. For the running trials, joint space values were extracted at each heelstrike and normalized to the subchondral distance of the first running trial. These normalized distances were then and plotted against time.

Differences between subject groups were assessed with SPSS software using a multiple-factor ANOVA (MANOVA). A MANOVA was used to look at differences between the subject groups in the initial loading phase of the leg press trial at full extension, and a separate MANOVA was used to look at differences between subject groups in the running trials. If MANOVA found significance (p<0.05), analysis was followed up with independent t-tests at different time points.

Results: Figure 2 shows the change in joint space during the step-loading activity at full extension during the initial loading phase (first 20 seconds of weight application), and the change in joint space during running. In terms of the leg press activity, significant differences are seen at 16.2, 17.45, and 18.7 seconds. Post-hoc testing reveals significant differences between the load-response curves of the partial meniscectomy group with softened articular cartilage and the uninjured control groups (p=.035, p=.028, p=.030, respectively), and differences trending on significance between the partial meniscectomy groups with softened and healthy articular cartilage (p=.078, p=.096, p=.069, respectively). Differences are not seen between the surgical group with healthy articular cartilage and the uninjured controls. There are no significant differences between any of the groups.
in the running activity. It should be noted that the leg press data from the 15° flexion trial are not included in this analysis. Subjects had trouble maintaining the flexion angle for the duration of the weight application, resulting in joint flexion/extension motion that confounded data analysis.

**Discussion:** The results of this study indicate that subjects with softened articular cartilage exhibit a different load-response curve than individuals with healthy articular cartilage. It is possible that cartilage softening is indicative of early mechanical damage in the cartilage’s collagen matrix, and that softened cartilage is more porous and allows water to escape more easily from its microstructure. These microscopic changes in the cartilage’s architecture manifest themselves as larger and faster changes in subchondral joint space over time in the leg press activity.

Interestingly, differences between the subject groups are only visible in the leg press activity and not in the repetitive loading of the running trials. These results mimic in vitro testing with cartilage specimens. Ronken, et al, performed confined creep and indentation tests on samples of bovine articular cartilage and measured the change in specimen thickness over time [3]. Similar to the current study, it was found that creep testing yielded differences in cartilage thickness while repetitive indentation testing did little to impact the thickness of the cartilage specimen over time. These similarities indicate that not only are there significant parallels between in vitro and in vivo work in this area, but also that softened and healthy articular cartilage are functionally similar in many activities.

In the future, we hope to use this data to develop a clinical diagnostic to be used in the clinic to aid in the early, non-surgical detection of cartilage damage. We would also like to segment the MRI scans of all subjects to generate cartilage maps and better understand any changes in cartilage contact area as a result of softened articular cartilage and/or partial meniscectomy.

**Significance:** The inability to detect cartilage damage before it advances into OA hinders the development or use of chondroprotective and OA-modifying treatments. Thus, the detection of OA before the appearance of significant cartilage damage would aid in treating and possibly reversing the disease.

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**References:**
Figure 1: Modified leg press inside Dynamic Stereo X-ray (DSX) system

Change in tibiofemoral subchondral joint space at full extension

Change in subchondral joint space during running

Figure 2: Normalized change in subchondral joint space during full extension and running. * represents trending significances, and + represents significant differences between groups.

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