In Vivo Cartilage Deformation Across a Series of Tasks in Adults with Knee Osteoarthritis

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INTRODUCTION: Articular cartilage's ability to perform its fundamental functions (load-bearing and lubrication) critically depends on the pressurization of interstitial fluid that is reacted by a high tensile modulus solid matrix. This interstitial fluid pressure effectively stiffens the cartilage by an order of magnitude or more. However, degenerative joint conditions such as osteoarthritis reduce the tensile modulus and increase the permeability of the matrix. In silico and ex vivo studies demonstrate that these changes lead to a reduction in the interstitial fluid pressure, a lower apparent tissue stiffness, and increased cartilage deformation. In this work we aimed to capture the deformation (strain) of cartilage in vivo in adults with knee osteoarthritis following a series of tasks designed to load the cartilage. We hypothesized that standing would produce compressive strain based on prior in vivo work, walking would partially recover strain due to the multiple recovery modes present during joint articulation, and that lying supine would recover strain based on prior in vivo work.

METHODS: Task Protocol: Following IRB approval and informed consent, eight adults (age: 46 to 67, sex: 4 male/4 female) with knee osteoarthritis defined by the National Institute for Health and Care Excellence performed a fixed series of tasks, each of which was followed by magnetic resonance imaging (MRI) to track acute changes in knee cartilage thickness. The order of tasks was as follows: 1) stand for 30 min, 2) walk for 10 min at 110 steps per min, 3) stand for 30 min, and 4) lie supine for 50 min. The walking task was performed on a hard surfaced linear track that was 16 m long and required participants to turn or pivot at each end. A 3T Siemens PRISMA scanner equipped with a 15 channel Tx/Rx knee coil was used to scan the affected knee of participants in the sagittal plane using a proton density weighted turbo spin echo sequence (TR = 9710 ms, TE = 37 ms, Flip Angle = 150 deg). The field of view was 13 × 13 cm [384 x 384 px] with a slice thickness of 1.5 mm. The resulting voxel size was 0.34 x 0.34 x 1.5 mm. The scan duration was 3:43 min.

Data Analysis: The femoral cartilage, tibial cartilage, and menisci were manually segmented following all 5 tasks. Each task-based segmentation was registered to the baseline to account for any rigid body motion between subsequent scans. Segmentation contours were resampled at a sub-voxel level. Cartilage thickness was measured as the Euclidean distance between the cartilage-bone interface and the cartilage surface. The axial deformation was quantified as the change in thickness at each location, and axial strain (engineering strain) was quantified by normalizing the axial cartilage deformation by the baseline cartilage thickness. The regional strain was reduced to 3 regions of interest on each joint surface: whole surface, cartilage-cartilage contact, and cartilage-meniscus contact, see **Fig 1A**. To avoid the effects of meniscus positioning on the analysis we used a fixed meniscus location based on its location in the baseline scan.

Statistics: Data are reported as the mean ± 95% confidence interval for engineering strain (**Fig 1**). We aimed to determine if task had a significant effect on cartilage strain in any of the regions. First, we assessed the data for normality using the Shapiro–Wilk test. All regions reported in this work met normality; therefore we used a parametric repeated analysis of variance test — Repeated Measures ANOVA test. While post-hoc testing was performed to detect significantly different pairs, we limit our discussion here to the results of the Repeated Measures ANOVA.

RESULTS: Femoral cartilage strain was not significantly affected by task for any regions (femoral surface, p=0.594; cartilage-cartilage contact, p=0.592; cartilage-meniscus contact, p=0.399). Tibial cartilage strain was significantly affected by task for the full surface and cartilage-meniscus contact (tibial surface, p=0.026; cartilage-cartilage contact, p=0.088; cartilage-meniscus contact, p=0.0009). Overall, the tibial cartilage underwent compressive strain during standing tasks (mean tibial compression = -4.47% strain), and recovery during walking (mean tibial recovery = 5.09% strain) and lying supine tasks (mean tibial recovery = 2.31% strain).

DISCUSSION: Standing, which produces a compressive and near static load on the cartilage, yielded a compressive strain that was greatest, during the first task, in the region of cartilage-cartilage contact on the tibial plateau (Standing 1 = -9.00% axial strain). Walking is known to load the joint more than standing, which would lead to the expectation of greater cartilage strain. However, walking also involves knee joint articulation, which may activate several modes of cartilage recovery that have been studied ex vivo and in vivo. **Fig 1C** demonstrates that walking induced cartilage recovery occurred across all regions on the tibial plateau. Interestingly we observed hyper-recovery following walking in the region of cartilage-meniscus contact. While this initially sounds implausible, it is important to note that participants were scanned at variable times throughout the day, they did not undergo a period of unloaded recovery prior to imaging, and we did not restrict their activity on day of or prior to imaging. Due to this, participants began the task series with a baseline level of compressive strain on their cartilage which may explain the observed hyper-recovery.

The results of this study have practical joint health implications. If brief bouts of walking can partially reverse the large compressive strains accrued during standing, incorporating short activity intervals may help limit daily strain accumulation. Furthermore, the results suggest that 10 min of walking may offer faster strain recovery when compared to 50 min of lying supine. While these results offer exciting potential for objectively detecting cartilage degeneration in vivo, there are several limitations we wish to acknowledge. First, this was a pilot study of 8 osteoarthritic participants. Osteoarthritis is a broad joint disorder with subcategories that we have not controlled for in this study. Second, strain was reduced to a single axis rather than a full tensor. Third, imaging was performed immediately after each task rather than during loading; thus, these measures represent the residual deformation. Lastly, the time of day and prior loading was not controlled for which may be linked to the variability between participants.

SIGNIFICANCE/CLINICAL RELEVANCE: This work provides initial evidence that osteoarthritic knee cartilage is responsive to different loading conditions in vivo.

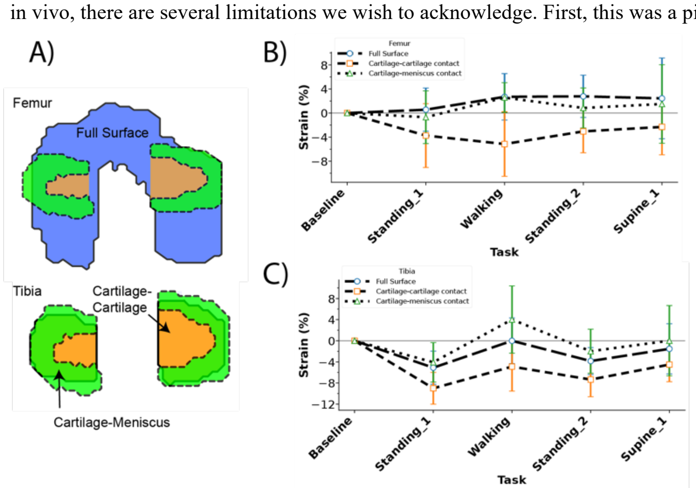

Figure 1. (A) Unrolled femoral/tibial cartilage maps: cartilage–cartilage (orange), cartilage–meniscus (green), outside meniscus (blue). (B & C) Regional strain in the femur and tibia versus task. Regions include: full surface (blue), cartilage–cartilage (orange), cartilage–meniscus (green).