Walking Decreases T1rho Relaxation Times in the Articular Cartilage of the Knee

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Introduction: Mechanical loading of articular cartilage plays an important role in normal cartilage homeostasis, while disruptions to normal loading patterns are associated with onset and progression of osteoarthritis [1]. However, the precise mechanisms through which mechanical loading leads to cartilage degeneration remain unclear. During activities of daily living, such as walking, significant loads of up to several times body weight are transferred across the joint [2]. In response to compressive loads, water is exuded from the cartilage matrix, which increases the relative concentration of highly charged proteoglycans within the tissue [3]. The charged proteoglycans retain dissolved ions as the water is exuded, leading to changes in the osmotic environment of the tissue. Since changes in osmotic pressure have been shown to influence chondrocyte metabolism [4, 5], data quantifying the influence of activities of daily living on proteoglycan concentration, and thus osmolarity, is important for understanding normal cartilage physiology. Furthermore, such data may be important for understanding the mechanisms through which altered mechanical loading contributes to the development of osteoarthritis.

There is currently limited data characterizing the effects of in vivo loading on proteoglycan concentration during activities of daily living. Thus, the goal of this study was to use T1rho-weighted MR imaging [6, 7] to analyze changes in proteoglycan concentration in knee articular cartilage in response to walking, one of the most frequent activities of daily living. T1rho relaxation is a non-invasive MR imaging technique that has been shown to be sensitive to changes in proteoglycan concentration [6, 7]. We hypothesize that mechanical loading experienced during walking will compress the cartilage matrix leading to expulsion of water and increased proteoglycan concentration which will be reflected by decreased T1rho relaxation times.

Methods: Six healthy subjects (3F, 3M; Age 22-27 years; mean 24 years) with normal BMI (22.3-26.4 kg/m2) were recruited to participate in this IRB approved study. Exclusion criteria included a history of knee injury, surgery, or symptomatic knee pain. All scans were performed first thing in the morning to minimize stress on the knee prior to testing. Upon arrival to the MRI suite, each participant rested in the supine position for 45 minutes to allow for cartilage equilibration [8].

Following the initial rest period, subjects were imaged using a 3T MRI scanner (Trio Tim, Siemens Medical Solutions USA, Malvern, Pennsylvania) and an eight-channel knee coil. Sagittal images were obtained using a 3D T1rho-weighted spin-lock pulse sequence (matrix=256 x 256, TR/TE = 3500/13 ms, B1 = 500 Hz, thickness = 3mm, spin lock pulse duration (TSL) = 5, 10, 40, 80 ms) and a Double Echo Steady State (DESS) sequence (field of view: 16×16 cm, resolution: 512×512 pixels, thickness: 1 mm, flip angle: 25°, TR: 17 ms, TE: 6 ms, DESS Scan = 9 minutes) [8]. Subjects then walked on the treadmill for a total of 20 minutes at 2.5 mph. Following completion of the walking exercise, subjects received a post activity T1rho scan using the same imaging parameters.
The bony and articular surfaces of the MR images were traced and stacked to form a wireframe model. An iterative closest point technique (Geomagic, Studio, Geomagic, Inc.) was used to align the pre and post activity models to allow for site-specific comparison of T1rho relaxation times. A grid sampling system was created on each osseous surface to span the joint (Figure 1). Image intensity was plotted against the corresponding spin lock time for each pixel [8] to create a relaxation curve from which T1rho values were extrapolated (Figure 2). A repeated measures ANOVA was used to analyze the effects of exercise and location (medial vs. lateral compartment) on T1rho relaxation.

**Results:** Following exercise, there was an overall 7% decrease in T1rho relaxation values across the tibiofemoral joint. T1rho values in the tibia decreased 3%, with pre-exercise values being significantly greater than post (p<0.01) and no significant difference between medial and lateral sides (p=0.5) (Figure 3). While not significant, a greater average decrease in T1rho values was observed in the lateral compartment (4%) than the medial compartment (2%). Similarly, on the femur, pre-exercise values were significantly greater than post-exercise by 7% (p<0.01) and there was no significant difference between medial and lateral sides (p=0.3) (Figure 3). While not significant, a greater average decrease in T1rho values was observed in the medial compartment (8%) than the lateral compartment (7%).

**Discussion:** This current study sought to quantify changes in proteoglycan concentration in response to in vivo activities of daily living. As the data illustrates, walking resulted in a significant decrease in T1rho relaxation times in both the tibial and femoral cartilage, corresponding to an increase in proteoglycan concentration. The loads transferred through the joint during ambulation have been shown to induce significant compressive cartilage strains [9]. These strains likely result in an expulsion of water from the tissue, which may require more than an hour to fully return through the low-permeability cartilage matrix [10]. This increase in proteoglycan concentration of the tissue was reflected in decreased T1rho relaxation times [7, 11]. This finding suggests that the repetitive cyclic loading of walking causes conformational changes of the extracellular matrix affecting the biochemical environment of the chondrocytes within the cartilage. In particular, these short term changes in proteoglycan concentration due to water exudation affect the osmolarity within the tissue. Chondrocytes are sensitive to secondary biophysical effects of loading, such as these changes in osmolarity [4, 5]. Thus, any alterations in the normal loading environment may affect the cues that chondrocytes use to maintain homeostasis and may contribute to the onset and progression of osteoarthritis.

**Significance:** Altered patterns of mechanical loading can change the osmotic environment of chondrocytes, which can disrupt normal cartilage homeostasis. Therefore, quantifying the effects of in vivo loading on proteoglycan concentration in cartilage is important for understanding how biomechanical factors can affect the development of osteoarthritis.
Figure 1. A grid system spanning the femur and tibia was created to provide site-specific measurements of the change in T1rho relaxation times before and after 20 minutes of walking on a treadmill. Eighteen points were created on the tibia and 36 on the femur. (L = Lateral and M = Medial)
Figure 2: Color maps illustrating changes in T1rho relaxation times before and after walking on a treadmill for a single grid sampling point on the tibia. The higher T1rho values observed before walking are representative of lower proteoglycan concentration as compared to that measured after walking.
Figure 3. Comparison of T1rho relaxation values pre- and post-walking activity for the tibia (top) and femur (bottom). On both the femur and the tibia, there was a statistically significant effect of activity on T1rho relaxation times ($p < 0.01$), with pre-activity being higher than post. No statistically significant effect of location (medial versus lateral) was observed ($p > 0.3$) and no significant interaction between location and activity was observed ($p > 0.25$).