

## Changes in T1rho and T2 Relaxation Times of Tibiofemoral Articular Cartilage with Acute Loading

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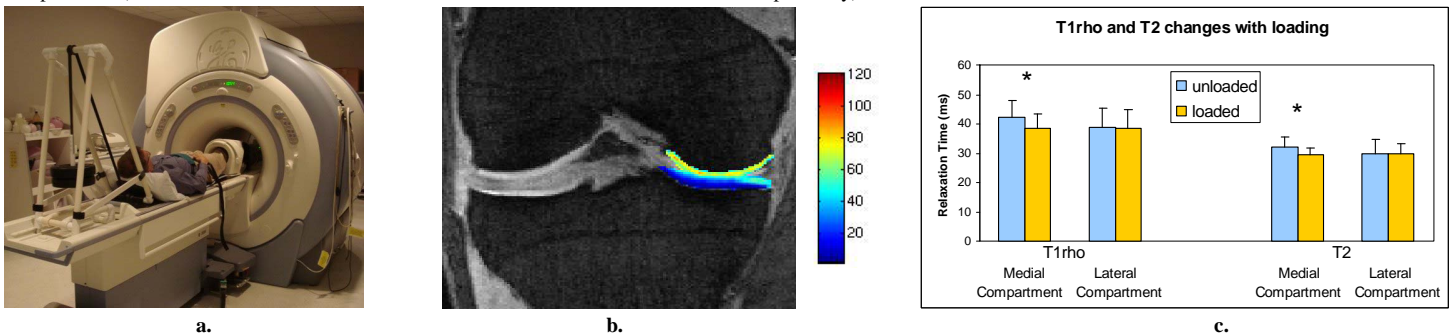
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**Introduction.** Osteoarthritis (OA) is a degenerative disease that is characterized by cartilage morphological and compositional changes. The initial signs of cartilage degeneration are molecular and biochemical changes within the extracellular matrix which occur long before any loss of joint space can be identified on radiographs. The earliest changes in OA have been reported to be decreased proteoglycan and increased water content. Recent advancements in MRI technology have led to an improved ability to monitor early signs of OA *in vivo*. Of particular interest in identifying the earliest changes of the cartilage matrix in patients with OA is the development of T1rho and T2 relaxation time mapping.<sup>1,2</sup> It is believed that cartilage loading plays a key role in the homeostasis of the cartilage biochemical environment. The effect of acute loading on T2 relaxation time has been studied by Nishi et al.<sup>3</sup> and Nag et al.<sup>4</sup> and both have shown some evidence of decreased T2 relaxation time (indicating a loss of water) with loading. To date, no one has studied the influence of acute loading on T1rho relaxation time. The objective of the current study is to determine the influence of acute mechanical loading on tibiofemoral cartilage T1rho and T2 relaxation times in 8 subjects. Our hypotheses are that loading will result in decreased T1rho and T2 relaxation times, indicating decreased water concentration and increased proteoglycan concentration.

**Methods.** Four healthy adult subjects and four subjects with mild-moderate OA based on radiological criteria participated in this study (mean age = 47 ± 15 years; mean weight = 69.7 ± 6.2 kg; mean height = 1.60 ± .09 m). Imaging was performed with a 3T GE MR scanner and an 8-channel phased array knee coil. The study consisted of two phases. First, subjects were positioned supine on top of a custom-designed loading device on the MR table with no load applied. Subjects' test lower extremity was positioned in 15 degrees of knee flexion (supported in a transmit-receive knee coil) and 10 degrees of foot external rotation (placed on the loading device footplate and supported in place.) Images of the subjects' knee were acquired as described below. During the second phase of the study, a load equal to 50% of the subjects' body mass was applied to the loading device resulting in loading of the subjects' lower extremity (Figure 1 a). Only the test lower extremity was placed on the loading device footplate, so all load was applied to the test extremity. An identical set of images was acquired for the loaded condition as described below.

**MR Analysis.** Coronal T1rho, and T2-weighted images were acquired using previously developed sequences based on a 3D-SPGR sequence (FOV = 14 cm, slice thickness = 3 mm, matrix: 256 x 192, TSL for T1rho = 0/10/40/80 ms, spin lock frequency for T1rho = 500 Hz; TE for T2 = 3.2/13.6/24.1/45 ms). Additionally, 3D high-resolution coronal water excitation spoiled gradient-echo (SPGR) images were acquired. T1rho maps were generated by fitting the T1rho-weighted images  $S(TSL) \propto \exp(-TSL/T1rho)$  pixel-by-pixel (Figure 1 b). The T2 map were reconstructed by fitting the image intensity pixel-by-pixel to the equation  $S(TE) \propto \exp(-TE/T2)$ . T1rho and T2 maps were then registered to high-resolution SPGR images for quantification of relaxation times. The cartilage was segmented semi-automatically in SPGR images using an in-house spline-based developed program. Slice selection was determined based on load bearing areas of the cartilage. All slices with cartilage on cartilage contact in the loaded images (with an additional 1 -2 slices both anterior and posterior) were segmented. The same number of slices was segmented in the unloaded and loaded conditions for each subject. Due to the difficulty in determining borders between femoral cartilage on tibial cartilage during loaded imaging, each compartment (medial and lateral) was assessed as a unit (i.e. medial femoral cartilage + medial tibial cartilage = medial compartment, etc.) The segmented masks from the 3D SPGR images were then applied to the registered T1rho and T2 maps. Mean of T1rho and T2 relaxation times for each compartment was compared between conditions (unloaded vs. loaded) using paired samples t-tests ( $\alpha = 0.05$ ).

**Results.** Mean ± standard deviation of T1rho and T2 relaxation times for the medial and lateral compartments are presented in Figure 1 c. Acute loading resulted in statistically significant differences in the medial (38.5 ± 4.8 vs. 42.3 ± 5.8 and 29.5 ± 1.9 vs. 32.2 ± 3.2 ms for T1rho and T2, respectively) but not the lateral compartment (38.4 ± 4.9 vs. 39.0 ± 6.4 and 29.8 ± 2.6 vs. 29.7 ± 5.4 for T1rho and T2, respectively).



**Discussion** It is believed that T2 relaxation time is primarily related to cartilage water content, in addition to collagen orientation and content. A decrease in T2 would suggest that loading of articular cartilage resulted in an expulsion of water. T1rho has been reported to be inversely related to proteoglycan content. The significant reduction in T1rho observed in the current study might have resulted from both an increase in proteoglycan concentration and a decrease in water content. It is not clear why this phenomenon was only observed in the medial compartment, but perhaps the anatomical shapes result in higher loads in the medial compartment. Clinically, OA is more frequently observed in the medial compartment. Thus, these findings may support a hypothesis that medial compartment loading occurs to a greater extent than the lateral compartment during acute loading. However, it is important to note that not all subjects displayed unchanged T1rho and T2 values in the lateral compartment. Rather it was the variability observed in the lateral compartment that resulted in a finding of no difference. Some individuals displayed large decreases in T1rho and T2, while others showed increases in values. Further work is needed to fully understand this issue. Our finding of significant decreases in T2 is consistent with the literature that has reported similar findings in various cartilage locations.<sup>3,4</sup> Differences between our study and previous investigations are primarily due to variations in cartilage region selection. In the current study we chose to combine the femoral and tibial cartilage to create a medial and lateral compartment. Future studies may want to collect additional images (perhaps T2-weighted FSE images) so that separation of femoral cartilage and tibial cartilage may be more successful. In conclusion, these data indicate that with acute loading of the medial compartment, T1rho and T2 values decrease suggesting that cartilage water content decreases and proteoglycan concentration increases. A better understanding of how loading influences cartilage biology may provide valuable in the treatment and prevention of OA.

**Reference** 1. Li X et al., 2007. Osteoarthritis Cartilage 15:789-97. 2. Dunn T et al., 2004. Radiology 232:592-8. 3. Nishi T et al., 2008. JMRI 28: 175-180. 4. Nag D et al. 2004. JMRI 19: 317-322.

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