Correlation of Cartilage Biochemical and Biomechanical Properties with $T_{1\rho}$ Relaxation

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Introduction: The biochemical composition of cartilage affords the tissue with its unique biomechanical properties. Proteoglycan (PG) is chiefly responsible for compressive properties with regard to stiffness and hydraulic permeability. Degenerative diseases affecting cartilage, including osteoarthritis (OA), can greatly affect the biochemical characteristics of cartilage and hence its mechanical integrity. The $T_{1\rho}$ parameter has been shown to closely track PG content in ex vivo tissue [1], animal models of OA [2], and osteoarthritic human specimens [3]. The aim of this study is to correlate changes in cartilage biomechanical and biochemical properties with $T_{1\rho}$ in a cytokine-induced model of degeneration.

Methods: Bovine cartilage explants were cultured in two groups: a control group in standard media and a treated group in media containing 30 ng/mL of IL-1β. The effects of IL-1β closely mimic the molecular events and pathology associated with OA, particularly with regard to loss of PG content [4]. Six samples from each group were removed from the media at days 0, 3, 6, and 10. $T_{1\rho}$ maps were created from MR images collected on a 4.7 Tesla Varian scanner with the following imaging parameters: resolution = 234 x 234 μm^2, TE/TR = 12/2000 ms, and slice thickness = 3 mm for five TSL times from 10 to 90 ms. The spin-lock pulse amplitude was set to 500 Hz (γB_1 = 500 Hz). Stress-relaxation biomechanical tests were conducted on a cylindrical sample using a confined compression apparatus. Linear biphasic theory was used to measure uniaxial aggregate modulus (H_A) and hydraulic permeability (k_0) from stress-relaxation data. Biochemical assays of adjacent tissue were performed to measure DNA, PG, collagen, and water content.

Results: Treatment with IL-1β resulted in a progressive loss of PG content compared to controls (Table 1). There were insignificant changes in DNA and collagen content and a small but insignificant increase in water content in treated samples compared to controls. Average proteoglycan content of each culture group was strongly correlated with average H_A (R^2 = 0.97) and k_0 (R^2 = 0.78). There was a progressive increase in $T_{1\rho}$ near the superficial surface and mid-zone of the cartilage as evident on the $T_{1\rho}$ maps (Figure 1). Measurements of average $T_{1\rho}$ were strongly correlated with average proteoglycan content (R^2 = 0.91), H_A (R^2 = 0.82), and k_0 (R^2 = 0.90) (Figure 2).

Discussion: The progressive decrease in PG with treatment of IL-1β in culture is consistent with data reported in previous studies [4]. The lack of changes in overall amount of collagen content does not rule out the possibility of changes in collagen organization which was not measured in this study. The relationship between PG, H_A, and k_0 has already been well established and examined in the literature [5] as well as the correlation between $T_{1\rho}$ and PG [1-3]. The salient contribution of this work is to combine these two relationships to demonstrate how $T_{1\rho}$ directly relates not only to the compositional but also the functional properties of cartilage. Previous studies have reported similar relationships between biochemical, biomechanical, and MR measurements including dGEMRIC [6] and T_2-mapping [5] methods. *Support from NIH grants RR02305 and R01-AR45404, and the Whitaker Foundation Graduate Research Fellowship.*

References: **1.** Akella SV, et al. Magn Reson Med 2001;46(3):419-23. **2.** Wheaton AJ, et al. Detection of changes in articular cartilage PG by $T_{1\rho}$ MRI. *J Ortho Res.* (in press). **3.** Wheaton AJ, et al. J Magn Reson Imaging 2004;20(3):519-25. **4.** Tyler JA. Biochem J 1985;225(2):493-507. **5.** Wayne JS, et al. Radiology 2003;228(2):493-9. **6.** Kurkijarvi KE, et al. Magn Reson Med 2004;52(1):41-6.
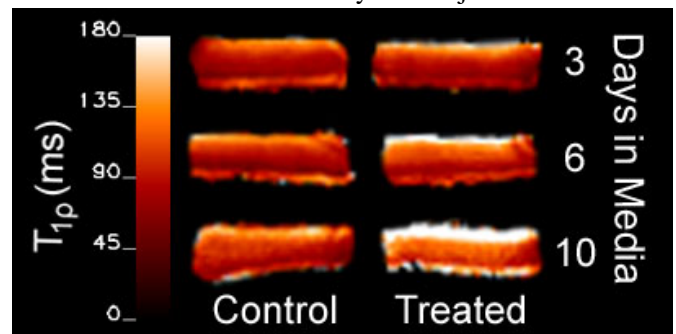
Figure 1: $T_{1\rho}$ maps of representative specimens.

Figure 2
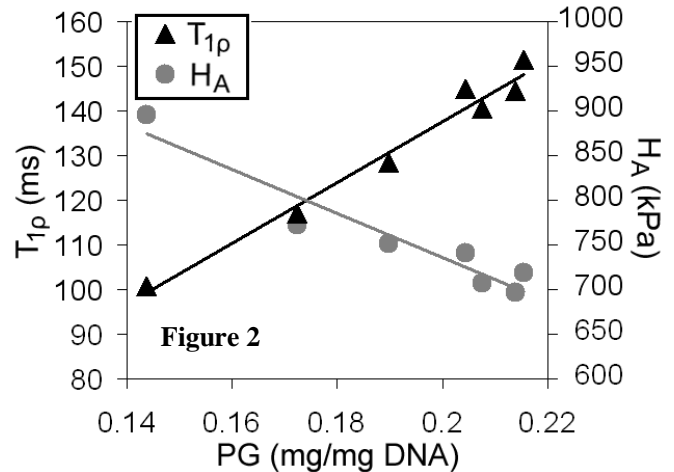
Days in Media	$T_{1\rho}$	H_A	k_0	PG	Collagen	Water
3	+6.3%	-12.0%*	+14.5%	-12.0%	-0.1%	-0.04%
6	+15.3%*	-14.9%*	+24.0%	-19.4%*	-5.4%	+1.24%
10	+37.3%*	-22.0%*	+217%*	-30.1%*	-5.2%	+1.93%

Table 1: Average percentage change in $T_{1\rho}$, H_A, k_0, proteoglycan, collagen, and water content in IL-1β-treated specimens with respect to time-matched control data. Statistically significant differences ($p < 0.05$) are indicated by an asterisk.