Detection of Proteoglycan Content in Human Osteoarthritic Cartilage Samples with Magnetic Resonance T1rho Imaging

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INTRODUCTION

Osteoarthritis (OA) is a heterogeneous and multifactorial disease characterized primarily by the progressive loss of hyaline articular cartilage. OA imaging is currently limited by the inability to directly visualize cartilage biochemical content. The current clinical evaluation of cartilage degeneration in OA relies primarily on plain radiography, which depicts only gross osseous changes that occur late in the disease. While standard clinical MRI techniques afford better clinical accuracy, these techniques are still limited to detecting cartilage morphologic changes that occur at a relatively late stage of degeneration. Changes in cartilage biochemistry are well known to be early markers of OA cartilage degeneration. One important change is the reduction of proteoglycan (PG) content [1], which results in the loss of integral mechanical properties, such as stiffness and reversible deformation [2]. T1ρ relaxation time in MRI is affected by low-frequency interactions between molecules. In cartilage, the water-PG interaction has been proposed to be the primary determinant of T1ρ, with a reduction in PG content causing an increase in the T1ρ relaxation time. Several studies have explored the effect of PG loss on T1ρ relaxation times using enzymatic degradation of bovine cartilage [3,4], but none have used human osteoarthritic cartilage to quantify such changes. The goal of this study was to evaluate the relationship between quantified PG loss in human osteoarthritic cartilage and the T1ρ relaxation time of these tissues.

MATERIALS AND METHODS

The tibial plateau and femoral condyle cartilage of 14 osteoarthritic knees (from 12 patients) were obtained during total knee arthroplasty surgery at the UCSF Medical Center. Immediately after surgery, the obtained cartilage pieces were scanned on a GE 3T MRI scanner using a quandrature transmit/receive wrist coil. The knee cartilage pieces were immersed in phosphate-buffered saline and scanned in their respective physiological positions to simulate *in vivo* imaging. The imaging protocol included a fat-suppressed spoil gradient echo (SPGR) sequence and a T2-weighted fast spin-echo (FSE) sequence, followed by a 3D T1ρ quantification sequence. The sagittal 3D T1ρ-weighted imaging sequence was composed of two parts: magnetization preparation based on spin-lock techniques as previously developed [5] for the imparting of T1ρ contrast, and an elliptical-centered segmented 3D SPGR acquisition immediately after T1ρ preparation during transient signal evolution. The imaging parameters are: TR/TE = 9.3/3.7 ms; FOV = 6-8 cm, matrix = 256 x 192, slice thickness = 2 mm, BW = 31.25 kHz, time of spin-lock (TSL) = 0, 10, 40, 80 ms, frequency of spin-lock (FSL) = 500 Hz. The T1ρ maps were reconstructed by fitting the T1ρ-weighted images pixel-by-pixel to the equation $S(TSL) \propto S*\exp(-TSL/T1\rho)$.

After imaging, a 50 mg sample of cartilage was obtained by a 3mm diameter biopsy punch. The biopsy punches were taken at standardized locations on each condyle or tibial plateau. The sample tissues were digested in papain and used for biochemical analyses. PG content was measured as previously described [6]. The locations of the punches were identified in the T1ρ maps based on anatomical distance and landmarks. The T1ρ values corresponding to the punch location were acquired using software developed in-house. Strength of correlation of T1ρ relaxation times to the PG content was assessed using the Spearman rank correlation coefficient (R).

RESULTS

A linear inverse correlation between the cartilage PG content and the T1ρ values was found (Figure 1). Significance was determined by using the Spearman rank correlation coefficient ($\rho = -0.3381$, $P < 0.05$). The mean %PG in the examined biopsy punches (n =37) was 3.67±1.20% wet weight (min = 1.45%, max = 7.05%) The mean T1ρ value for the examined tissues was 70.06±13.51 ms (min= 49.8 ms, max = 112.41 ms).

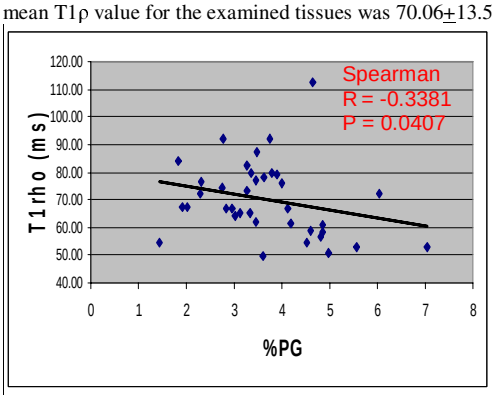

Figure 1: A plot of T1ρ of biopsy punches and the corresponding biochemical analyses is shown. There is a significant linear inverse correlation between T1ρ and PG content ($P < 0.05$)

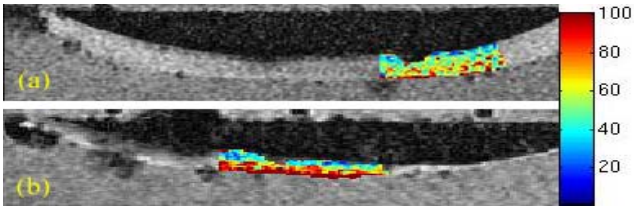

Figure 2: T1ρ colormap with a color bar in milliseconds
(a) A region of high PG (4.86%) is seen as low T1ρ (60.85±28.58ms) in the lateral femoral condyle of Patient A
(b) A region of low PG (2.30%) is seen as high T1ρ (76.56±46.49ms) in the lateral femoral condyle of Patient B

DISCUSSION

The negative correlation between the proteoglycan measurements and T1ρ values suggests that T1ρ imaging is capable of reliably detecting changes in the PG content of articular cartilage. Previous studies have studied PG loss versus T1ρ in enzymatically degraded bovine cartilage specimens *ex vivo* [3,4], but comparison of quantified PG content and T1ρ relaxation times in fresh, human osteoarthritic cartilage has not been documented.

The ability to non-invasively detect changes in proteoglycan content of cartilage is clinically significant, since PG depletion is an early step in OA etiology and occurs before discernible pain or morphological damage to cartilage [1]. PG loss leads to a decrease in cartilage mechanical properties and renders the tissue susceptible to further mechanical injury, leading to cartilage tissue loss. Therefore, non-invasively detecting these early stage biochemical changes has significant clinical implications. Previous *in vivo* studies have shown that OA subjects have significantly higher T1ρ values compared to normal controls [5]. Correlation results from this study between PG concentration and *ex vivo* T1ρ values may have the potential to calibrate PG quantification *in vivo*. Our results demonstrate that T1ρ imaging may provide a non-invasive method for early differentiation of degenerated from normal cartilage.

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