Comparison of T1ρ, T2 mapping, and sodium MRI of osteoarthritic cartilage *in vivo*

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Introduction

Proteoglycan depletion has been identified as a marker for the early development of osteoarthritis [1]. However, traditional proton MRI only permits visualization of morphological cartilage changes that often occur late in the disease process. Therefore several MRI techniques – including T1ρ, T2 mapping, and sodium imaging – have been developed to assess the biochemical composition of articular cartilage, which may facilitate earlier detection of osteoarthritic changes. T2 mapping has been correlated with changes in cartilage water content and collagen structure [2]. Meanwhile, sodium MRI is able to measure proteoglycan content directly, due to the attraction between negatively-charged glycosaminoglycan (GAG) side chains of the proteoglycans and positively-charged sodium ions [3]. Previous research has produced mixed results regarding the biochemical properties measured by T1ρ. Specifically, *ex vivo* proteoglycan depletion studies have shown strong correlations between T1ρ relaxation and MRI measures of fixed charge density, suggesting that T1ρ provides a measure of proteoglycan content [4, 5]. However, other *in vivo* human studies have found no such correlation or have identified correlations between T1ρ and T2 relaxation times, suggesting that collagen changes may influence T1ρ measures more than initially thought [6, 7]. This study therefore evaluates the correlations between T1ρ and T2 versus sodium images of osteoarthritic subjects *in vivo* in order to better identify the properties affecting T1ρ in a clinical model.

Methods

Nine knees of subjects (age 50-69) were imaged in the sagittal plane using a GE Signa Excite 3.0T MRI scanner (GE Healthcare, Milwaukee, WI). Subjects were all diagnosed with radiographic OA, and each had a Kellgren-Lawrence grade of 1 or 2. T1ρ and T2 images were acquired using an eight-channel proton knee coil, while sodium images were obtained using a custom sodium quadrature knee coil. T1ρ images were acquired using a prototype magnetization-prepared spoiled gradient echo sequence (TR/TE 5.1/0, 10, 30, and 70ms, 256 x 192 matrix size, 3mm slice thickness, 16cm FOV, 70-degree flip angle, receiver bandwidth ±62 kHz, 10 min imaging time) [7]. T2 images were obtained using TR/TE 2000/8.8, 16.5, 26.3, 35, 43.8, 52.5, 61.3, and 70ms, 320 x 160 matrix size, 3mm slice thickness, 16cm FOV, and receiver bandwidth ± 41 kHz with a 10 min imaging time. A fast gradient-spoiled sequence using the 3D cones *k*-space trajectory was used to obtain sodium images (TR/TE 35/0.6 ms, flip angle 70 degrees, 28 signal averages, resolution 1.25 x 1.25 x 4 mm, 21 min imaging time) [8]. A test tube containing 100-mmol saline was placed within the coil for normalization.

For each subject, T1ρ and T2 fit maps were generated and relaxation times as well as sodium signals were measured using OsiriX from the following regions of interest (Fig. 1): medial and lateral anterior, central, and posterior femoral condyle, medial and lateral anterior and posterior tibia, and medial and lateral superior and inferior patellar cartilage. Sodium signal was normalized to the saline test tube signal. Linear regression analysis was performed on each pair of T1ρ, T2, and sodium data, and Student's t tests were used to determine correlation coefficient significance.

Results

As shown in Figure 2, linear regression analysis showed no correlation between T1ρ relaxation times and sodium signal (R^2=0.0091, P=0.28) or between T2 relaxation times and sodium signal (R^2=0.0008, P=0.97). However, a moderate correlation was found between T1ρ and T2 relaxation times (R^2=0.5755, P<0.001). Regional analysis of T1ρ, T2, and sodium signal in the medial and lateral femoral, tibial, and patellar regions yielded similar results.

Discussion

These results suggest that T1ρ-weighed imaging may not be exclusively dependent on one macromolecule. The lack of correlation between T1ρ and sodium signal correspond to findings by Taylor et al., who reasoned that the development of osteoarthritis is a complex process and that depletion of fixed charge density may not necessarily correlate precisely with loss of proteoglycan mass [6]. Moreover, whereas the *ex vivo* studies isolated proteoglycan degradation with exogenous enzymes, the degenerative processes occurring *in vivo* are likely more complicated, and both proteoglycan content and collagen structure may have already been damaged in these subjects. The moderate T1ρ and T2 correlation suggests that collagen condition, or perhaps interactions between several macromolecules, provide a stronger influence on T1ρ than proteoglycan content alone. Together these results indicate that T1ρ, T2, and sodium MRI may be able to provide complementary rather than overlapping information about articular cartilage biochemistry, but that our understanding of the early processes characterizing development of OA and its effects on T1ρ relaxation may not yet be complete.

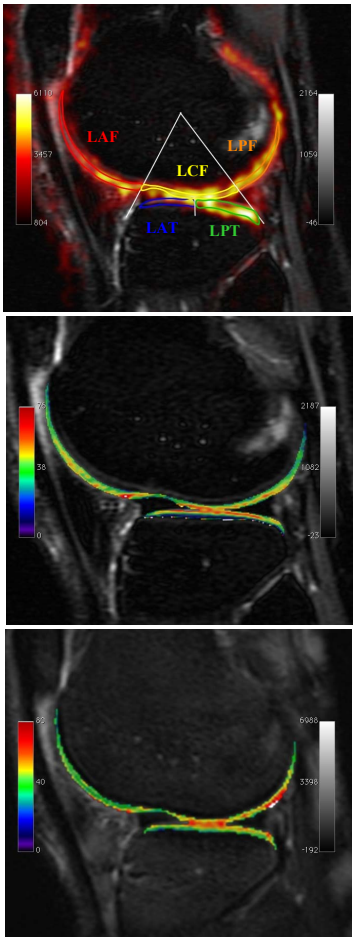

Figure 1. A) Overlay of sodium image on proton image. Examples of lateral ROIs are illustrated. B, C) Fit maps of T2 & T1ρ ROIs overlaid on grayscale T2 & T1ρ images, respectively.

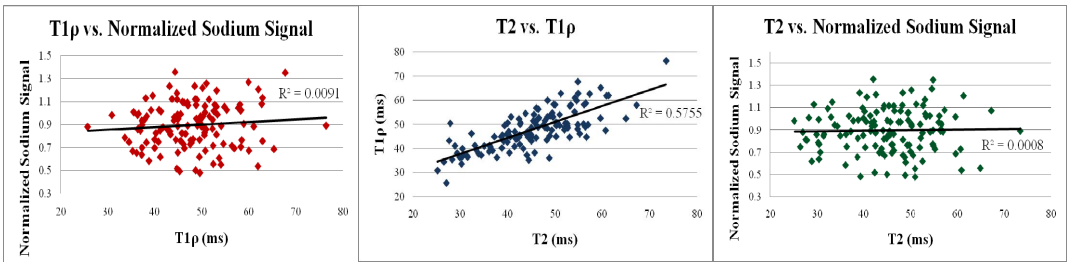

Figure 2. Comparison of T1ρ relaxation times, T2 relaxation times, and sodium signal normalized to signal measured from a test tube containing 100-mmol saline. Only T1ρ and T2 were found to be significantly correlated (P<0.001).

Acknowledgements: NIH EB002524, EB005790, GE Healthcare, SCBT/MR

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