Correlation of T1ρ and T2 Relaxation Times Values with Glycosaminoglycan and Water Content of Articular Cartilage

Ali Hosseini, PhD¹, Yang Wang², Martin Torriani, MD¹, Alan J. Grodzinsky, PhD², Guoan Li, Ph.D.¹.
¹Massachusetts General Hospital/Harvard Medical School, Boston, MA, USA, ²Massachusetts Institute of Technology, Cambridge, MA, USA.

Disclosures:  A. Hosseini: None.  Y. Wang: None.  M. Torriani: None.  A.J. Grodzinsky: None.  G. Li: 1; Received Loyalties form MAKO Surgical Corp and Stryker. 5; K2M, DePuy Synthes.

Introduction: Osteoarthritis (OA) is one of the most common diseases that causes pain and limits joint mobility. Biochemical changes in the glycosaminoglycan and collagen constituents of cartilage extracellular matrix can lead to morphological and structural changes in cartilage tissue which are associated with OA [1]. Early in the OA disease process, these biochemical alterations include a decrease in the glycosaminoglycan concentration and proteoglycans size [2] and inevitability an increase in water content [3]. Detecting biochemical changes within the cartilage tissue is critically important for early diagnosis of OA or monitoring the progression of the disease. New techniques based on quantitative MR imaging (qMRI) have shown promising outcomes for detecting changes in cartilage before abnormalities are observed on radiographs and/or morphological MR images. The purpose of this study was to validate whether the T2 and T1ρ values are associated with controlled changes in the cartilage water content and glycosaminoglycan content, and to evaluate the extent of water or GAG content changes that can be detected by each of these signals.

Methods: Cylindrical cartilage disks ~3.5 mm thick and 9 mm in diameter were harvested from the patellofemoral grooves of 1-2-week-old bovine calves. These disks were randomly divided into 2 groups for controlling GAG content or water content of the cartilage. In the 1st group, plugs were digested with trypsin (1mg/mL) for 0 (control), 0.5, 6 and 21 hours to create a range of different GAG contents. The disks of the 2nd group were compressed to either 25% or 50% in specialized static compression chambers designed to create a range of different water contents. These chambers were then mounted within the MR scanner. Four plugs were assigned for each condition in each group. Using a 3T MR scanner, T1ρ and T2 scans of the plugs were collected. All relaxation times were calculated from a mono-exponential fit. The images corresponding to the central section of the plugs were used for T1ρ and T2 analysis (Figure 1). Next, the GAG content of each plug was measured using the DMMB assay and normalized to the wet weight of the sample. The correlations of GAG and water content with T1ρ and T2 times were investigated. Water content was defined as the weight difference before and after lyophilizing the sample, normalized to the wet weight. Next, T1ρ and T2 mapping techniques were used to examine in vivo cartilage compositional changes after ACL reconstruction. A patient (male, 30 years old at injury) with a unilateral ACL injury was recruited three years following clinically successful ACL reconstruction with bone-patellar tendon-bone autograft. Both intact and ACL reconstructed knees were scanned using a 3T MRI scanner. T1ρ and T2 values at weight bearing regions of medial compartment were analyzed and compared.
**Results:** A weak negative correlation was detected between T2 relaxation time and cartilage GAG content ($r = -0.37$, $p = 0.19$, Figure 2A). However, $T_{1p}$ relaxation times showed a moderately strong negative correlation with cartilage GAG content ($r = -0.64$, $p = 0.01$, Figure 2B).

A strong correlation was observed between T2 relaxation times and cartilage water content ($r = 0.90$, $p = 0.000$, Figure 2C). A relatively strong correlation was observed between $T_{1p}$ relaxation times and cartilage water content ($r = 0.73$, $p = 0.02$, Figure 2D).

With regard to in vivo results three years following ACL reconstruction, the $T_{1p}$ and T2 values were higher in the femoral cartilage (F) and tibial cartilage (T) of the ACL reconstructed knees compared to those of intact contralateral sides (Figure 3).

**Discussion:** This study tested the hypothesis that $T_{1p}$ and T2 time values correlate with GAG content and water content of the articular cartilage. The data show that both T2 and $T_{1p}$ relaxation times decreased by reduction of water content (due to cartilage compression). The T2 values are strongly predictive of water content within cartilage, more than $T_{1p}$ measures. This is in agreement with the mobility of water molecules in the extracellular matrix of the cartilage and T2 signals (which are shorter than $T_{1p}$ signals) can predict the water content better. On the other hand, the $T_{1p}$ values are moderately predictive of GAG content within cartilage, more so than T2 time measures. Our in vivo data imply that in this case three years post-operatively, the water content of the cartilage of the ACL reconstructed knee is increasing, and the GAG content is decreasing, even though the patient outcome was reported “clinically stable knee” having “no pain”. The results of this study suggest that $T_{1p}$ and T2 values may be more reliable for monitoring GAG changes and Water content changes in articular cartilage, respectively, which may help evaluate the joint degeneration and its progression.

**Significance:** $T_{1p}$ and T2 quantification could be a reliable tool for diagnosis of joint degenerative disease. We have implemented $T_{1p}$ and T2 scans in vivo, and could detect signal changes within the cartilage of an ACL reconstructed joint compared to its corresponding healthy contralateral side. This is a powerful tool which can be used noninvasively to monitor the disease progression and evaluate therapeutic procedures.
Figure 1: (A) T2 relaxation time maps of GAG depleted plugs (Group 1), The variation of T2 values with GAG contents; (B) T1p Relaxation time maps of GAG depleted plugs (Group 1), The variation of T1p values with GAG contents.
Figure 2: (A) Weak negative correlation between T2 relaxation time and cartilage GAG content ($r = -0.37$, $p = 0.19$). (B) Moderate negative correlation between T1p relaxation time and cartilage GAG content ($r = -0.64$, $p = 0.01$). (C) Strong correlation between T2 relaxation times and cartilage water content ($r = 0.90$, $p = 0.000$). (D) Relatively strong correlation between T1p relaxation times and cartilage water content ($r = 0.73$, $p = 0.02$).
Figure 3: T1\text{p}, T2 relaxation time maps of the medial articular cartilage of (A) the intact contralateral knee and (B) the knee three years after ACL reconstruction.

T1: Central, without overlaying meniscus  
T2: Overlaying anterior meniscus  
T3: Overlaying posterior meniscus  
F1: Central, without overlaying meniscus  
F2: Overlaying anterior meniscus  
F3: Overlaying posterior meniscus  
F4, 5: anterior, posterior cartilage