T1ρ and T2 Show Regional Variation in Degenerate Human Menisci: Correlation with Biomechanics and Matrix Composition

Min-Sun Son[1], Marc Levenston[2], Brian Hargreaves[3], Weitian Chen[4], Stuart Goodman[5], and Garry Gold[6]

[1]*Bioengineering, Stanford University, Stanford, CA, United States,* [2]*Mechanical Engineering,* [3]*Radiology, Stanford University,* [4]*GE Healthcare,* [5]*Orthopaedic Surgery, Stanford University,* [6]*Radiology*

INTRODUCTION: Degenerative changes and tears in the meniscus have been shown to precede cartilage degeneration and contribute to osteoarthritis (OA) progression[1,2]. Detection of these changes via MRI would provide a powerful diagnosis and research tool for early-stage OA. While T1ρ and T2 values have been proposed to reflect such changes in biochemical composition in articular cartilage,[3,4] no studies have investigated this relationship in the meniscus. In this study, we examine zonal variations in T1ρ and T2 values in relation to the biochemical composition and mechanical properties in OA human menisci.

METHODS: ***Imaging*** Ten menisci (5 lateral, 5 medial) were obtained as incidental surgical waste from patients undergoing total knee replacement (TKR) procedures. Each specimen was fixed in a container filled with perfluorooctyl bromide to minimize artifacts from air-tissue interface. T1ρ- and T2-weighted images were acquired using a Magnetization-Prepared Angle-Modulated Partitioned k-Space Spoiled Gradient Echo Snapshots (3D MAPSS) sequence that has a magnetization preparation followed by an immediate SPGR acquisition during transient signal evolution[3]. Coronal images were taken with a 3T GE MR scanner (GE Healthcare, Waukesha, WI) in an 8-channel wrist coil where the main circumferential collagen fibers were oriented perpendicular to B_0 in order to avoid any magic angle effects. Imaging parameters were TR 7.5 ms, FOV 10cm, matrix 256x256, BW ±31.25kHz, number of excitations (NEX) 1, and 1mm slice thickness. To optimize the sequence for the short T2 meniscus, the pulse sequence was designed to achieve TE 3.6ms for SPGR readout. T1ρ-weighted images (Fig. 1A) were collected at 6 spin-lock durations (TSL) (0, 4, 12, 20, 30, and 40ms) with spin-lock frequency 500Hz, and T2-weighted images (Fig. 1C) were collected at 6 echo times (0, 6.4, 12.8, 19.3, 38.5, and 64.2ms). 3D Fast GRE images (TR 7.2ms, TE 3.4ms, 256X256, FOV 14cm, 1.5mm thickness, FA 30°, BW ±31.25kHz, NEX 3) were used to define the anterior, body, posterior and inner, middle, outer regions (Fig. 2). Pixel intensities for different TSLs and TEs were fit via Matlab with a mono-exponential equation to obtain the T1ρ and T2 time constants for all pixels from each region. ***Biochemistry*** Sulfated glycosaminoglycan (sGAG) and collagen content from each region were obtained from 1,9-dimethylmethylene blue and hydroxyproline assays, respectively. ***Histology*** Qualitative distribution of proteoglycans were observed sections stained with Safranin-O/Fast Green in the anterior, body, and posterior regions ***Mechanical Testing*** 4mm diameter, 2mm thickness cores from the anterior, body, and posterior regions were subject to dynamic shear (0.1Hz, 1.5%) in addition to static and dynamic unconfined compression tests (0.1Hz, 10%). ***Statistics*** Regional differences were evaluated using a General Linear Model with Tukey's test for pairwise comparisons, treating the donor as a random variable. The relationships between different parameters were examined via Pearson's correlation coefficient. Significance was set at $p<0.05$.

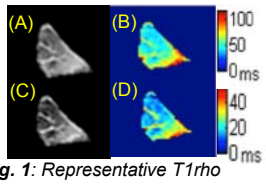

Fig. 1*: Representative T1rho (A,B) and T2 (C,D) images at the third echo and*

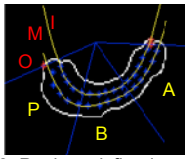

Fig. 2*: Regions defined circumferentially Anterior (A), Body (B), Posterior (P) and radially Inner (I), Middle (M) and Outer (O).*

RESULTS: T1ρ and T2 showed significantly lower values in the body region compared to the anterior and posterior horns; however, they did not vary radially among the inner, middle and outer regions (Fig. 3). sGAG content was significantly higher in the middle region (Fig.4), consistent with Safranin-O staining of histology sections (not shown), but collagen content did not significantly vary among regions. The dynamic shear modulus (14.5±2.8kPa), dynamic compressive modulus (156±38.6kPa) and equilibrium compressive modulus (33.8±9.27kPa) did not significantly differ among regions. However, interesting correlations were observed for all regions pooled together. T1rho and T2 showed strong correlation with one another (r=0.873, p<0.001, Fig.5) and with water content (T1ρ r=0.73, p<0.001; T2 r=0.71, p<0.001). sGAG content per wet mass was negatively correlated with only T1ρ (r=-0.436, p<0.001) whereas collagen per wet mass was negatively correlated with both T1rho (r=-0.411, p<0.001) and T2 (r=-0.475, p<0.001). On the other hand, neither sGAG per dry mass nor collagen per dry mass significantly correlated with T1rho or T2. Mechanical properties showed moderate, negative correlations with both T1rho and T2 (dynamic shear modulus T1ρ r=-0.512, p=0.006; T2 r=-0.41, p=0.034; dynamic compressive modulus T1ρ r=-0.434, p=0.024; T2 r=-0.389, p=0.045; equilibrium compressive modulus T1ρ r=-0.431, p=0.025; T2 r=-0.358, p=0.067), which also showed correlations with sGAG and collagen content per wet mass (sGAG r=0.58, p=0.002; collagen r=0.612, p=0.001). sGAG and collagen per wet mass were not significantly correlated (r=0.001, p=0.993).

DISCUSSION: Consistent regional variation in T1ρ and T2 values were detected in degenerated human menisci. While these patterns did not match those of sGAG or collagen contents, higher T1ρ and T2 values were associated with higher water content, as had been previously shown with articular cartilage for T2[5]. The strong correlation between T1ρ and T2 despite the apparent lack of correlation between sGAG and collagen suggest the correlations to sGAG and collagen per wet mass are primarily due to water content, which is known to increase in degenerative menisci with low collagen and sGAG content[6]. The mechanical properties observed in this study were lower than values reported for non-osteoarthritic human menisci, as would be expected from severely degenerated menisci taken from TKR surgeries[7,8]. T1ρ and T2 values were also longer than values previously reported for menisci *in-vivo*[9], which may also reflect the more degenerative state of these specimens. The higher sGAG content in the middle region is extremely interesting, as the inner region is known to be more cartilage-like with higher sGAG content in normal menisci. This may indicate significant proteoglycan loss in the inner region for OA menisci and the detection of this loss with imaging parameters will be important. ***Conclusion***: The findings in this study provide insight to understanding the physical meaning of T1ρ and T2 values. Both parameters were found to strongly correlate with water content and moderately with mechanical properties in osteoarthritic menisci. However, future work should include similar studies in non-diseased menisci, as this will be essential to develop protocols for detection of early degenerative changes in the meniscus.

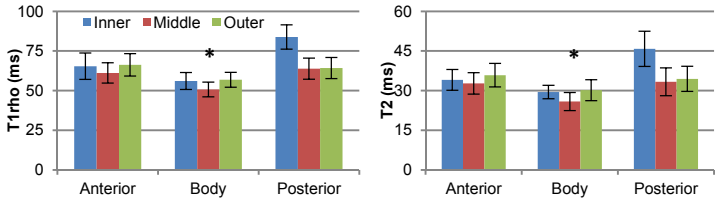

Fig. 3*: Zonal variation of T1ρ and T2 values in the meniscus. * indicates the body region is significantly different from the anterior and posterior regions.*

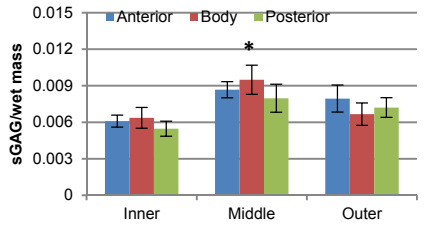

Fig. 4*: Zonal variation of sGAG content. *The middle region is significantly different from the inner and outer regions.*

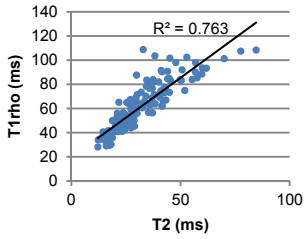

Fig. 5*: Strong positive correlation is seen between T1ρ and T2 values.*

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References: **1.**Lohmander+ *J Sports Med* 2007 **2.**Englund+ *Rheum Dis Clin N Am* 2009 **3.**Li+ *Mag Res Med* 2008 **4.**Bydder+ *Ske Rad* 2009 **5.**Chou+ *Ost Cart* 2009 **6.**Herwig+ *Ann Rheum Dis* 1984 **7.**Bursac+ *Biorheology* 2009 **8.**Lewis+ *Orth Res* 2008 **9.**Zarins+ *Ost Cart* 2010