T1ρ Assessment of Human Cartilage in an Impact Injury Model

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Introduction: Magnetic resonance imaging (MRI) continues to be the gold standard imaging modality for assessment of cartilage morphology and visualization of defects. However, the appearance of morphological changes in cartilage occurs long after the initial degenerative processes have begun. Proteoglycan (PG) loss is among the first tissue-level changes appearing in the early stages of osteoarthritis (OA), making the cartilage vulnerable to subsequent mechanical injury. These biochemical changes are not visible using routine MRI acquisition protocols.

T1ρ is an additional relaxation parameter that has shown promise as a sensitive indicator of changes in PG content in tissues. Numerous studies have validated the effect of PG content on T1ρ relaxation times[1-3] both in vitro and in vivo[4-5]. Low-frequency interactions between bulk water and macromolecules influence T1ρ relaxation. In cartilage, the main determinant of T1ρ relaxation time appears to be the interactions between water and PG, where a reduction in PG content decreases these interactions and yields an increase in observed T1ρ relaxation time. In this study, a single mechanical impact model was used to initiate the post-injury biologic cascades. The purpose of this study was to observe the PG changes in impacted fresh human cartilage and to assess the ability of T1ρ imaging to accurately detect and portray the time course of the associated PG depletion.

Methods: Four 1-cm wide osteochondral specimens (tibial plateau, 2 medial, 2 lateral) were taken from a fresh knee joint from an above-knee amputation of a 50-year-old male with no known history of OA. Three of the specimens were subjected to a single mechanical impact from a drop tower at a height of 5 cm, yielding an impact of 2.47 J/cm^2. The fourth specimen served as the control.

All specimens were serially imaged on day 1, day 3, and day 6 after impact testing with T1ρ imaging. Images were acquired on a Varian INOVA 4.7-T small-bore scanner (Varian Medical Systems,Palo Alto, CA) equipped with a 3.75-cm diameter quadrature RF coil, with the specimens immersed in nutrient media. The imaging protocol utilized a fast spin-echo pulse sequence with a T1ρ magnetization preparation block prepended. The T1ρ preparation block included a +90$_x$° square pulse, a 1000 Hz spin lock pulse, a -90$_x$° square tip-up pulse, and a final crusher gradient to destroy any residual transverse magnetization. Images at seven different spin lock durations (ranging from 5 to 80 ms) formed the basis for subsequent quantitative estimation of T1ρ relaxation time. The fast spin-echo pulse sequence parameters were TR/TE=4000/11 ms, echo train length of 4, and 512 x 128 matrix. The field of view ranged from 72 mm x 16 mm to 72 mm x 20 mm (depending on the thickness of the specimen) with a slice thickness of 1.5 mm and spacing of 2-3mm (depending on the specimen width) and two slices collected for each specimen. A nonlinear curve fitting algorithm computed the T1ρ relaxation maps on a pixel-by-pixel basis over the cartilage regions of interest (ROI) for each specimen slice.

After the final imaging session, each specimen was segmented into 5-6 samples for PG assay and histologic staining with safranin-O to determine PG content. The histology slides served as the basis for registration of the samples with equivalent regions of interest on the final (day 6) T1ρ maps for direct comparison of PG and T1ρ measures.

Day 1: Mean T1ρ = 61   Day 3: Mean T1ρ = 60   Day 6: Mean T1ρ = 70
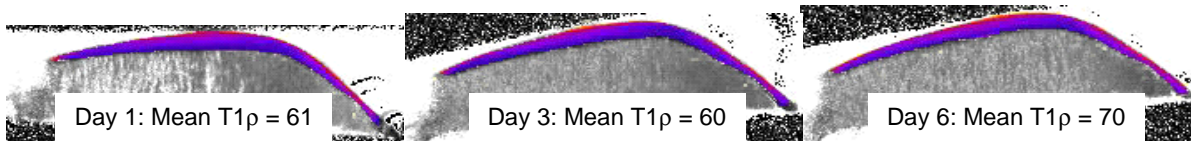
Figure 1: T1ρ maps acquired from an impacted sample over a six day period. Increasing mean T1ρ relaxation time by day 6 suggests overall PG depletion in the sample.
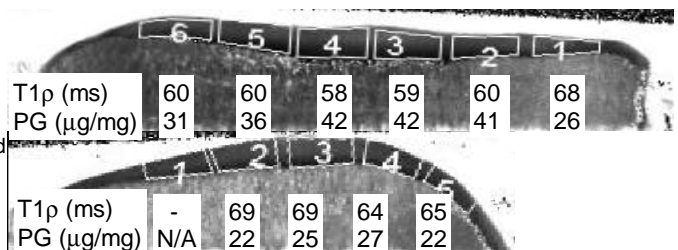
Results: Figure 1 displays sample T1ρ maps for one of the impacted specimens at all three imaged time points. The overall increase in T1ρ time suggests early loss of PG content, which was in fact decreased compared to the control sample. Figure 2 shows defined regions for T1ρ and PG measurements in an impact and control specimen. All regions of the cartilage specimen subjected to impact demonstrated reduced PG content and increased T1ρ relaxation time compared to the control specimen. Figure 3 compares the PG content and T1ρ relaxations for all 18 samples and regions of interest where PG content was available. T1ρ relaxation times correlated well with PG content, with increases in T1ρ corresponding to measurably reduced PG content occurring within 6 days after impact.

Discussion: The significant correlation between T1ρ relaxation times and PG measurements furthers the hypothesis that PG depletion resulting from mechanical impact or injury can be assessed noninvasively with T1ρ imaging. While direct comparison to PG content is not available for the earlier imaging times, the evidence from the T1ρ maps suggests that changes in PG content manifest within a few days of injury. The ability to follow the time course of PG depletion in a non-destructive and noninvasive fashion may thus serve as an important imaging biomarker for assessment of cartilage degradation in vivo in early stages of OA. This study represents further validation of the ability of noninvasive MRI techniques to quantitatively measure cartilage function, potentially yielding more objective early stage appraisals of OA and injury as well as follow-up treatment modalities.
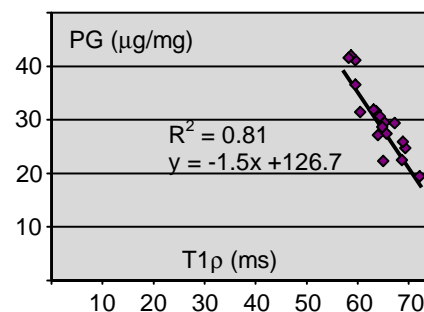

	6	5	4	3	2	1
T1ρ (ms)	60	60	58	59	60	68
PG (µg/mg)	31	36	42	42	41	26

	1	2	3	4	5
T1ρ (ms)	-	69	69	64	65
PG (µg/mg)	N/A	22	25	27	22

Figure 2: Regional T1ρ times at day 6 and corresponding PG measurements for control (top) and impacted (bottom) samples.

Figure 3: Comparison of T1ρ relaxation and PG content from biochemical assay in 18 cartilage regions.

$R^2 = 0.81$
$y = -1.5x + 126.7$

References
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