T1ρ MRI of Human Articular Cartilage at 3T: Topographic Variations and Correlation with Indentation Biomechanical Properties

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INTRODUCTION: In joint diseases such as osteoarthritis, articular cartilage undergoes structural, compositional, and functional alterations. Such changes include cartilage roughening and wear,[9] loss of proteoglycans (PG),[10] and diminished biomechanical integrity as indicated by decreased indentation stiffness.[2,7] Conventional MRI has been useful in evaluating structure of cartilage,[4] but not composition and function. Recently PG-sensitive methods such as T1ρ[5] and dGEMRIC[3] have been developed, with the former not requiring the use of contrast agent. Establishing a relationship between mechanical indentation[2] and T1ρ properties of human cartilage would extend the implications of T1ρ imaging. Thus, for human patellar cartilage, we determined , topographic variations in indentation stiffness and T1ρ values, and the correlation between these parameter values.

METHODS: ***Sample Preparation.*** Axial bone-cartilage slices (5 mm thick) were obtained from the center of two cadaveric (77±0 yrs) patellae, and kept hydrated during testing with saline with proteinase inhibitors.[6] ***T1ρ MR Imaging.*** Apparatus. A GE 3T Signa Twinspeed MR scanner was used with a 1" quadrature coil. T1ρ Sequence. For T1ρ MRI, a segmented elliptic-centric T1ρ sequence[14] was used to obtain 6 images with different spin lock times (TSL) with the following settings: TR=1500 ms, TSL=0, 10, 20, 40, 60 and 80 ms, spin lock frequency=500 Hz,, image matrix=256x256, FOV=5 cm, slice=2.4 mm, flip angle=90°. Samples were submerged in perfluorocarbon during scanning. T1ρ Quantification. Using Matlab (v7.5), MR images taken at multiple TSL were analyzed by voxel-wise mono-exponential fitting of signal intensity to: $S(TSL) = S_0 \cdot \exp(-TSL/T1\rho)$. This, along with masks representing areas of articular cartilage, provided T1ρ maps. ***Indentation Testing.*** Conventional. To determine topographic biomechanical integrity of each sample, sites (~1 mm apart) on the articular surface were tested. Sites were aligned (**Fig.1A**) normal to an indenter (0.8 mm dia., plane-ended) fitted onto a mechanical tester (V500, Biosyntech). A tare load (3 mN) was applied, followed by 100 μm compression, a hold for 1 s, and a release. This was repeated 3 times per site. Indentation stiffness was determined as the average of resultant forces divided by the applied displacement. Photographs were taken to register indentation sites to MRI. Side-Indentation. To determine depth-associated variations in indentation stiffness, a side-indentation method was used. Test sites on a 2-D grid (0.5 mm apart, **Fig.1A**) on the cut sample surface were indented using a micro-scale tip (0.125 mm dia.). The testing protocol and data reduction were performed as described above, except with smaller tare load (0.3 mN) and depth (50 μm). ***Data Analysis & Statistics.*** T1ρ vs. Conventional Indentation. To compare conventional indentation stiffness to regional T1ρ values, semi-circular regions of interest (ROI) centered about each indentation site (**Fig.1B**) were analyzed on T1ρ maps (**Fig.2AB**). A ROI diameter of 1.2 mm was chosen since it encompasses regions of cartilage undergoing strain during indentation.[1] For each ROI, T1ρ values were averaged and plotted (**Fig.2CD**), along with indentation stiffness (**Fig.2EF**). In addition, regional T1ρ were determined for different diameters of ROI (1.2, 2.4 and 4.8 mm) and correlated with indentation stiffness (log-transformed due to a large range) using Systat software (α=0.05). The overall T1ρ values and indentation stiffness between the two samples were compared using t-test. T1ρ vs. Side-Indentation. Subsets of a T1ρ map (dotted area, **Fig.1A** and **4A**) was compared to a map of side-indentation stiffness values (**Fig.4B**) from the same area.

RESULTS: T1ρ maps (**Fig.2AB**) exhibited large topographic variations, including depth-wise and focal differences. In general, deeper layers of cartilage had low values (~50 ms) of T1ρ that increased towards the surface. High regional T1ρ values (**Fig.2CD**) usually corresponded to lower values of indentation stiffness (**Fig.2EF**). Both the overall T1ρ ($p<0.001$ for all ROI diameters) and indentation stiffness ($p<0.05$) varied between samples. The strength of correlation between T1ρ and indentation stiffness was the highest ($R^2=0.22$, $p<0.001$, **Fig.3A**) when ROI diameter was 1.2 mm, and it decreased with increasing ROI diameter (**Fig.3BC**). Depth-varying topography of side-indentation stiffness (**Fig.4B**) was similar to corresponding subset from a T1ρ map (**Fig.4A**).

DISCUSSION: These results indicate that overall and topographic variations in T1ρ values correlate inversely with indentation stiffness, and that the strength of correlation depended on the size of ROI. The inverse relation is consistent with the increase of T1ρ[12] and decrease in mechanical integrity[2,10] with joint degeneration. The present study extends studies relating MR and biomechanics[11,13] by elucidating 2-D maps of biomechanical properties (**Fig.4B**) that closely mimicking T1ρ maps. While loss of PG is one mechanism for reduced indentation stiffness, collagen network integrity is another important factor[8] whose relationship to T1ρ would be useful to determine. The present study has implications for the use of T1ρ MRI to evaluate the structure, composition and function of a joint.

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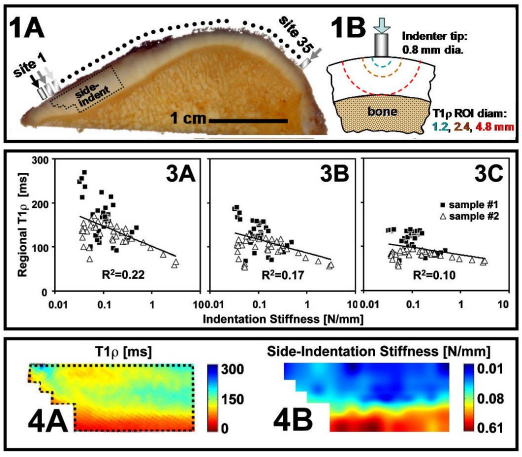

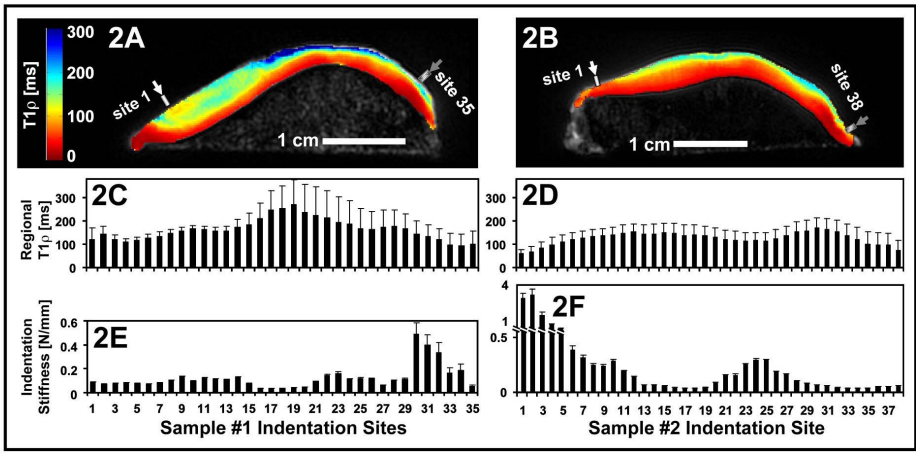

Fig.1: (**A**) Photograph of sample #1 and indentation sites. (**B**) Schematic of regions of interest (ROI) for regional T1ρ analysis.
Fig.2: (**AB**) T1ρ maps, (**CD**) regional T1ρ values, and (**EF**) conventional indentation stiffness values for samples (**ACE**) #1 and (**BDF**) #2.
Fig.3: Correlation between conventional indentation stiffness and regional T1ρ determined using ROI diameter of (**A**) 1.2, (**B**) 2.4, and (**C**) 4.8 mm.
Fig.4: (**A**) Subset of T1ρ map compared with (**B**) side-indentation stiffness map.