INTRODUCTION: Degeneration of articular cartilage involves structural, compositional, and functional alterations. Such changes include cartilage roughening,\(^1\) loss of glycosaminoglycans (GAG),\(^2\) and diminished biomechanical integrity.\(^3\) Conventional MRI has been useful in evaluating structure of cartilage,\(^4\) but not composition or function. GAG-sensitive MRI such as T1\(\rho\) and dGEMRIC\(^5\) have been introduced, with the former not requiring the use of contrast agent. Establishing a relationship between T1\(\rho\) properties, indentation stiffness\(^6\) and GAG content of human cartilage would extend the implications of T1\(\rho\) imaging. Thus, for human patellar cartilage, we determined topographic variations in indentation stiffness, water and GAG content, and T1\(\rho\) values, and correlation between the measures.

METHODS: Samples. Axial bone-cartilage slices (5 mm thick) were obtained from the center of five cadaveric patellae (80–4 yrs; Collins grade 3), and kept hydrated with saline containing proteinase inhibitors.\(^7\) MRI. GE 3T Sigma HDx was used with a 1" birdcage coil. T1\(\rho\) Sequence. A 2D spiral sequence with T1\(\rho\) preparation pulse was used to obtain 6 images: TR=1500 ms, TSL (spin lock time)=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\(^\circ\). T1\(\rho\) Quantification. Using Matlab, T1\(\rho\) maps were created by voxel-wise mono-exponential fitting of signal intensity to: \(S(T1\rho) = S_0 \cdot \exp(-TSL/T1\rho)\). Additionally, T1\(\rho\) values in local regions of interest (ROI) were determined (Fig. 1) for comparison to indentation stiffness as well as biochemical content.

Indentation. To determine biomechanical integrity, topographic sites (~1 mm apart) on the articular surface were tested by indentation with a 0.8-mm diameter plane-ended tip. Sites were aligned (Fig.1A) normal to the tip, a tare load (3 mN) was applied, followed by 100 \(\mu\)m compression, a hold for 1 s, and a release. Indentation stiffness was determined as the resultant force divided by the applied displacement.

Biochemical Content. Evenly-sized cartilage fragments (Fig.1A, dashed lines) were obtained by resection. Water content was determined by wet-and dry-weighing, and sulfated GAG (sGAG) content was determined by DMB assay,\(^7\) and normalized to wet and dry weights. Data Analysis & Statistics. T1\(\rho\) vs. Indentation Stiffness. Semi-circular ROI centered about each indentation site (Fig.1B) were analyzed to determine regional T1\(\rho\) values. Since cartilage undergoes complex intra-tissue strain during indentation,\(^8\) varying ROI diameters of 1.2, 2.4, and 4.8 mm were analyzed to determine the sensitivity of ROI selection to the strength of correlation. For each ROI, T1\(\rho\) values were plotted (Fig.2B) and along with indentation stiffness (Fig.2C). For correlation, indentation (log-transformed due to a large range) and T1\(\rho\) data were compared using linear regression (Systat). T1\(\rho\) vs. Content. Rectangular ROI (Fig.1A), based on photographs taken after sequential resection, were analyzed to determine region T1\(\rho\) values. These were compared to water and sGAG contents (log-transformed) using univariate and multivariate linear regression.

RESULTS: T1\(\rho\) maps (Fig.2A) exhibited large topographic variations, including depth-wise differences. In general, deeper layers of cartilage had low values (~50 ms) of T1\(\rho\) that increased (~250 ms) towards the surface. High regional T1\(\rho\) values (Fig.2B) usually corresponded to lower values of indentation stiffness (Fig.2C). The strength of correlation between T1\(\rho\) and indentation stiffness was the highest (\(R^2=0.25\), \(p=0.0001\), Fig.3B) when ROI diameter was 2.4 mm, and it was the lowest (\(R^2=0.22\)) when ROI diameter was 4.8 mm (Fig.3C). There was a trend of positive correlation between T1\(\rho\) and water content (Fig.4A): \(R^2=0.06\), \(p=0.06\), and a significant correlation between T1\(\rho\) and sGAG content (Fig.4B): \(R^2=0.06\), \(p=0.06\). (Correlation with sGAG per wet weight was weak, \(R^2=0.0\), \(p=0.97\)). In multivariate analysis (Fig.4C.), water (\(p=0.08\)) and sGAG (\(p=0.01\)) contents accounted for 14% of variation seen in T1\(\rho\) (\(R^2=0.14\), \(p=0.05\)).

DISCUSSION: These results indicate that overall and topographic variations in T1\(\rho\) 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 T1\(\rho\) and decrease in mechanical integrity\(^6\) with joint degeneration. The dependence on the size of ROI suggests choice of ROI in MR analysis is important for sensitivity to mechanical function. Generally weak correlation between biochemical content and T1\(\rho\) may be because the samples were from older donors and were somewhat degenerate. A positive correlation between sGAG content and T1\(\rho\), seemingly contrary to the convention that high GAG concentration results in low T1\(\rho\), may be due to the fact that concentration of GAG in cartilage may depend not only on the content of GAG, but other factors such as integrity of collagen network which helps to keep GAG within matrix.


ACKNOWLEDGMENTS: NIH, General Electric