

Comparison of Quantitative Imaging of Cartilage for Osteoarthritis: T2, T1rho, dGEMRIC, and Contrast-Enhanced CT

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Introduction Osteoarthritis (OA) is a chronic degenerative disease characterized primarily by the loss of articular cartilage. Although radiography is the primary clinical method of evaluating OA, radiographs lack the ability to directly image soft tissues and hence is limited to the detection of OA only at late stages of disease progression and is relatively insensitive to biochemical cartilage changes. In contrast, magnetic resonance imaging (MRI) can assess cartilage morphology directly and has shown promise for the detection of soft tissue changes. For example, T2 relaxation times have been correlated with degradation of cartilage matrix², T1ρ relaxation times with macromolecular degradation³, and T1 values using delayed gadolinium enhanced MR imaging of cartilage (dGEMRIC) with proteoglycan content of cartilage^{4,5}. In addition, contrast-enhanced computed tomography (CT) has also been proposed as an alternative to dGEMRIC⁶. In the wake of the development of new imaging methods for assessment of cartilage biochemistry, there is a need for a careful, systematic comparison of the proposed imaging parameters to assess the ability of each. The focus of this work is to compare MRI (T1, T2, and T1ρ) and contrast-enhanced CT in human articular cartilage, in both the presence and absence of gadolinium-based contrast agent.

Methods Five human osteochondral specimens were obtained from OA patients undergoing total knee arthroplasty surgeries. Baseline MR images were obtained; then specimens were soaked overnight at 4°C in an isotonic saline solution containing 1mM Gd in preparation for contrast-enhanced MRI; specimens were again soaked overnight in solution containing 250 mM Gd for contrast-enhanced CT studies. MRI data were acquired on a 3T GE Excite Signa system using a quadrature transmit/receive wrist coil. The protocol included four sequences: sagittal three-dimensional water excitation high-resolution SPGR imaging, T1 mapping using a fast spin-echo inversion recovery sequence (TI = 50, 130, 200, 400, 800, 2100ms), T1ρ mapping employing a spin-lock technique and a 3D SPGR sequence developed previously (time of spin-lock (TSL) = 0, 10, 40, 80 ms, frequency of spin-lock = 500 Hz), and T2 mapping using a nonselective T2 preparation and a SPGR sequence as for T1ρ mapping (TE = /4.1, 14.5, 25, 45.9 ms). T1ρ and T2 maps were generated by fitting the data pixel-by-pixel to the equation $S(TSL) \sim \exp(-TSL/T1\rho)$ and $S(TE) \sim \exp(-TE/T2)$ respectively. T1 maps were generated with a pixel-by-pixel 3-parameter fitting program. CT images were obtained on a Scanco XtremeCT, and reconstructed at 21μm using software provided with the system. Resulting images underwent rigid registration using the VTK CISM toolkit. Cartilage was segmented semiautomatically using the first echo T1ρ images via a Bezier spline-based MATLAB program also developed in-house; the median value for each image slice was computed and used to compute Spearman rank correlations between imaging parameters. T1ρ and T2 values before and after contrast injection were compared using a paired t-test. To illustrate spatial relationships between imaging parameters, a colormap of each was generated and overlaid on the anatomical SPGR image, and pixel-by-pixel Spearman correlations were computed for the slice shown in the figure.

Results T2 values were found to correlate moderately well with postcontrast T1 values (r=-0.58) and also with precontrast T1ρ values (r=0.52), which might be expected due to the influence of water mobility. In addition, postcontrast T1 was found to correlate equivalently well with T1ρ and T2 (r=-0.58 vs. -0.58). Moreover, contrast-enhanced CT values correlated better with both T1ρ (r=0.76) and postcontrast T1 (r=-0.69) better than T2 (r=0.45), as expected since T1ρ is considered to be more sensitive than T2 to destruction of high molecular weight proteoglycans. Spearman correlation data are shown in the table below, with p<0.01 indicated by an asterisk. Figure 1 illustrates the spatial distribution of T1, T2, T1ρ, and CT attenuation values before and after the addition of contrast in sample images from one specimen. Both T1ρ and T2 values

	T2	Precontrast T1	Postcontrast T1	Delta T1/T1pre	CT Attenuation (1/cm)
T1ρ	0.52*	0.25	-0.58*	-0.52*	0.76*
T2		0.11	-0.58*	-0.41	0.45*
Precontrast T1			0.05	-0.58*	0.29
Postcontrast T1				0.72*	-0.69*
Delta T1 / T1pre					-0.64*

after contrast injection were significantly different from those before contrast (P < 0.001).

Spatial comparison of the distribution of imaging parameters within the cartilage was performed using individual pixel data. Pre- and postcontrast T2 values were found to be quite different (pixel-by-pixel t-test p<0.005) and only mildly correlated with each other (pixel-by-pixel Spearman r=0.29). Similar results were found for T1ρ, although spatial correlation was stronger (t-test p<0.005, Spearman r=0.55). Finally, postcontrast T1 was found to be highly correlated on a spatial pixel-by-pixel basis with CT data (Spearman r=-0.71). Postcontrast T1 and CT data were also correlated with T1ρ spatially (r=-0.47 and 0.39, respectively) but not with T2 (r=0.16 and 0.04, respectively). Similarities in the spatial distributions of T1ρ, CT attenuation, and postcontrast T1 values are shown qualitatively in the figure.

Discussion There has been much recent interest in the use of imaging techniques to quantify biochemical status and molecular pathways within living organisms. In the area of OA this interest has been directed toward assessment of the molecular state and health of articular cartilage. In particular, dGEMRIC imaging of cartilage has received attention for its intuitive mechanistic appeal relating to measurement of fixed charge density and hence its ability to characterize spatial variations of proteoglycans in cartilage. Employing methodology similar to that of dGEMRIC imaging, contrast-enhanced CT techniques have also been studied as a potential method for imaging proteoglycans in cartilage; as expected, CT attenuation values in this study were found to correlate on both a regional and a spatial basis with postcontrast T1. Moreover, contrast-enhanced CT has a potential advantage in that it detects the presence of contrast agent by directly sensing its electron density instead of relying indirectly on its effect on tissue relaxation times. At the present time, however, concerns related to radiation exposure and administration of increased contrast agent dose will likely require some technological advancement before its use becomes widespread in human studies. Interestingly, although T2 and T1ρ values correlated equally well on a regional basis with postcontrast T1, T1ρ correlated more highly on a spatial basis with postcontrast T1 than did T2. T1ρ was also correlated much better with CT data than was T2, both on a regional and spatial level. Although both T2 and T1ρ are influenced by water motility, this result might be expected partially on the basis that T1ρ is sensitive to large molecular weight proteoglycans, whose degradation may not necessarily correlate on a spatial basis with fluid accumulation. Together, this indicates that T1ρ, T2, contrast-enhanced techniques may provide complementary information about the molecular environment in cartilage during the evolution of OA, and that further study will expand our understanding of the relationships between them.

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