Relationship of T2 and dGEMRIC with histologically verified degeneration of human cartilage at 1.5T

E. Lammentausta[1], P. Kiviranta[2], J. Töyräs[3], I. Kiviranta[4], M. T. Nieminen[5], J. S. Jurvelin[1,6]

[1]Department of Applied Physics, University of Kuopio, Kuopio, Finland, [2]University of Kuopio, Kuopio, Finland, [3]Department of clinical Neurophysiology, Kuopio University Hospital, Kuopio, Finland, [4]Department of Orthopaedics and Traumatology, Jyväskylä Central Hospital, Jyväskylä, Finland, [5]Department of Diagnostic Radiology, Oulu University hospital, Oulu, Finland, [6]Department of Clinical Physiology, Kuopio University Hospital, Kuopio, Finland

INTRODUCTION

Articular cartilage constituents, i.e. proteoglycans (PGs), the three-dimensional collagen network and interstitial water, as well as their interactions have a major role in the mechanical response of cartilage [1]. T2 and dGEMRIC (delayed Gadolinium-Enhanced MRI of Cartilage) mapping of cartilage have been reported to be sensitive to cartilage constituents, T2 particularly to collagen and dGEMRIC to proteoglycan [2,3]. Earlier, both parameters have been related to mechanical properties of animal [4,5] and human cartilage at 9.4T [6]. The aim of the present study was to determine the ability of T2 and dGEMRIC, as obtained at a clinically applicable field strength, to quantitatively distinguish healthy and degenerated cartilage tissue.

METHODS

Patellae of human cadavers (N=14, 12 male, 2 female, age 55 ± 18 years) were equilibrated overnight in 0.5mM Gd-DTPA(2-) solution. It has been previously shown that, at low contrast agent concentrations, the T2 relaxation time of cartilage is insignificantly affected by Gd-DTPA(2-) [7]. For MRI measurements (GE Signa 1.5T, GE Healthcare, Milwaukee, WI), articular surface of intact patellae were oriented parallel to B0 to emulate clinical patient positioning. T2 maps were calculated from multi-slice multi-echo spin echo experiments (GE prototype sequence with improved slice profile, TR=1000ms, 8 TEs between 10.3-82.4ms, ETL=8, 3-mm slice thickness, 0.313mm in-plane resolution at room temperature) and dGEMRIC maps were obtained from single-slice inversion recovery fast spin echo experiments (TR=1700ms, TE=11ms, 6 TIs between 50-1600ms). Subsequently, full-thickness cartilage disks (dia. = 4 mm) without subchondral bone were prepared from specified locations. A total of 76 regions of interest (width 3 mm) were analyzed. Superficial T2 and dGEMRIC values from the first three pixels (0.938mm) of each region were averaged to characterize the superficial tissue. Bulk values for full thickness tissue were also calculated by averaging all pixels in the ROI.

Prior to biomechanical testing the cartilage disks were equilibrated in phosphate buffered saline solution for at least two hours to wash-out the contrast agent. Stress-relaxation tests in unconfined geometry were conducted with 10% pre-strain and three 2% steps using a relaxation time of 30min to determine the Young's modulus from the equilibrium response, and the dynamic modulus from the peak-to-peak stress-strain relation from sinusoidal loading of 5 cycles with 1% amplitude and 1 Hz frequency [8]. After biomechanical testing, the samples were processed for microscopic analyses of PG content (assessed with optical density measurements of safranin-O stain [9]) and collagen (assessed with Fourier Transformed Infrared Imaging [10]). Mankin score of the samples [11] was evaluated by three of the authors independently from blind-coded sections. As the samples were detached from subchondral bone, the integrity of the tidemark could not be evaluated.

RESULTS

The samples were divided into three groups based on their Mankin score. Samples with Mankin scores from 0 to 3.3 (n=29) were defined to represent healthy tissue. The samples with early cartilage degeneration were identified by Mankin scores between 3.3 and 5.0 (n=23). Samples with Mankin scores greater than 5.0 represented advanced degeneration (n=25). Values of superficial and bulk T2, Young's modulus, dynamic modulus, PG and collagen content were statistically different ($p < 0.01$) between advanced degeneration and other groups (Figure 1). Statistically significant linear correlations were demonstrated between T2, mechanical properties and cartilage composition (Table 1). There were no significant differences in superficial or bulk dGEMRIC values between different groups. The only significant linear correlation between dGEMRIC and mechanical properties of tissue composition was that of superficial dGEMRIC values and Young's modulus ($r=0.30$, $p < 0.01$).

Table 1. Linear correlation coefficients between T2, mechanical and compositional parameters.

	Young's Modulus	Dynamic Modulus	Collagen Content	PG Content
$T2_{,sur}$	-0.55**	-0.64**	-0.59**	-.052**
$T2_{,bulk}$	-0.42**	-0.47**	-0.45**	-0.39**
Young's m.			0.68**	0.55**
Dynamic m.			0.74**	0.58**

** $p < 0.01$

DISCUSSION

Based on the present results, significant, degeneration dependent variation existed in superficial and bulk T2 values as well as in mechanical and compositional parameters of human patellar cartilage. These results indicate that elevated T2 relaxation time values effectively identify advanced degeneration of articular cartilage while dGEMRIC correlates relatively poorly with mechanical or compositional parameters in this setting. The results (Table 1) suggest that T2 serves as an indicator of cartilage mechanical quality, collagen and PG contents, and thereby, provides a noninvasive tool for evaluation of OA development. While dGEMRIC, measured at higher magnetic fields, has previously been successfully related to cartilage PG content [2,3] and mechanical properties [4,6] we were unable to reproduce these findings at 1.5T. The contrast agent distribution in the most degenerated samples may not be controlled by electrostatic forces because of increased fluid mobility in extensively damaged extracellular matrix. This also suggests that collagen disruption is the major mechanism behind the inferior structural and functional integrity of tissue in spontaneous cartilage degeneration

REFERENCES

1. Mow VC et al, Biomaterials 13: 67-97, 1992
2. Bashir A et al., MagnReson Med 41:857-865, 1999
3. Nieminen MT et al, Magn Reson Med 43: 676-681, 2000
4. Nissi MJ et al, J Orthop Res 22: 557-564, 2004
5. Nieminen MT et al, J Biomech 37: 321-328, 2004
6. Kurkijärvi JE et al, Magn Reson Med 52: 41-46, 2004
7. Nieminen MT et al. Magn Reson Med 51: 1147-1152, 2004
8. Jurvelin JS et al, J Biomech 30: 235-241, 1997
9. Panula HE et al., Ann Rheum Dis 57:237-245, 1998
10. Gamacho et al., Biopolymers 61:1-8, 2001
11. Mankin HJ et al., J Bone Joint Surg Am 53:523-537, 971

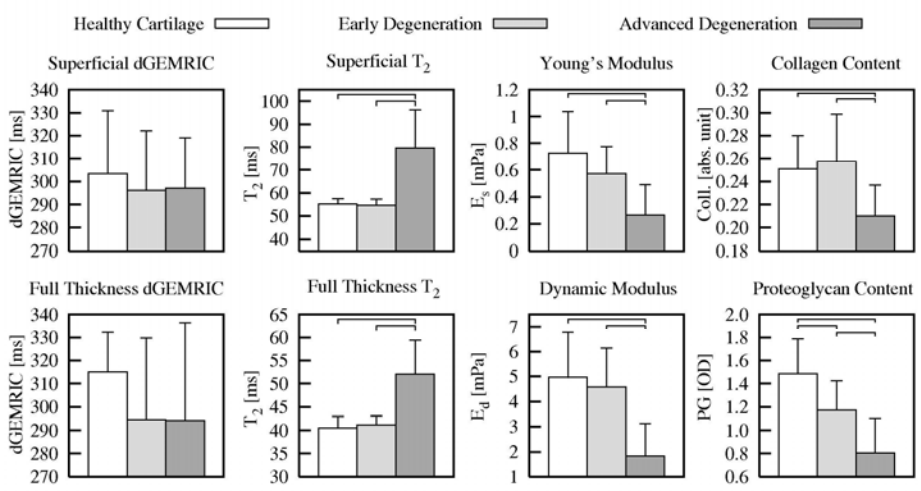

Figure 1. Mean ± SD of MRI, mechanical and compositional parameters of human patellar cartilage as divided in three categories based on their Mankin score. Statistical significant difference ($p<0.01$) between groups is indicated with brackets.