In-situ Response Measurement of Degenerated Articular Cartilage to the Loading in 3-T MRI

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Abstract. *The aim of this study was to assess the changes in MRI parameters during applied load directly in MR scanner and correlate these changes with biomechanical parameters of human articular cartilage. Cartilage explants from patients who underwent total knee replacement were examined in the micro-imaging system in 3-T scanner. Concerning MRI parameters, T_1 without- and T_1 with contrast agent as a marker of proteoglycan content, T_2 as a marker of collagen network anisotropy and ADC as a measure of diffusivity were calculated in pre- and during compression state. Subsequently, these parameters were compared to the biomechanical properties of articular cartilage, instantaneous modulus (I), equilibrium modulus (Eq) and time of tissue relaxation (τ). Significant load-induced changes of T_2 and ADC were recorded. High correlation between T_{1Gd} and I was found (r = 0.6324), and between ADC and Eq (r = -0.4884). Multi-parametric MRI may have great potential in analysing static and dynamic biomechanical behaviour of articular cartilage.*

Keywords: Articular cartilage, MRI, biomechanics, loading

1. Introduction

Only limited information is currently available on the relationship between cartilage compression and signal changes in T_1, T_2 and diffusion weighted images as a consequence of biochemical and biomechanical alterations during and after compression. However, in order to interpret medical images from MRI correctly, one should know several circumstances that precede measurement itself. Cartilage compression can be considered as one of these factors. Cartilage tissue consists of several macromolecules that provide basic functions: to distribute the load within a joint and provide a smooth surface for articulation. Load distribution in the joint is influenced by cartilage anatomy and mechanical properties, the presence of menisci and ligaments, bone stiffness and anatomy, and loading direction and kinetics. MR imaging has become the method of choice in the evaluation of normal [1] and damaged [2] cartilage due to the improved soft tissue contrast and multi planar capability without radiation exposure. Several studies were performed in the field of mechanical testing of cartilage during compression [3]. Biochemical and biomechanical changes were observed: fluid-flow and internal deformation, intrinsic viscoelasticity, changes in the water content or catabolism and loss of proteoglycans [4]. Investigators attempted to use MRI to evaluate mechanical properties of cartilage after applying load. In some cases, an MR-compatible device was built for controlled loading of cartilage explants and intact joints [5]. In another study, the rate and degree of deformation were increased after trypsin degradation [6]. A recent in vivo study demonstrated the ability to measure changes in cartilage volume as a function of mechanical stress (i.e. exercise) [7]. These studies imply that MRI is a modality with sufficient sensitivity to evaluate load-induced changes in cartilage tissue.

The goal of this study was to evaluate common MRI parameters of human articular cartilage and their changes as a consequence of static compression by a special designed non-magnetic device for indentation tests of cartilage tissue and correlate these with selected biomechanical parameters.

2. Subject and Methods

Cartilage samples were prepared from joints of 10 patients, who underwent a total knee joint replacement. The samples were cuboid-shape, with 10x10x6 mm in dimension. Study was performed on a Bruker 3T Medspec whole-body scanner (Bruker, Ettlingen, Germany) using BGA-12 micro-gradients (capable of delivering 200mT/m) with a special designed compression device built for this gradient system. Cartilage sample was compressed in the way that 15% of thickness decrease was accomplished. T_1 mapping was performed after filling the water-proof chamber of the compression device with a 2 mmol solution of gadopentetate dimeglumine (Gd-DTPA, Schering, Berlin, Germany) and soaking cartilage sample in solution for 24 hours. Then inversion recovery spin echo pulse sequence with TI times were 15, 30, 60, 160, 400 and 2000 ms. For T_2 mapping a multi-echo multi-slice spin echo sequence with TE times 15, 30, 45, 60, 75 and 90 ms was applied. ADCs were calculated from data from pulsed gradient spin echo (PGSE) with 6 different b-values (10.472, 220. 627, 452.8, 724.5 and 957.7). Each of parameters was calculated by fitting to appropriate exponential function. Fitting routines were written in IDL (Interactive Data Language, Research Systems, Inc.) using *mpcurvefit* routine. Regarding biomechanical parameters, *Eq* (equilibrium modulus), *I* (instantaneous modulus) and τ (time of tissue relaxation) were measured by indentation tests on a Zwick Z050 universal testing device with a 20N-load cell of 1mN resolution. OA status was determined by histogical evaluation using hematoxylin-eosine staining. Biomechanical and MR parameters were compared using Pearson correlation coefficient and statistical significance was determined by pair T-test (p-value lower than 0.05 was considered as statistical significant).

3. Results

Calculated MR parameters in pre- and during compression states are summarized in Table 1. The summary of Pearson correlation coefficients between MR and biomechanical parameters can be found in the Table 2. The example of MR appearance of articular cartilage sample is depicted in the Fig. 1.

Table 1. Values of T_1, T_2 and ADC, comparison of pre- and during-compression states

	ADC [10^{-3}mm^2/s]	T_1 [ms]	T_2 [ms]
number of pixels in ROI	166	110	108
without compression	**0.96 ± 0.40**	180 ± 30	**30 ± 9**
with compression	**0.85 ± 0.39**	230 ± 30	**27 ± 8**
change (%, p value)	**11% (<0.05)**	22% (0.238)	**10% (<0.05)**

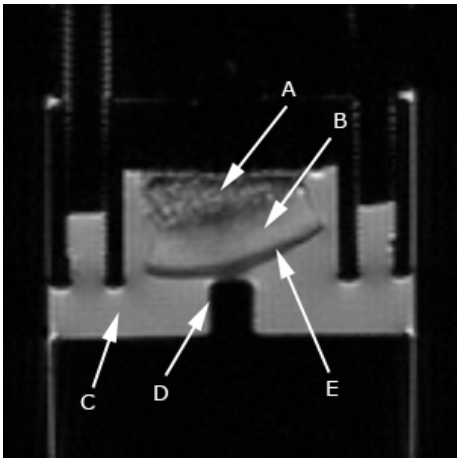

Fig. 1. Cartilage specimen in micro-imaging system (IR, TI = 60ms, TR = 4s, TE = 15ms): A - bone tissue, B – deep zone of cartilage, C - PBS + Gd-DTPA^{2-} solution, D - compressive piston, E - superficial zone of cartilage

Table 2. Pearson correlation coefficients between MR parameters during loading and biomechanical parameters measured by indentation tests

	Eq [MPa]	I [MPa]	I/Eq	T [s]
T1c/T1w	-0.1884	**0.6324**	**-0.5275**	**0.6092**
T2c/T1w	0.3620	0.1118	-0.0860	0.0257
ADCc/ADCw	**-0.4884**	0.1276	-0.2612	**0.5039**

The rows are expressed as a ratio of the MR parameters during compression (c-index) and without compression (w-index).

4. Discussion

It is generally known that the response of cartilage to compressive load is not uniform [8]. Therefore, the ability to spatially localize the response of cartilage to compression is necessary. While interpreting data in comparison with in-vivo conditions there are two important factors affecting resulting deformation: first one is the dynamics of loading and second one is the distribution of loading. Dynamics of loading strongly affects load displacement relationship. T_2 values decreased after compression in 10%. These observations agree well with published results and support the hypothesis that cartilage compression results in greater anisotropy of superficial collagen fibers, because region of interest was defined very close to piston head, i.e. mostly in superficial part of cartilage. Eckstein et al demonstrated a 5 to 6% decrease in patellar cartilage volume after compressive loading induced by performing 50 deep knee bends [9]. Besides tissue consolidation and the resulting decrease in water content due to efflux of water as a possible factor responsible for the observed change in cartilage T_2 prior ex vivo studies designed for the evaluation of changes in collagen fiber orientation with loaded conditions suggest that changes in fiber orientation is the dominant factor for T_2 shortening [10]. T_1 values of cartilage after penetration of Gd-DTPA^{2-} allow assessment of the proteoglycan (GAG) component of articular cartilage [11]. Applying compression to cartilage sample invokes changes in water content in cartilage tissue. Amount of proteoglycans stays unaltered, but amount of liquid part decreases. Due to squeezing liquid content from cartilage, concentration of Gd-DTPA^{2-} decreases as well. In contrast to T_{1Gd}, which reflects changes in chemical composition, diffusion constants may reflect microstructural degradation of the cartilage matrix. ADC correlates with structural changes rather than with changes in chemical composition [12]. Compression may induce cartilage matrix impairment which leads to decreasing of ADC. Since *Eq* and *I* reflect dynamic mechanics of cartilage, they correlate mostly with proteoglycans content (T_{1Gd}) and diffusivity of water molecules (ADC)

5. Conclusions

It was shown that multi-parametric MRI has a great potential in analysis the static and dynamic biomechanical behaviour of articular cartilage.

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