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The in vivo effects of unloading and compression on T1-Gd (dGEMRIC) relaxation times in healthy articular knee cartilage at 3.0 Tesla

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Abstract *Purpose:* The purpose was to investigate the in vivo effects of unloading and compression on T1-Gd relaxation times in healthy articular knee cartilage. *Materials and methods:* Ten volunteers were enrolled, and dGEMRIC images of their right knee joints were obtained using 3.0-T MR at three timepoints: directly following exercise ("baseline"), approximately 15 min after unloading ("unloading") and during application of a compressive force (50% of the body weight) generated by a loading device via a footplate ("compression"). *Results:* Our analysis of variance of pooled data from all cartilage zones demonstrated a significant mean T1-Gd decrease of 56.6 ms between baseline and compression ($p<0.001$), and a significant mean decrease of 42.1 ms between unloading and compression ($p<0.001$). No significant difference was found between baseline and unloading. Higher mean T1-Gd values were observed in the cartilage contact zone (central femoral and tibial zones; 698.3±162.2 ms) than in the non-contact zone (anterior and posterior femoral and tibial zones, and dorsal femoral zone; 662.9±149.3 ms; $p<0.01$). *Conclusion:* T1-Gd times appear to be sensitive to mechanical cartilage stress, and thus, further studies are warranted that investigate the relationship between the biochemical load response and the biomechanical properties of articular cartilage.

Keywords Articular cartilage/disorders · MR imaging/diagnosis · 3T MR imaging

Introduction

T1 mapping in the presence of Gd-DPTA^{2-} (delayed gadolinium-enhanced MRI of cartilage, dGEMRIC) is a well-accepted biochemical magnetic resonance imaging (MRI) technique for the quantitative evaluation of articular cartilage [1–3] and chondrocyte implants [4]. The T1-Gd relaxation time is recognized as a specific, indirect measure of glycosaminoglycan (GAG) concentration, which, in turn, represents an important indicator of cartilage quality [5, 6]. The ultimate goal of dGEMRIC is to detect the early stages of abnormal cartilage wear, which are associated

with GAG loss, before macroscopic tissue damage has occurred and the cartilage may be beyond repair [7].

Ex vivo experiments have demonstrated that T1-Gd relaxation times are correlated with the mechanical properties of cartilage, as reflected by elastic and dynamic moduli, and adequately reproduce the topographical differences of both mechanical and biochemical cartilage properties [6, 8–12]. Despite these encouraging ex vivo findings, several open questions remain that are important for the in vivo applicability of T1-Gd as a biomarker for the functional status of cartilage. Specifically, little is presently known about the biochemical response of articular cartilage to mechanical stress in vivo, as reflected by changes in T1-Gd relaxation times.

In the present study, it was our aim to determine, in vivo, the effects of unloading and, more importantly, compression on T1-Gd relaxation times in healthy articular knee cartilage. It was our hypothesis that T1-Gd relaxation times would be sensitive to mechanical stress induced by compression and that this effect would be particularly pronounced in the central femoral and tibial cartilage zones, which are exposed to a higher mechanical load.

Materials and methods

Patients and study design

We enrolled ten asymptomatic volunteers (seven men and three women; mean age, 27.2±4.5 years; age range, 22 to 31 years) in our study. The study was approved by the local Institutional Review Board, and written informed consent was obtained from all subjects. Criteria for exclusion from the study were a history of cartilage damage or other musculoskeletal disorders of the right knee, including trauma within the last 6 months. Furthermore, volunteers who had had previous surgery or other interventions that involved the right knee were also excluded from participation in the study. On the morphological MR images that were obtained in the present study (see below), no focal knee cartilage defects, and no significant signal inhomogeneities, were observed.

MR imaging

MRI of the right knee was performed using 3.0-T MR (Magnetom Trio; Siemens, Erlangen, Germany) with a gradient strength of 40 mT/m, equipped with a dedicated, flexible, eight-channel knee array coil (Noras, Wuerzburg, Germany). The joint space of the extended knee was placed in the middle of the coil.

For morphological evaluation, we used an isotropic three-dimensional, double-echo steady-state (DESS) sequence with the following acquisition parameters: TR, 15.1 ms; TE, 5.1 ms; flip angle, 25°; field of view (FOV), 150×150 mm; matrix size (MTX), 250×250; isotropic voxel size, 0.6×0.6×0.6 mm; and total acquisition time, 6 min 32 s.

For T1-Gd mapping, we used a 3D gradient echo (GRE) sequence with the following parameters: TR, 15 ms; TE, 1.95 ms; flip angles, 5° and 18.6°; FoV, 160×160 mm; MTX, 384×384; voxel size 0.4×0.4×3.0 mm; bandwidth, 480 Hz/pixel; 22 slices; and total acquisition time, 3 min 40 s. T1-Gd maps were calculated on a pixel-by-pixel basis, as previously described [13], using the equations below:

$$T1c_{j,k} = \frac{TR}{1n\left[\frac{\sin(\alpha_1)*\cos(\alpha_2) - Q_{j,k}\sin(\alpha_2)*\cos(\alpha_1)}{\sin(\alpha_1) - Q_{j,k}*\sin(\alpha_2)}\right]}$$

$$Q_{j,k} = \frac{mess\_1_{j,k}}{mess\_2_{j,k}}$$

where $T1c_{j,k}$ denotes the T1 value, and $Q_{j,k}$ denotes the quotient of the two signal intensities for the pixel (j,k).

DESS images, as well as T1-Gd maps, were obtained in the supine position at three timepoints:

(1) baseline: 90 min after a bolus injection of 0.2 mmol per kilogram body weight of Gd-DTPA^{2-} (Magnevist; Schering, Berlin, Germany), including a time period of 20 min, starting approximately 30 min post injection, during which the patient exercised the knee by walking up and down stairs (enhanced MR imaging protocol recommended by Burstein et al. [14]);
(2) unloading: directly following the first mapping, i.e., approximately 15 min after unloading of the knee joint with the volunteer remaining inside the MR gantry;
(3) compression:" directly following the second mapping, during application of a compressive force, which was generated by a custom-made loading device (Noras, Wuerzburg, Germany), and was transmitted to the knee joint via a foot plate (Fig. 1).

The magnitude of the compressive force was set to 50% of body weight individually for each volunteer with the intention of simulating static weight-bearing conditions in the standing position [15].

Fig. 1 Custom-made loading device, with footplate, for generation of a compressive force (50% of body weight) on the knee joint

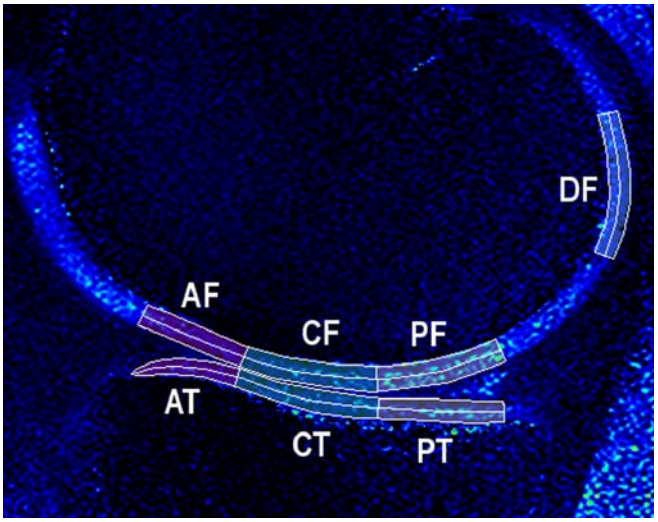

Fig. 2 Sagittal dGEMRIC image of the knee joint depicting the seven cartilage zones evaluated: anterior femoral (AF); central femoral (CF); posterior femoral (PF); dorsal femoral (DF); anterior tibial (AT); central tibial (CT); posterior tibial (PT), with respect to the position of the anterior and posterior horn of the meniscus. Each cartilage zone was divided into a deep and a superficial cartilage layer, yielding a total of 14 ROIs for analysis

Patient positioning and MR imaging plane orientation, with regard to their reproducibility, received particular attention to enable a comparison of the results of quantitative cartilage analysis on T1-Gd maps across the different timepoints. For this reason, localizers in the axial, coronal and sagittal imaging planes were repetitively obtained until a match among the three examinations was achieved, with regard to the slice positions.

Image analysis

To determine T1-Gd relaxation times at different cartilage sites, all images were analyzed in consensus by a senior musculoskeletal radiologist and a fourth-year resident in radiology. The two raters were blinded to the sequence being analyzed (i.e., baseline, unloading or compression). Independently for each of the three T1-Gd maps (corresponding to the three points in time), we manually defined seven regions of interest (ROI) on either of two reconstructed, adjacent sagittal sections that depicted the central portion of the medial, femoro-tibial knee joint compartment. The seven ROIs corresponded to the anterior, central, posterior and dorsal femoral cartilage zones, and to the anterior, central and posterior tibial cartilage zones, with respect to the position of the meniscus (Fig. 2). Anterior and posterior zones were defined as being covered by the anterior and the posterior horn of the medial meniscus, respectively. Central zones were located between the anterior and posterior zones (i.e., not covered by the meniscal horns). The mean cartilage thickness, calculated across all cartilage zones of all analyzed baseline images, was 2.1 mm (~4.9 pixels). Each ROI was further subdivided into a superficial and a deep layer of approximately the same size, yielding a total of 28 ROIs (7 ROIs × 2 layers × 2 slice positions) per subject for each point in time. Special care was taken to ensure that measurement sites (i.e., MR slice positions), as well as ROI positions, were consistent between T1-Gd maps on the one hand and across all timepoints on the other hand. This was achieved by direct visual comparison of the slice positions, and by copying the ROIs of the baseline examination to the corresponding image sections of the unloading and compression examinations.

Data and statistical analysis

For all measured T1-Gd values, (estimated marginal) means and standard deviations (SD) were calculated, independently for each cartilage zone and layer, and separately for each timepoint. For the assessment of quantitative differences among the three examinations (baseline, unloading and compression), we used a three-way analysis of variance (ANOVA) with random effects, taking into account the different measurements in each patient. Tukey's post-hoc testing was used for pairwise group comparisons, where appropriate.

In addition to the evaluation of pooled data from individual cartilage zones, we also quantitatively compared T1-Gd relaxation times for two supplementary cartilage

Table 1 Differences in mean T1-Gd relaxation times (ms) among the seven individual cartilage zones (combination of results obtained from deep and superficial cartilage layers) at baseline, unloading and compression

	Baseline	Unloading	Compression
Anterior femoral	664.73±137.57	635.67±122.57	602.65±144.71
Central femoral	712.3±158.36	703.64±152.96	657.07±172.71
Posterior femoral	743.56±185.29	733.57±180.28	676.12±175.02
Dorsal femoral	677.04±141.39	647.54±154.22	618.8±126.57
Anterior tibial	641.23±129.91	633.59±143.18	612.16±132.48
Central tibial	726.84±159.43	732.54±165.5	657.5±156.29
Posterior tibial	711.51±122.62	688.67±128.12	656.6±133.47

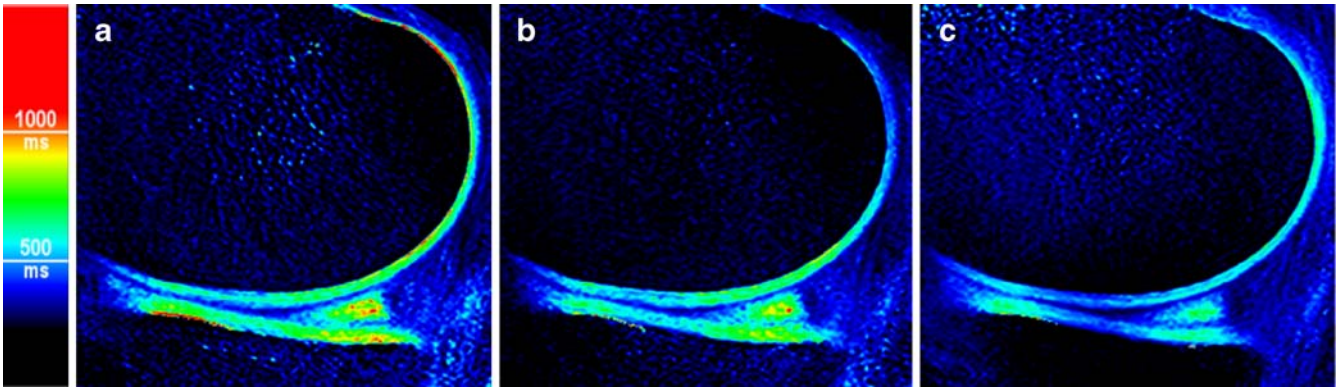

Fig. 3 Sagittal dGEMRIC images of the knee joint, obtained at baseline (**a**), unloading (**b**) and compression (**c**) at identical window levels. While there is no significant difference, with regard to T1-Gd relaxation times, between baseline and unloading, there is a significant T1-Gd decrease between baseline and compression, and between unloading and compression. This decrease is most obvious in the central femoral and tibial cartilage zones, and also in the posterior femoral and tibial zones

zones: the "cartilage contact zone" (all ROIs of the central femoral and central tibial cartilage, which are in direct contact with each other during compression) and the "cartilage non-contact zone" (all ROIs of the anterior and posterior femoral and tibial cartilage zones, as well as the dorsal femoral cartilage).

To determine the reproducibility of our measurements, MR images of five of the ten subjects were evaluated a second and a third time, by the same raters who had performed the original assessment, with a time interval of 2 weeks between the ratings. Based on these data, coefficients of variation (root mean square average) were calculated separately for the different time points and cartilage zones.

All calculations were performed using the SPSS 16.0 for Windows software package (Chicago, IL). The specified level of significance was 5% for all statistical tests.

Results

The ANOVA of pooled data from all cartilage zones demonstrated statistically significant differences in the mean T1-Gd relaxation times among baseline (696.7±151.4 ms), unloading (682.2±154.5 ms) and compression (640.1±150.6 ms) ($p=0.025$). Groupwise comparisons revealed that these differences were significant only between baseline and compression ($p<0.001$), and between unloading and compression ($p<0.001$), but not between baseline and unloading (Table 1, Fig. 3). We also observed significant T1-Gd differences between the individual cartilage zones ($p<0.001$), and between deep and superficial cartilage layers ($p<0.001$) across all examinations/timepoints (Table 2).

Our evaluation of supplementary cartilage zones revealed significantly higher T1-Gd values in the cartilage contact zone (mean, 698.3±162.2 ms) than in the non-contact zone (mean, 662.9±149.3 ms), across all points in time ($p<0.001$). However, we did not observe a significant interaction between these supplementary zones and timepoints, i.e., there was no significant change in the mean T1-Gd difference between contact and non-contact zones from one examination to another. Nevertheless, a graphic depiction showed a trend towards a more pronounced decrease in T1-Gd relaxation times in the superficial layers of the contact zone compared with the superficial layers of the non-contact zone during compression (Table 3).

Reproducibility was very high for all measurements, across all timepoints and cartilage zones, with coefficients of variation below 1% (Table 4).

Table 2 Differences in mean T1-Gd relaxation times (ms) among deep and superficial cartilage layers, calculated for the seven individual cartilage zones (combination of results obtained at baseline, unloading and compression)

	Deep layer	Superficial layer
Anterior femoral	643.25±130.65	625.46±142.7
Central femoral	704.56±160.34	677.45±163.93
Posterior femoral	739.52±172.93	695.99±188.03
Dorsal femoral	678.73±136.22	616.86±142.02
Anterior tibial	628.36±123.53	629.63±146.14
Central tibial	705.43±163.54	705.82±163.32
Posterior tibial	692.04±122.42	679.14±136.12

Table 3 Changes in mean T1-Gd relaxation times (ms) for cartilage contact and non-contact zones between baseline, unloading and compression. In the superficial cartilage layer, the mean T1-Gd decrease during compression appears to be more pronounced in the contact zone than in the non-contact zone

	Deep layer		Superficial layer	
	Contact	Non-contact	Contact	Non-contact
Baseline	729.26±158.87	716.44±172.45	709.88±158.66	658.79±142.75
Unloading	724.18±158.42	674.78±144.09	712.01±161.38	660.84±157.33
Compression	661.56±161.56	637.92±132.1	653.01± 167.67	628.61±157.07

Discussion

In the present study, we investigated the in vivo effects of unloading and compression on T1-Gd relaxation times of healthy articular cartilage in the medial knee joint compartment. This topic has, to our knowledge, not been previously investigated. Our results clearly show that prolonged unloading has no significant impact on the T1-Gd relaxation times, whereas mechanical cartilage stress, comparable to that generated under static weight-bearing conditions in the standing position, leads to a significant decrease in T1-Gd relaxation times (Fig. 3). The most likely explanation for this T1-Gd decrease is a higher density (i.e., an increase in the relative concentration) of Gd-DTPA^{2-} molecules within the cartilage tissue because of a reduction of cartilage thickness under compression. A reduction of cartilage thickness under compression, as a result of water and ionic movement as well as collagen deformation, has been previously established both in vivo and ex vivo [15–18], and even under a mechanical load of the same magnitude as the one used in the present study (50% of the body weight) [15].

It is striking that a T1-Gd decrease has previously been observed in degenerative disease because of a loss of glycosaminoglycans (GAG) and thus a higher Gd-DTPA^{2-} uptake in cartilage tissue [6, 19]. GAGs are negatively charged side chains of proteoglycans (PG) that attract protons, and are thus important for water influx and hydrodynamic pressure, and consequently, load distribution and compressive stiffness of cartilage [5, 6, 20]. It seems highly unlikely that a GAG loss was responsible for the T1-Gd decrease that we observed in the present study because of the short time interval between the application of the compressive force and image acquisition. Thus, even if a GAG concentration change had occurred under mechanical loading, the Gd-DTPA^{2-} molecules would have needed more time to redistribute between the poroviscoelastic cartilage tissue and the synovial fluid in order to reflect the new GAG concentration.

Based on our limited sample size, a T1-Gd decrease of approximately 50 ms may be regarded as a normal response of healthy articular knee cartilage to static weight-bearing stress in the standing position, at least in a younger population (20 to 30 years of age). This finding not only increases our basic understanding of cartilage contrast enhancement dynamics in vivo, but also may have implications for clinical dGEMRIC applications. It has been demonstrated previously that the recovery of cartilage thickness after increased or repetitive mechanical loading does not occur instantly, but requires a certain amount of time [21]. As the widely accepted enhanced MR imaging protocol by Burstein et al. also involves exposure of the knee joint to an increased mechanical load (20 min of walking up and down stairs) to support the Gd-DTPA^{2-} uptake in cartilage [14], artificially lower T1-Gd values might be observed if imaging is performed directly or early after loading. In the latter scenario, the observed influence of mechanical loading on cartilage T1-Gd values may thus represent a pitfall in the interpretation of T1-Gd relaxation times, and an ample time interval between mechanical loading and imaging is necessary to avoid this.

Nishii et al. recently reported an in vivo decrease in T2 relaxation times of articular knee cartilage under compression with a force of 50% of the body weight, which

Table 4 Coefficients of variation (%) for T1-Gd relaxation time measurements, based on three ratings in five subjects

	Baseline	Unloading	Compression
Anterior femoral	0.44	0.51	0.49
Central femoral	0.33	0.32	0.40
Posterior femoral	0.32	0.52	0.34
Dorsal femoral	0.54	0.58	0.44
Anterior tibial	0.41	0.50	0.34
Central tibial	0.39	0.42	0.36
Posterior tibial	0.44	0.35	0.47

suggests both a decrease in the water content and changes in the collagen network architecture [15]. These authors hypothesized that this method of examining the load response of articular cartilage enables the assessment of biomechanical tissue characteristics, which, in turn, might be useful for the detection of localized stress concentrations. Based on the latter assumption, it was our hypothesis that compression would lead to a greater T1-Gd change in the cartilage contact zone compared with the non-contact zone. This contact zone included the centrally located femoral and tibial cartilage zones of the medial knee joint compartment, which are in close contact with each other during compression (i.e., not covered by the stress-absorbing meniscal horns), and are thus exposed to a higher mechanical pressure [22]. While we did observe a more pronounced T1-Gd decrease in the superficial layers of the contact zone during compression (Table 3), this trend was not significant, and thus, our hypothesis could not be directly confirmed. This lack of statistical significance, however, may be a result of the rather small number of subjects that were included in the present study, which undoubtedly led to a high variance of results, particularly within the different subgroups. Thus, further investigations that are based on a larger population are warranted with regard to this topic.

Our study results demonstrated consistently higher T1-Gd values in deep cartilage zones than in superficial zones, which is quite in accordance with previous research in the field [23]. Notably, we also observed significantly higher T1-Gd values, suggestive of a higher GAG concentration, in the contact zones of the femoral and tibial cartilage, compared with the femoral and tibial non-contact zones. This finding may be attributed to the fact that these cartilage contact zones are exposed to a higher pressure during everyday life activities than all other cartilage zones of the knee joint. This interpretation is supported by the results of previous studies, which investigated the adaptive capacity of articular knee cartilage and reported that exercise stimulates GAG synthesis in an attempt to increase compressive stiffness [24, 25]. Although our study was not designed to investigate this topic, our findings may lend further credibility to the alleged role of continuous, moderate, physical exercise for the prevention of cartilage disease.

We note the limitations of our study. Our assignment of individual cartilage zones to two supplementary zones (cartilage contact and non-contact zones) may be subject to critique, because we made no attempt to directly correlate these supplementary zones with the weight-bearing zones. However, determination of weight-bearing zones, particularly in a supine lying position under static loading conditions, represents a difficult task and would have exceeded the scope of the study. We also did not assess changes in cartilage thickness in the different cartilage zones, because there is clear evidence that cartilage thickness is reduced under mechanical loading [15–18]. As mentioned above, the small sample size prevented us from performing a more in-depth analysis of dynamics in the GAG and contrast media distributions among cartilage zones and layers after mechanical stress.

In conclusion, the results of our study demonstrate a significant decrease in T1-Gd relaxation times in healthy articular knee cartilage under a mechanical load similar to that generated under static weight-bearing conditions in the standing position. This T1-Gd decrease appears to be more pronounced in the superficial layers of the femoral and tibial cartilage contact zones, although not significantly. It is important to note that the observed T1-Gd decrease is obviously not associated with a GAG loss and may represent a pitfall for the interpretation of T1-Gd values in certain situations. Further studies, particularly in patients with early degenerative cartilage disease, are necessary to determine whether the change in T1-Gd relaxation times during cartilage compression enables an indirect assessment of biomechanical cartilage properties.

References

1. Bashir A, Gray ML, Boutin RD, Burstein D (1997) Glycosaminoglycan in articular cartilage: in vivo assessment with delayed Gd(DTPA)(2-)-enhanced MR imaging. Radiology 205:551–558
2. Link TM, Stahl R, Woertler K (2007) Cartilage imaging: motivation, techniques, current and future significance. Eur Radiol 17:1135–1146
3. Burstein D, Gray ML (2006) Is MRI fulfilling its promise for molecular imaging of cartilage in arthritis? Osteoarthritis Cartilage 14:1087–1090
4. Trattnig S, Millington SA, Szomolanyi P, Marlovits S (2007) MR imaging of osteochondral grafts and autologous chondrocyte implantation. Eur Radiol 17:103–118
5. Heinegaard D, Bayliss M, Lorenzo P (2003) Biochemistry and metabolism of normal and osteoarthritic cartilage. In: Brandt KD, Doherty M, Lohmander LS (eds) Osteoarthritis. 2nd edn. Oxford University Press, New York, pp 72–82
6. Wayne JS, Kraft KA, Shields KJ, Yin C, Owen JR, Disler DG (2003) MR imaging of normal and matrix-depleted cartilage: correlation with biomechanical function and biochemical composition. Radiology 228:493–499
7. Williams A, Oppenheimer RA, Gray ML, Burstein D (2003) Differential recovery of glycosaminoglycan after IL-1-induced degradation of bovine articular cartilage depends on degree of degradation. Arthritis Res Ther 5:97–105

8. Korhonen RK, Laasanen MS, Töyräs J, Rieppo J, Hirvonen J, Helminen HJ et al (2002) Comparison of the equilibrium response of articular cartilage in unconfined compression, confined compression and indentation. J Biomech 35:903–909
9. Kurkijärvi JE, Nissi MJ, Kiviranta I, Jurvelin JS, Nieminen MT (2004) Delayed gadolinium-enhanced MRI of cartilage (dGEMRIC) and T2 characteristics of human knee articular cartilage: topographical variation and relationships to mechanical properties. Magn Reson Med 52:41–46
10. Nieminen MT, Töyräs J, Laasanen MS, Silvennoinen J, Helminen HJ, Jurvelin JS (2004) Prediction of biomechanical properties of articular cartilage with quantitative magnetic resonance imaging. J Biomech 37:321–328
11. Nissi MJ, Rieppo J, Töyräs J, Laasanen MS, Kiviranta I, Nieminen MT et al (2007) Estimation of mechanical properties of articular cartilage with MRI - dGEMRIC, T2 and T1 imaging in different species with variable stages of maturation. Osteoarthr Cartil 15:1141–1148
12. Juras V, Bittsansky M, Majdisova Z, Szomolanyi P, Sulzbacher I, Gäbler S et al (2008) In vitro determination of biomechanical properties of human articular cartilage in osteoarthritis using multi-parametric MRI. J Magn Reson. doi:10.1016/j.jmr.2008.11.019
13. Trattnig S, Mamisch TC, Pinker K, Domayer S, Szomolanyi P, Marlovits S et al (2008) Differentiating normal hyaline cartilage from post-surgical repair tissue using fast gradient echo imaging in delayed gadolinium-enhanced MRI (dGEMRIC) at 3 Tesla. Eur Radiol 18:1251–1259
14. Burstein D, Velyvis J, Scott KT, Stock KW, Kim YJ, Jaramillo D et al (2001) Protocol issues for delayed Gd (DTPA) (2-)-enhanced MRI: (dGEMRIC) for clinical evaluation of articular cartilage. Magn Reson Med 45:36–41
15. Nishii T, Kuroda K, Matsuoka Y, Sahara T, Yoshikawa H (2008) Change in knee cartilage T2 in response to mechanical loading. J Magn Reson Imaging 28:175–180
16. Rubenstein JD, Kim JK, Henkelman RM (2006) Effects of compression and recovery on bovine articular cartilage: appearance on MR images. Radiology 201:843–850
17. Grunder W, Kanowski M, Wagner M, Werner A (2000) Visualization of pressure distribution within loaded joint cartilage by application of angle-sensitive NMR microscopy. Magn Reson Med 43:884–891
18. Herberhold C, Faber S, Stammberger T, Steinlechner M, Putz R, Englmeier KH et al (1999) In situ measurement of articular cartilage deformation in intact femoropatellar joints under static loading. J Biomech 32:1287–1295
19. Chen CT, Fishbein KW, Torzilli PA, Hilger A, Spencer RG, Horton WE Jr (2003) Matrix fixed-charge density as determined by magnetic resonance microscopy of bioreactor-derived hyaline cartilage correlates with biochemical and biomechanical properties. Arthritis Rheum 48:1047–1056
20. Owman H, Tiderius CJ, Neuman P, Nyquist F, Dahlberg LE (2008) Association between findings on delayed gadolinium-enhanced magnetic resonance imaging of cartilage and future knee osteoarthritis. Arthritis Rheum 58:1727–1730
21. Liess C, Lüsse S, Karger N, Heller M, Glüer CC (2002) Detection of changes in cartilage water content using MRI T2-mapping in vivo. Osteoarthr Cartil 10:907–913
22. Chen MI, Branch TP, Hutton WC (1996) Is it important to secure the horns during lateral meniscal transplantation? A cadaveric study. Arthroscopy 12:174–181
23. Kurkijärvi JE, Nissi MJ, Rieppo J, Töyräs J, Kiviranta I, Nieminen MT et al (2008) The zonal architecture of human articular cartilage described by T2 relaxation time in the presence of Gd-DTPA2-. Magn Reson Imaging 26:602–607
24. Roos EM, Dahlberg L (2005) Positive effects of moderate exercise on glycosaminoglycan content in knee cartilage: a four-month, randomized, controlled trial in patients at risk of osteoarthritis. Arthritis Rheum 52:3507–3514
25. Tiderius CJ, Svensson J, Leander P, Ola T, Dahlberg L (2004) dGEMRIC (delayed gadolinium-enhanced MRI of cartilage) indicates adaptive capacity of human knee cartilage. Magn Reson Med 51:286–290