Osteoarthritis and Cartilage (2002) **10,** 907–913

1063–4584/02/$35.00/0
doi:10.1053/joca.2002.0847, available online at http://www.idealibrary.com on IDEAL®

Osteoarthritis and Cartilage

ICRS International Cartilage Repair Society

OARSI OSTEOARTHRITIS RESEARCH SOCIETY INTERNATIONAL

Detection of changes in cartilage water content using MRI T_2-mapping *in vivo*

C. Liess*, S. Lüsse†, N. Karger‡, M. Heller* and C.-C. Glüer*
**Department of Diagnostic Radiology, Medical Physics, Christian-Albrechts University Kiel, Michaelisstr. 9, D-24105 Kiel, Germany; †Technologiestiftung Schleswig-Holstein, Lorentzendamm 21, D-24103 Kiel, Germany; ‡ABX Advanced Biochemical Compounds, Biomedizinische Forschungsreagenzien GmbH, Schillerstr. 23, D-01326 Dresden, Germany*

Summary

Objectives: Osteoarthritis (OA) is the most prevalent chronic disease in the elderly, and it is generally diagnosed at an advanced state when treatment is difficult if not impossible. The early form of OA is characterized by an elevated water content in the cartilage tissue. The purpose of this study was to verify *in vivo* if changes in the water content of patellar cartilage typically occurring in early OA can be detected using T_2 mapping MRI methods.

Design: Twenty healthy volunteers performed 60 knee bends in order to compress their patellar cartilage thereby reducing its water content. MR images of the patellar cartilage were acquired immediately following exercise and after 45 min of rest. Patellar cartilage thickness and T_2 maps were determined and their difference between the time points evaluated.

Results: Cartilage thickness increased by 5.4±1.5% from 2.94±0.15 mm to 3.10±0.15 mm ($P<0.001$) following 45 min of rest, while T_2 increased by 2.6±1.0% from 23.1±0.5 ms to 23.7±0.6 ms ($P<0.05$).

Conclusion: Small, physiologic changes in the water content of patellar cartilage and the concomitant change in proteoglycan and collagen density following exercise can be detected using MRI. The proposed T_2-mapping method, together with other non-invasive MR cartilage imaging techniques, could aid in the early diagnosis of OA. © 2002 OsteoArthritis Research Society International. Published by Elsevier Science Ltd. All rights reserved.

Key words: Early osteoarthritis, Water content, MRI, T_2-mapping.

Abbreviations: dGEMRIC, Delayed Gadolinium Enhanced Magnetic Resonance Imaging of Cartilage; FLASH, Fast Low Angle Shot; IDL, Interactive Data Language; MR, Magnetic Resonance; MRI, Magnetic Resonance Imaging; OA, Osteoarthritis; PG, Proteoglycan; RARE, Rapid Acquisition with Relaxation Enhancement; ROI, Region of Interest; SC_1, Initial percentage solid content of cartilage; SEM, Standard Error of the Mean; SNR, Signal to Noise Ratio; $V_{1,2}$, Cartilage volume pre- and post-exercise; ΔWC, Percentage reduction of cartilage water content following exercise.

Introduction

Osteoarthritis (OA) is the most prevalent chronic disease in the elderly[1,2] and is characterized by progressive degeneration and eventual loss of cartilage tissue. Despite its high incidence OA is still poorly understood (e.g. see[3,4]), which may be attributed to the fact that it is generally detected at an advanced stage. As OA is a debilitating disease with a negative prognosis and a high socio-economic impact, it is crucial to develop techniques for its early detection.

Before structural changes manifest, the cartilage tissue is subjected to biochemical alterations, including a loss of proteoglycans (PG) and a concomitant increase in water content (e.g. see[5,6] in recent reviews). These early changes cannot be detected using 'classical' methods such as radiography, the use of biochemical markers or arthroscopy. Only magnetic resonance imaging (MRI) has been shown to do so, with the PG content being determined non-invasively using contrast agent-based T_1-weighted imaging[7], and the water content by using proton density[8,9] or T_2-weighted imaging[10,11]. For the early detection of OA using MR methods, the water content may be the parameter of choice, as it requires neither a lengthy study time nor the administration of contrast agents.

Previous studies have shown that the water content in OA affected cartilage may increase by around 10%[12,13]. The water content may be determined directly using proton density weighted imaging[8,9], but this method is not very sensitive to the small water content changes observed in the early stages of OA. Instead the T_2 time was recently demonstrated to be very sensitive to the water content in cadaveric knee cartilage specimen[11,14]. However, it is not clear if T_2 might also be related to the water content *in vivo*, and if this method would be sensitive enough to detect small changes in knee cartilage water content typically occurring in early OA.

It was therefore the aim of this work to investigate if small, physiologic changes in the water content of human patellar cartilage can be detected *in vivo* by monitoring cartilage T_2 in a standard clinical 1.5T system. The change

---

Received 6 November 2001; accepted 29 July 2002.
Address correspondence to: Dr C. Leiss, Department of Diagnostic Radiology, Medical Physics, Christian-Albrechts University Kiel, Michaelisstr. 9, D-24105 Kiel, Germany. Tel.: +49-431-597-3156; Fax: +49-431-597-3127; E-mail: carsten@rad.uni-kiel.de

in water content can be induced by knee bends compressing the patellar cartilage thus decreasing its thickness and forcing a small amount of water out of the cartilage[15–17]. Mechanical deformation of cartilage has been investigated using MR by several authors to study material properties of cartilage[18–21]. Such stress leads to a reduced water content which is accompanied by an increase in the PG and collagen density and together these factors cause a decrease in T_2. This may then be monitored by generating T_2 maps of the patellar cartilage[22–27].

HYPOTHESIS

During the relaxation phase after the knee bends the compression effect is reversed; both the mean thickness and T_2 of the patellar cartilage are likely to increase because water is reabsorbed back into the cartilage, causing the proteoglycan and collagen density to decrease. Thus, while PG and collagen contents remain constant, the water content will increase in time to its level prior to exercise. Using literature data, both the expected thickness and T_2 increase may be estimated. According to Eckstein and colleagues a 3% increase in thickness would be expected after 45 min of rest following knee bends[17]. In a different study, Lüsse and co-workers measured T_2 as a function of water content in cadaveric tibial and femoral cartilage[14]; according to their data, the average water content would be expected to change by 1.3% from 69.5 wt.% immediately following the knee bends to 70.4 wt.% after 45 min of rest (see appendix). This would correspond to a T_2 increase of 1.5 ms.

OA patients show water content increases by around 10%[12,13]. Hence should the proposed method show a significant change in T_2 following knee bends, then it would be sensitive enough to detect changes associated with degenerating cartilage typically occurring in OA patients.

Methods

SUBJECTS AND STUDY DESIGN

Twenty asymptomatic volunteers (four female, 16 male, 28±6 years) took part in the study. After approval by the local ethics committee, informed consent was obtained from all participants. Volunteers were positioned supine in a 1.5T Siemens Magnetom Vision scanner (Siemens Medizintechnik, Erlangen, Germany), with an 8 cm surface coil over their right knee to image the patellar cartilage. The right leg was immobilized at thigh, knee and foot level using cushions and straps. Scout FLASH images were acquired and the T_2 scan (see below) was planned. Volunteers were then asked to perform 60 knee bends outside the magnet, after which they were scanned without further delay using the previously planned T_2 scan. The exercise was supervised to ensure identical conditions among subjects, with 3 s for each knee bend and a constant 90° flexion. Knee bends and repositioning took about 5 min after which MR data for thickness and T_2 determination of patellar cartilage were acquired and again after 45 min of rest in the magnet.

MR MEASUREMENTS

After repositioning in the magnet, the thickness and the T_2 of patellar cartilage was measured using a fat-saturated multislice multi-spin–echo pulse sequence with a TR of 3500 ms and 8 TE values (13, 33, 53, 75, 100, 150, 200 and 300 ms). One of the rationales behind choosing a spin–echo rather than a gradient echo pulse sequence (as done by other authors for cartilage thickness measurements, e.g. see[28,29]), was to be able to acquire T_2 maps and thickness information at the same time. Ten contiguous 2 mm axial slices of the knee were acquired. The field-of-view was set to 40×80 mm and the matrix 128×256, yielding a resolution of 313 μm per pixel. With the given timing parameters, a set of 10 slices took 7.5 min to acquire.

As a test for the reproducibility of this method, three of the volunteers were measured again three months after their first session using the same protocol as outlined above. The reproducibility of the individual T_2 and thickness measurement was calculated the RMS average coefficient of variation, %CV.

DATA PROCESSING

T_2 maps of the patellar cartilage in each of the 10 slices were generated using a mono-exponential fitting routine written in IDL (Research Systems, Boulder, CO, U.S.A.). To avoid fitting noise, pixels having intensity values below a global threshold in the TE=13 ms image, and those for which the fit failed, were assigned a T_2 value of zero. Generally, the proportion of cartilage pixels for which the fit failed was below 1%. Following generation of the maps, the mean T_2 over all patellar cartilage voxels was determined.

The mean cartilage thickness from the bone–cartilage interface to the cartilage–joint space surface was determined as described before[30]. Briefly, an ROI of the patellar cartilage was defined by hand; here the hypointense region at the cartilage bone interface (see Fig. 1) was assumed to be bone in all subjects. After a binary image of the cartilage was created, the bone–cartilage interface and the cartilage–joint space surface were fitted to a fourth-order polynomial, and lines perpendicular to these functions were generated to measure the distance across the cartilage. The mean cartilage thickness was then calculated by averaging over all distances.

Finally, the T_2 and thickness changes of the patellar cartilage between the first (t~8 min) and the last measurement (t~53 min) were calculated; these parameters were tested for differences from zero using Student's t-test with significance assumed for $P<0.05$. Cartilage thickness and T_2 values are presented as mean±S.E.M. if not stated otherwise.

Results

Following data acquisition no visible movement artefacts were seen on the images. Figure 1 shows typical images of a patella immediately following exercise at t=8 min (a) and after 45 min of rest (b). No obvious thickness change could be detected by eye in these images. Generally the patellar cartilage could be separated from the femoral cartilage although defining the interface between the two was occasionally difficult.

Figure 2 shows the change in cartilage thickness for each individual, with the dashed lines indicating a reduction and the solid lines an increase after 45 min of rest. The majority of volunteers showed an increase in cartilage thickness; the mean thickness increase over all volunteers

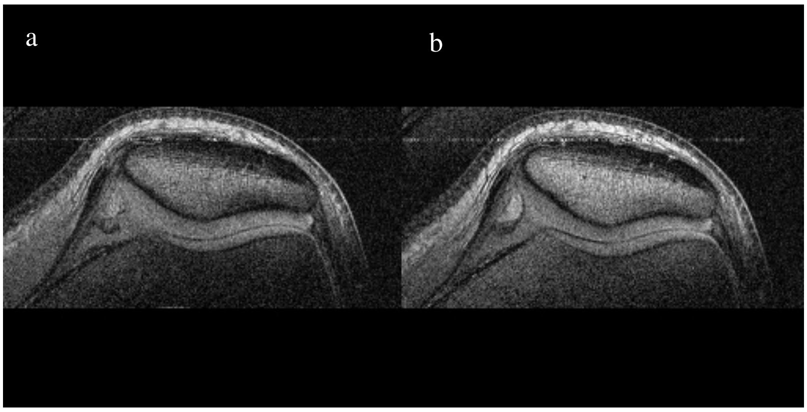

Fig. 1. Typical axial images of a healthy knee showing the patellar and tibial cartilage areas following exercise (a) and after 45 min of rest (b). A change in the patellar thickness is difficult to be seen by eye, but becomes apparent when applying image and statistical analysis (see Fig. 2).

was 5.4±1.5% (0.16±0.04 mm) from 2.94±0.15 mm to 3.10±0.15 mm [Fig. 2(b), $P<0.001$].

Following exercise, the average cartilage T_2 value increased in 13 of the 20 subjects [Fig. 3(a)], although to a somewhat less obvious degree than the cartilage thickness; the mean T_2 increase over all volunteers was 2.6±1.0% (0.6±0.2 ms) from 23.1±0.5 ms to 23.7±0.6 ms after 45 min of rest [Fig. 3(b), $P<0.05$]. There was a correlation between the change in cartilage T_2 and cartilage thickness, with $r=0.57$ ($P<0.01$).

The reproducibility measurements of cartilage thickness revealed that the coefficient of variation (%CV) in individuals ranged from 3.9% to 11.6%, with an average %CV of 7.7%. The %CV in the T_2 measurements ranged from 0.3% to 2.2% in individuals, with an average %CV of 1.7%.

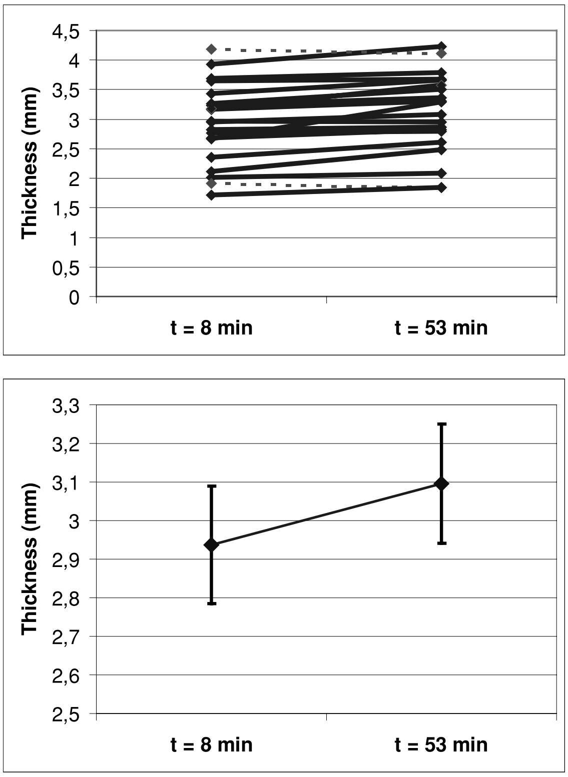

Fig. 2. (a) Graph showing the change of the mean cartilage thickness following knee bends (t=8 min) to after 45 min of rest (t=53 min) for each subject. Solid lines indicate increases, dashed ones decreases in cartilage thickness. (b) The mean overall change showed an increase from 2.94±0.15 mm to 3.10±0.15 mm ($P<0.001$). Note the different scales in (a) and (b).

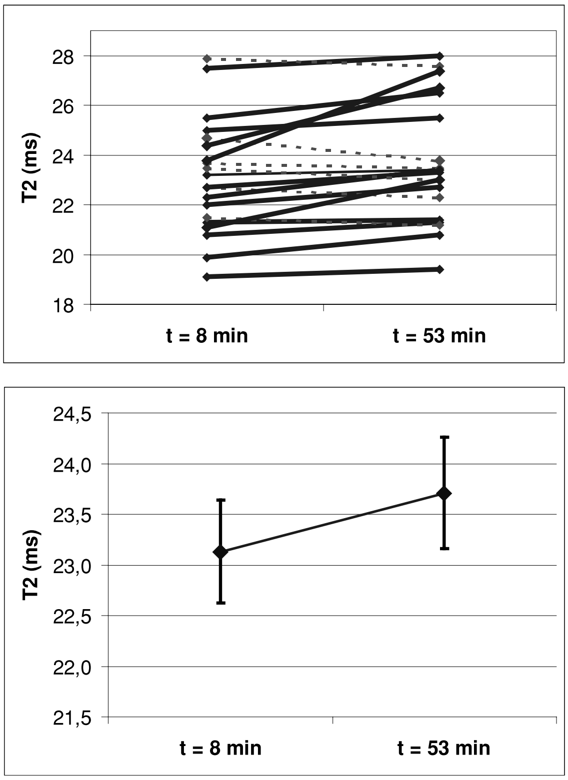

Fig. 3. (a) Graph showing the change of the mean cartilage T_2 just after exercise and after 45 min of rest in each subject. Increasing T_2 values are represented by solid lines, decreasing ones by dashed lines. The majority of volunteers showed an increase of the mean T_2 value. (b) The overall increase of 0.58±0.24 ms in patellar cartilage T_2 of all volunteers was significant ($P<0.05$). Note the different scales in (a) and (b).

Discussion

The correlation of water content and T_2 has been known for some time[14] but, to the best of our knowledge, this is the first *in vivo* study based on that relation. Following 45 min of rest, the mean cartilage thickness increased by 5.4% while the mean T_2 increased by 2.6%. Thus the thickness increase was twice that measured by Eckstein and colleagues[17], while the T_2 increased about one-third compared with the expected value based on Lüsse's *in vitro* study[11].

CARTILAGE THICKNESS

The current picture of water movement from cartilage tissue is based on a biphasic model, which assumes that cartilage consists of a fluid (and hence displaceable) phase and a solid phase[31,32]. Physiological loading such as knee bends leaves the *contents* of the solid phase unaffected, but causes an increase in its density through the concomitant displacement of cartilage water. This water leaks out into the joint space and, upon relaxation, will be re-absorbed back into the cartilage matrix because of the negative hydrostatic pressure. The re-absorption is a slow process, such that recovery from exercise will require extensive periods of rest. For instance, in the study by Eckstein and co-workers a volume change of the order of 6% following 50 knee bends took about 90 min to recover[17].

In our work we observed twice that recovery rate. A number of reasons may have contributed to this effect. First, the rate of cartilage recovery is known to correlate closely with the level of deformation caused by mechanical stress. Hence the fast recovery rate obtained in our study implies a higher degree of cartilage deformation, perhaps caused by more strenuous knee bends compared to those in Eckstein's study. Second, it is also known that there are considerable interindividual variations in the degree of cartilage compression[16,20], which is supported by the range of recovery rates depicted in Fig. 2. Therefore a larger number of volunteers is necessary to obtain more solid data. Third, the rate of cartilage thickness recovery was assumed to be linear over 90 min, i.e. recovery would be half completed after 45 min. However, it is conceivable that the thickness increase following knee bends might be described by an exponential function, such that the degree of recovery after 45 min of rest in our study would be higher compared to a linear recovery. Furthermore, not only are there considerable differences in cartilage morphology among subjects[6], but there may be different recovery functions, too. Finally it is possible that the measured thickness changes are larger in our study because only the central part of the joint surface was considered where most of the changes are bound to occur.

The reproducibility error of the cartilage thickness measurement was 7.7% such that changes in cartilage thickness could be detected in the group of volunteers (with $P<0.001$, as indicated above), but not in the individual volunteer. The %CV in the T_2 measurement was smaller than the standard deviation of the T_2 change of the volunteers. Hence the accuracy of the T_2 change measurement should be sufficient to monitor water content changes of the cartilage after 45 min of rest.

CARTILAGE T_2 CHANGES

Based on the data of Lüsse and co-workers, the inverse water content is a linear function of $1/T_2$ with an intercept of 1.2 and a slope of $4.4*10^{-3}$ s; thus an average water content of 71.3 wt.% corresponds to a T_2 of 21.7 ms. Taking these numbers as a reference and assuming a linear recovery rate, the water content would have been 69.5 wt.% immediately after the knee bends, and 70.4 wt.% following 45 min of rest. This corresponds to changes in T_2 from 18.4 ms to 20.0 ms, about three times what was measured in this study. A number of factors might be responsible to this difference; Lüsse's study was carried out on *in vitro* tibial and femoral cartilage, whereas our work focused on patellar cartilage. It is known that there are differences in structure and composition of various types of cartilage, and these are also present upon compression (see e.g.[20,33]). In addition, Lüsse and co-workers found the average water content to vary from 61.5 wt.% to 78.9wt.% and the slope from $3*10^{-3}$ s to $5*10^{-3}$ s, depending on the type of cartilage[11], thus yielding a large range of T_2 values. Hence a direct comparison of our data to those acquired by Lüsse should not be made, and it should be stressed that the predicted T_2 changes from Lüsse's data can only serve as a landmark. Consequently, although desirable in the clinical environment, the determination of the absolute water content from the T_2 relaxation time would have been prone to error and was not attempted.

POSSIBLE ERROR SOURCES

There are three types of errors that could have an effect on the accuracy of the thickness and T_2 measurements; these may be subdivided into subject-based differences, assumptions about water uptake and release from the patellar cartilage, and MR-related limitations.

The first of these points provides the highest potential for the spread of thickness and T_2 data among subjects. Anatomical variations, differences in motor strategies and neuromuscular control patterns among subjects may have led to various degrees of patellar cartilage compression. Volunteers were young with no history of knee problems, and their cartilage was assumed to be 'healthy'; however, it is possible that undetected microscopic alterations existed (for instance caused by injury or early OA). The volunteers were mainly students and had a similar daily movement regime, but it cannot be excluded that some subject their patellar cartilage to larger forces during the day than others. Moreover, subject stature as expressed by body mass index (although not measured) differed substantially. The MR measurements were always carried out at the same time of day such that diurnal variation[34] should not contribute to the spread of data.

Second, for the estimation of the expected T_2 changes during the rest period, it was assumed that the re-uptake of water into the patellar cartilage can be described by a linear function, as may be inferred from Eckstein and co-workers[16]. If this was not so, e.g. if an exponential recovery function was assumed, the expected T_2 change would be different. Another point to consider is the water movement from the patellar cartilage. It was assumed that the displaced water leaks out into the joint space. It could also be possible that cartilage water is only displaced internally to areas that were not subjected to large compression forces. Immediately after the knee bends this would lead to a focal T_2 and thickness increase in areas that are not subjected to large forces. Unfortunately, due to the limitations of the MR system (see below), we were unable to detect such focal increases in the t=8 min measurement. With better hardware one may attempt to monitor only those parts of the cartilage in which to expect the largest changes in thickness (and T_2). This would allow a rough estimate as to how water is displaced in patellar cartilage upon compression. Furthermore, it should be noted that knee bends not only cause a change in cartilage water content but also an increase in collagen and proteoglycan density. This change will also contribute to a decrease in T_2 upon compression. Finally, an obvious extension of the study protocol would be to acquire baseline T_2 maps and cartilage thickness data. We have implemented that aspect in our future studies.

Third, the quality of the acquired data depends strongly on the MR hardware. In this *in vivo* study an acceptable compromise between resolution (313 μm) and signal-to-noise ratio (5:1 in cartilage for the TE=13 ms image) was chosen. The patellar cartilage was covered by between 6 and 12 pixels, depending on the cartilage thickness; therefore partial volume effects occur predominantly in thinner cartilage layers. It is anticipated that the SNR and/or the resolution may be improved using stronger gradients and/or faster, e.g. RARE based, pulse sequences. Such sequences have been used before for the detection of cartilage lesions[35–37], and are known to deliver an increased accuracy for T_2 values compared to multi-echo spin echo sequences[38]. The latter are sensitive to RF pulse imperfections, resulting in an estimated T_2 error of around 10% in this application[11].

We used a spin echo rather than a gradient echo based sequence in order to determine both thickness and T_2 at the same time. Gradient echo sequences have been used and validated for cartilage thickness measurements by other authors (see e.g.[28,29,39]). However, although the spin echo sequence has not been precisely matched to *ex vivo* anatomic sections of cartilage, it is nevertheless a valid approach, particularly in view of the refocusing effects of the spin echo. We acknowledge that a proper validation of the sequence would be desirable, and that acquiring an additional fat-suppressed gradient echo sequence would improve our protocol.

It is also known that T_2 strongly depends on the angle between the main magnetic field and the cartilage layer[40,41]. Although the volunteers were identically positioned in the magnet, differences in cartilage orientation may still have been present, thus having an impact on T_2. In addition, the orientation of the collagen may change during the relaxation phase, which could also influence T_2.

OUTLOOK

We are currently accumulating more data to establish mean T_2 values of patellar cartilage in a set of volunteers, which is to be compared to patients suffering from various degrees of OA. In such patients, considerable mechanical degradation of cartilage tissue will result in water content changes substantially larger than the small change induced by knee bends in our study; for instance Mankin and co-workers found a 9% increase in water content in human arthritic femoral cartilage[13], while a 13% increase was detected in a canine model of OA[12].

Even if this T_2-mapping method might initially not be diagnostic in the individual patient, it would, together with other non-invasive MR techniques such as dGEMRIC[7,42] and magnetization transfer methods[43,44], aid in the early diagnosis of OA. More importantly, using T_2 maps as an early indicator of OA would also potentially allow monitoring the effects of treatment strategies in patients.

Conclusion

We have demonstrated that the re-uptake of water into, and the concomitant decrease in proteoglycan and collagen density in, the patellar cartilage following knee bends lead to a thickness increase and T_2 increase. The recovery rates of the thickness and T_2 relaxation times after knee bends varied considerably among volunteers and so may the actual recovery function. Furthermore, it seems that for the observed change in cartilage thickness after recovery, the T_2 change obtained was smaller than expected. Comparing our data to previous *in vitro* work in the literature, this implies a reduced *in vivo* sensitivity of T_2 to the cartilage water content. Nevertheless, our data indicate that, in future experiments, water content changes in OA may be detected using the proposed method.

References

1. Peyron JG. Osteoarthritis. The epidemiologic viewpoint. Clin Orthop 1986;213:13–9.
2. Felson DT, Zhang Y, Hannan MT, Naimark A, Weissman BN, Aliabadi P, *et al*. The incidence and natural history of knee osteoarthritis in the elderly. The Framingham Osteoarthritis Study. Arthritis Rheum 1995;38(10):1500–5.
3. Cicuttini FM, Spector TD. What is the evidence that osteoarthritis is genetically determined? Baillieres Clin Rheumatol 1997;11(4):657–69.
4. Radin EL, Burr DB, Caterson B, Fyhrie D, Brown TD, Boyd RD. Mechanical determinants of osteoarthrosis. Semin Arthritis Rheum 1991;21(3 Suppl 2):12–21.
5. Aigner T, McKenna L. Molecular pathology and pathobiology of osteoarthritic cartilage. Cell Mol Life Sci 2002;59(1):5–18.
6. Eckstein F, Reiser M, Englmeier KH, Putz R. In vivo morphometry and functional analysis of human articular cartilage with quantitative magnetic resonance imaging—from image to data, from data to theory. Anat Embryol (Berl) 2001;203(3):147–73.
7. Bashir A, Gray ML, Boutin RD, Burstein D. Glycosaminoglycan in articular cartilage: in vivo assessment with delayed Gd(DTPA)(2-)-enhanced MR imaging. Radiology 1997;205(2):551–8.
8. Hohe J, Faber S, Stammberger T, Reiser M, Englmeier KH, Eckstein F. A technique for 3D in vivo quantification of proton density and magnetization transfer coefficients of knee joint cartilage. Osteoarthritis Cart 2000;8(6):426–33.
9. Shapiro EM, Borthakur A, Kaufman JH, Leigh JS, Reddy R. Water distribution patterns inside bovine articular cartilage as visualized by 1H magnetic resonance imaging. Osteoarthritis Cart 2001;9(6):533–8.
10. Recht MP, Resnick D. Magnetic resonance imaging of articular cartilage: an overview. Top Magn Reson Imaging 1998;9(6):328–36.
11. Lüsse S, Claassen H, Gehrke T, Hassenpflug J, Schunke M, Heller M, *et al*. Evaluation of water content by spatially resolved transverse relaxation

times of human articular cartilage. Magn Reson Imaging 2000;18(4):423–30.

12. Guilak F, Ratcliffe A, Lane N, Rosenwasser MP, Mow VC. Mechanical and biochemical changes in the superficial zone of articular cartilage in canine experimental osteoarthritis. J Orthop Res 1994;12(4): 474–84.
13. Mankin HJ, Thrasher AZ. Water content and binding in normal and osteoarthritic human cartilage. J Bone Joint Surg Am 1975;57(1):76–80.
14. Lüsse S, Knauss R, Werner A, Grunder W, Arnold K. Action of compression and cations on the proton and deuterium relaxation in cartilage. Magn Reson Med 1995;33(4):483–9.
15. Eckstein F, Lemberger B, Stammberger T, Englmeier KH, Reiser M. Patellar cartilage deformation in vivo after static versus dynamic loading. J Biomech 2000;33(7):819–25.
16. Eckstein F, Tieschky M, Faber S, Englmeier KH, Reiser M. Functional analysis of articular cartilage deformation, recovery, and fluid flow following dynamic exercise in vivo. Anat Embryol (Berl) 1999;200(4): 419–24.
17. Eckstein F, Tieschky M, Faber SC, Haubner M, Kolem H, Englmeier KH, *et al*. Effect of physical exercise on cartilage volume and thickness in vivo: MR imaging study. Radiology 1998;207(1):243–8.
18. Rubenstein JD, Kim JK, Henkelman RM. Effects of compression and recovery on bovine articular cartilage: appearance on MR images. Radiology 1996; 201(3):843–50.
19. Grunder W, Kanowski M, Wagner M, Werner A. Visualization of pressure distribution within loaded joint cartilage by application of angle-sensitive NMR microscopy. Magn Reson Med 2000;43(6):884–91.
20. Herberhold C, Faber S, Stammberger T, Steinlechner M, Putz R, Englmeier KH, *et al*. In situ measurement of articular cartilage deformation in intact femoropatellar joints under static loading. J Biomech 1999; 32(12):1287–95.
21. Kaufman JH, Regatte RR, Bolinger L, Kneeland JB, Reddy R, Leigh JS. A novel approach to observing articular cartilage deformation in vitro via magnetic resonance imaging. J Magn Reson Imaging 1999; 9(5):653–62.
22. Dardzinski BJ, Mosher TJ, Li S, Van Slyke MA, Smith MB. Spatial variation of T2 in human articular cartilage. Radiology 1997;205(2):546–50.
23. Frank LR, Wong EC, Luh WM, Ahn JM, Resnick D. Articular cartilage in the knee: mapping of the physiologic parameters at MR imaging with a local gradient coil—preliminary results. Radiology 1999; 210(1):241–6.
24. Nieminen MT, Rieppo J, Toyras J, Hakumaki JM, Silvennoinen J, Hyttinen MM, *et al*. T2 relaxation reveals spatial collagen architecture in articular cartilage: a comparative quantitative MRI and polarized light microscopic study. Magn Reson Med 2001; 46(3):487–93.
25. Mosher TJ, Smith H, Dardzinski BJ, Schmithorst VJ, Smith MB. MR imaging and T2 mapping of femoral cartilage: in vivo determination of the magic angle effect. AJR Am J Roentgenol 2001;177(3):665–9.
26. Smith HE, Mosher TJ, Dardzinski BJ, Collins BG, Collins CM, Yang QX, *et al*. Spatial variation in cartilage T2 of the knee. J Magn Reson Imaging 2001;14(1):50–5.
27. Xia Y, Farquhar T, Burton-Wurster N, Ray E, Jelinski LW. Diffusion and relaxation mapping of cartilage-bone plugs and excised disks using microscopic magnetic resonance imaging. Magn Reson Med 1994;31(3):273–82.
28. Eckstein F, Sittek H, Milz S, Schulte E, Kiefer B, Reiser M, *et al*. The potential of magnetic resonance imaging (MRI) for quantifying articular cartilage thickness—a methodological study. Clin Biomech (Bristol, Avon) 1995;10(8):434–40.
29. Burgkart R, Glaser C, Hyhlik-Durr A, Englmeier KH, Reiser M, Eckstein F. Magnetic resonance imaging-based assessment of cartilage loss in severe osteoarthritis: accuracy, precision, and diagnostic value. Arthritis Rheum 2001;44(9):2072–7.
30. Lüsse S, Karger N, Heller M, Glüer CC. Spatially resolved relaxation times T2 of human articular cartilage—an in vitro and in vivo MRI study. Z Med Phys 2000;10:34–42.
31. Mow VC. Biphasic rheological properties of cartilage [proceedings]. Bull Hosp Joint Dis 1977;38(2): 121–4.
32. Mow VC, Kuei SC, Lai WM, Armstrong CG. Biphasic creep and stress relaxation of articular cartilage in compression? Theory and experiments. J Biomech Eng 1980;102(1):73–84.
33. Froimson MI, Ratcliffe A, Gardner TR, Mow VC. Differences in patellofemoral joint cartilage material properties and their significance to the etiology of cartilage surface fibrillation. Osteoarthritis Cart 1997;5(6):377–86.
34. Waterton JC, Solloway S, Foster JE, Keen MC, Gandy S, Middleton BJ, *et al*. Diurnal variation in the femoral articular cartilage of the knee in young adult humans. Magn Reson Med 2000;43(1):126–32.
35. Bredella MA, Tirman PF, Peterfy CG, Zarlingo M, Feller JF, Bost FW, *et al*. Accuracy of T2-weighted fast spin-echo MR imaging with fat saturation in detecting cartilage defects in the knee: comparison with arthroscopy in 130 patients. AJR Am J Roentgenol 1999;172(4):1073–80.
36. Uhl M, Allmann KH, Ihling C, Hauer MP, Conca W, Langer M. Cartilage destruction in small joints by rheumatoid arthritis: assessment of fat-suppressed three-dimensional gradient-echo MR pulse sequences in vitro. Skeletal Radiol 1998;27(12): 677–82.
37. White LM, Schweitzer ME, Johnson WJ, Amster BJ, Oliveri MP, Russell K. The role of T2-weighted fast-spin-echo imaging in the diagnosis of meniscal tears. J Magn Reson Imaging 1996;6(6):874–7.
38. Liney GP, Knowles AJ, Manton DJ, Turnbull LW, Blackband SJ, Horsman A. Comparison of conventional single echo and multi-echo sequences with a fast spin-echo sequence for quantitative T2 mapping: application to the prostate. J Magn Reson Imaging 1996;6(4):603–7.
39. Glaser C, Faber S, Eckstein F, Fischer H, Springer V, Heudorfer L, *et al*. Optimization and validation of a rapid high-resolution T1-w 3D FLASH water excitation MRI sequence for the quantitative assessment of articular cartilage volume and thickness. Magn Reson Imaging 2001;19(2):177–85.
40. Rubenstein JD, Kim JK, Morova-Protzner I, Stanchev PL, Henkelman RM. Effects of collagen orientation on MR imaging characteristics of bovine articular cartilage. Radiology 1993;188(1):219–26.

41. Xia Y, Farquhar T, Burton-Wurster N, Lust G. Origin of cartilage laminae in MRI. J Magn Reson Imaging 1997;7(5):887–94.
42. Bashir A, Gray ML, Burstein D. Gd-DTPA2- as a measure of cartilage degradation. Magn Reson Med 1996;36(5):665–73.
43. Vahlensieck M, Dombrowski F, Leutner C, Wagner U, Reiser M. Magnetization transfer contrast (MTC) and MTC-subtraction: enhancement of cartilage lesions and intracartilaginous degeneration in vitro. Skeletal Radiol 1994;23(7):535–9.
44. Wolff SD, Chesnick S, Frank JA, Lim KO, Balaban RS. Magnetization transfer contrast: MR imaging of the knee. Radiology 1991;179(3):623–8.

Appendix

The calculation of the percentage reduction of water content in patellar cartilage following exercise assumes that the reduction in volume is solely due to loss of cartilage water, with the volume of the cartilage matrix being constant. Thus the percentage reduction of cartilage water, ΔWC, is given by

$$\Delta WC = SC_1 \frac{V_1 - V_2}{V_2} \qquad \text{(A1)}$$

where SC_1 is the initial percentage solid content and $V_{1,2}$ the cartilage volume pre and post exercise. As a typical example, suppose a 6% reduction in cartilage volume from V_1=4500 mm^3 to V_2=4230 mm^3 at an initial water content of 71.3 wt.% (i.e. SC_1=28.7%). According to eqn (A1), this results in a water content reduction of 1.8 wt.% to 69.5 wt.%.