In Vivo Reproducibility of Three-Dimensional Cartilage Volume and Thickness Measurements with MR Imaging

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OBJECTIVE. Previous studies suggest that MR imaging is capable of providing accurate data on knee joint cartilage volume and thickness in vitro, but the reproducibility of these data in living subjects has not been analyzed rigorously. Our aim was therefore to determine the in vivo reproducibility of volume and thickness measurements from replicated data sets, applying three-dimensional (3D) postprocessing methods.

SUBJECTS AND METHODS. Eight healthy volunteers were imaged six times at a resolution of $2 \times 0.31 \times 0.31$ mm with a fat-suppressed fast low-angle shot 3D sequence, the knee being repositioned in between replicated examinations. Three-dimensional reconstructions of the articular cartilage surfaces were obtained from sagittal data sets, and the cartilage volumes were calculated. The thickness distribution was analyzed throughout the joint surfaces independent of the section orientation, using a previously validated 3D minimal-distance algorithm.

RESULTS. In the volunteers, the coefficient of variation for replicated volume measurements ranged from 1.3% (patella) to 3.4% (lateral tibia), and the standard deviation of the individual cartilage volumes ranged from ±16% (lateral tibia) to ±22% (femur). The intraclass correlation coefficient ranged from .959 (lateral tibia) to .995 (patella). The interobserver evaluation was similar to the interscan reproducibility. The mean interscan deviation of the maximal cartilage thickness interval ranged from 0.1 to 0.3 cartilage thickness intervals (of 0.5 mm); only in rare cases did we record deviations greater than one thickness interval.

CONCLUSION. MR imaging can be used to determine cartilage volume and thickness in the knee joints of living subjects with high precision, provided that a fat-suppressed gradient-echo sequence with adequate resolution and 3D digital image processing are used.

Received July 7, 1997; accepted after revision August 27, 1997.

Some of the presented data have been acquired as part of the doctoral thesis (in preparation) of J. Westhoff of the Ludwig-Maximilians Universität München.

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AJR 1998;170:593–597

0361–803X/98/1703–593

The ability of articular cartilage to function effectively during joint movement and loading depends on the ultrastructural composition and integrity of the proteoglycan–collagen matrix and on the quantitative distribution of the tissue within the joint surfaces. Precise data on articular cartilage thickness are therefore required for the evaluation of both normal and abnormal joints, for the determination of cartilage material properties from arthroscopic indentation tests [1], and for the construction of computer models to assess preoperatively the effects of orthopedic interventions [2–4].

Previously, MR imaging has been used to noninvasively quantify cartilage volume [5–10], local cartilage thickness [8–9, 11–14], and the cartilage thickness distribution throughout entire joint surfaces [15–17]. Using various in vitro methods for validating these measurements, investigators have shown that accurate data on the quantitative distribution of the cartilage can be obtained with MR imaging if fat-suppressed gradient-echo sequences are selected [5, 6, 9, 10, 15–17]. In sectional images, however, the apparent cartilage thickness depends on its orientation relative to the imaging plane, the true thickness being overestimated by the cosecant of the angle between the images and the cartilage layer [18, 19]. Because identical section locations and orientations cannot be obtained in longitudinal studies, it is impossible to reliably quantify changes of cartilage thickness over time from serial images [5, 6, 15–19]. For these reasons, three-dimensional (3D) approaches have been developed and validated, which allow the articular cartilage thickness to be measured independent of the original section plane [18–21].

The objective of our study was to determine the in vivo reproducibility of cartilage volume and thickness measurements under clinically realistic imaging conditions, based on a previ-

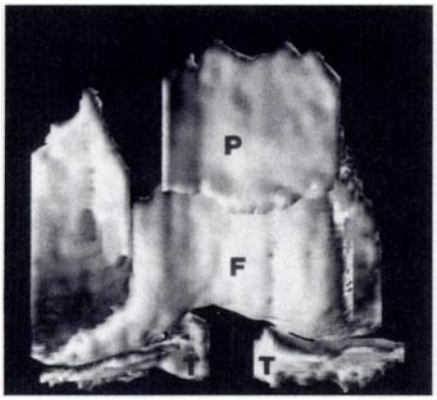

Fig. 1.—Anterior view of three-dimensional (3D) reconstruction of knee joint cartilage plates of 26-year-old healthy volunteer (P = patella , F = femur, T = tibia), obtained with optimized surface-reconstructing algorithm [22] after semiautomatic segmentation of MR images. The image data were acquired with a high-resolution fat-suppressed fast low-angle shot 3D sequence (60/11 [TR/TE]; flip angle, 30°; resolution, 2 × 0.31 × 0.31 mm).

ously validated fat-suppressed gradient-echo sequence [5, 6, 10, 15–17], 3D computer reconstruction, and digital image processing [19–21].

Subjects and Methods

Volunteers and Imaging Protocol

Eight volunteers who had no musculoskeletal disorders or internal derangements of the knee were examined (six men and two women, 23–50 years old). A 1.5-T magnet (Magnetom Vision; Siemens, Erlangen, Germany), a circularly polarized transmit–receive knee coil, and a previously validated high-resolution, fat-suppressed 3D gradient-echo fast low-angle shot sequence (60/11 [TR/TE]; flip angle, 30°; number of acquisitions, one; readout bandwidth, 65 Hz; imaging time, 20 min) were used [16, 17, 19–21]. Sagittal images were obtained at a partition thickness of 2 mm and an in-plane resolution of 0.31 × 0.31 mm (field of view, 160 mm; matrix, 512 × 512 pixels). Saturation pulses were used to reduce flow artifacts produced by the femoral and popliteal vessels. Six data sets of the right knee were obtained for each volunteer, and the volunteers were asked to move and reposition the joint in between replicated acquisitions. The studying protocol had been ratified by the local ethics committee, and informed consent had been obtained from the volunteers.

TABLE 1 Cartilage Volumes in Eight Volunteers on MR Imaging

Joint Surface	Mean (mm^3)	SD (mm^3)	CV%
Patella	3,512	711	20
Femur	13,851	3,042	22
Medial tibia	2,328	469	20
Lateral tibia	2,794	442	16

Note.—CV% = coefficient of variation in percent (SD / mean × 100).

Digital Image Processing

The digital data were converted to a workstation-compatible format and transferred to a symmetric multiprocessing computer with a high-performance graphic system (Onyx; Silicon Graphics, Mountain View, CA). Segmentation of the patellar, femoral, and tibial cartilage plates was performed semiautomatically section by section using a region-growing algorithm [19–21]. Areas of relatively low contrast between the cartilage and adjacent tissue (e.g., the joint contact zones and the marginal recesses, where the cartilage is in direct contact with synovial folds) were marked manually. We then placed in the center of the cartilage a seed pixel that was programmed to expand automatically into all directions until either a strong gradient of signal intensity or a manually traced border was reached. The performance of the algorithm was controlled visually in each section. An isotropic voxel size was then obtained by a trilinear interpolation routine, and each cartilage plate was reconstructed three-dimensionally with an optimized surface-constructing algorithm [22]. From these reconstructions (Fig. 1), the cartilage volumes were computed. To assess the intraobserver and interobserver reproducibility, one knee joint was analyzed at four different occasions by the same observer and by four different observers.

The distribution patterns of cartilage thickness were obtained by determining the minimal 3D distance of each surface voxel to the bone–cartilage interface in the 3D reconstructed cartilage plates using a previously validated algorithm [20, 21]. Finally, the thickness distribution was visualized using a texture-mapping technique by projecting color-coded thickness intervals of 0.5 mm onto the 3D reconstructed joint surfaces.

Statistical Analysis

The interscan reproducibility of the patellar, femoral, and tibial volume measurements was assessed by calculating the coefficient of variation in percent (CV% = SD / mean × 100) of the sixfold determination of each cartilage plate in the eight volunteers. Because the reliability of a method in a transverse study depends on the reproducibility of the method and on the variability of the parameter in the population, the methodologic variation was related to the biologic one by calculating the intraclass correlation coefficient on the basis of the analysis of variance [23, 24]. The intraclass correlation coefficient can be a potential maximum of 1.0 and relates the CV% of the repetitive measurements to the CV% of the mean values in the group. From the average interscan precision we also estimated the minimal number of individuals required for a reliable demonstration of 2% volume changes (95% confidence level) in the cartilage surfaces in a longitudinal study, applying a sample size calculation involving the *t* test (paired type, $\alpha = 0.01$, power = 95%).

The reproducibility of the cartilage thickness distribution was evaluated by identifying in each pattern the maximal cartilage interval in the patellar surface, in the femoral trochlea (facies patellaris femoris), in the medial femoral condyle, in the medial tibial plateau, in the lateral femoral condyle, and in the lateral tibial plateau. In each case, the maximal interval was numbered (0–0.5 mm = 1, 0.5–1.0 mm = 2, 1.0–1.5 mm = 3..., 5.5–6.0 mm = 12, >6.0 mm = 13) and the means and SDs of the maximal cartilage intervals were calculated from the transformed values. Then, for each volunteer all six thickness plots were compared with one another (15 paired comparisons). The deviations were determined in terms of the differences of the maximal cartilage interval (0, ±1 interval, ±2 intervals, etc.), and the mean of these differences for each of the eight volunteers was calculated for all six joint regions.

Results

Cartilage Volume Measurements

The cartilage volumes in the patellae of the volunteers ranged from 2831 to 4795 mm^3, in the femur from 10,015 to 19,306 mm^3, in the medial tibial plateau from 1915 to 3343 mm^3, and in the lateral plateau from 2128 to 3458 mm^3. The mean, SD, and CV% are shown in Table 1 and Figure 2. The interscan reproducibility of the cartilage volume was on average 1.3% in the patella, 1.8% in the femur, 3.0% in the medial tibial plateau, and 3.4% in the lateral tibial plateau, the maximum being 2.7%, 4.7%, 5.1%, and 6.2%, respectively (Table 2 and Fig. 2). The intraclass correlation coefficient ranged from .959 in the lateral tibia to .995 in the patella (Table 2). An estimate of the cartilage volume differences that may be reliably detected when several individuals are included in a longitudinal study (paired study type) showed that a minimum of six individuals is required in the case of the patella, 10 in the femur, 28 in the medial tibia, and 33 in the lateral tibia to show a statistically significant difference of 2% of the cartilage volume. Fourfold semiautomatic analysis of the same data set by the same observer yielded a CV% of 1.6% for the patella, 1.6% for the femur, 3.7% for the medial tibial plateau, and 2.2% for the lateral tibial plateau; analysis by four different observers yielded a CV% of 1.8% for the patella, 2.6% for the femur, 1.1% for the medial tibial plateau, and 4.6% for the lateral tibial plateau.

Cartilage Thickness Measurements

The maximal cartilage thickness interval ranged from greater than 4 mm to greater than 6 mm in the patella, from greater than 2 mm to greater than 3.5 mm in the femoral trochlea, from greater than 2 mm to greater than 2.5 mm in the medial and lateral femoral condyles, from greater than 3 mm to greater than 4.5 mm in the medial tibial plateau, and from greater than 2.5 mm to greater

than 3.5 mm in the lateral plateau. The mean of the maximum was greater than 5 mm in the patella (SD = 1.5 intervals, CV% = 13%), greater than 2.5 mm in the femoral trochlea (SD = 1.1 intervals, CV% = 17%), greater than 2.0 mm in the medial femoral condyle (SD = 0.5 interval, CV% = 10%) and in the lateral condyle (SD = 0.5 interval, CV% = 9%), greater than 4.0 mm in the medial tibia (SD = 1.2 intervals, CV% = 13%), and greater than 3.0 mm in the lateral tibia (SD = 0.7 interval, CV% = 11%). Distribution patterns of cartilage thickness of one volunteer (as obtained from the six different data sets) are shown in Figure 3, the femur being taken as an example. With regard to the maximal thickness interval, only rarely were deviations of more than one interval observed in replicated measurements (Table 3). The evaluation of the mean deviation of the maximal thickness in each of the eight volunteers yielded an average difference of 0.3 intervals (of 0.5 mm) in the patella, the femoral trochlea, and the medial and lateral tibial plateaus and of 0.1 and 0.2 intervals in the medial and lateral femoral condyles, respectively (Table 3).

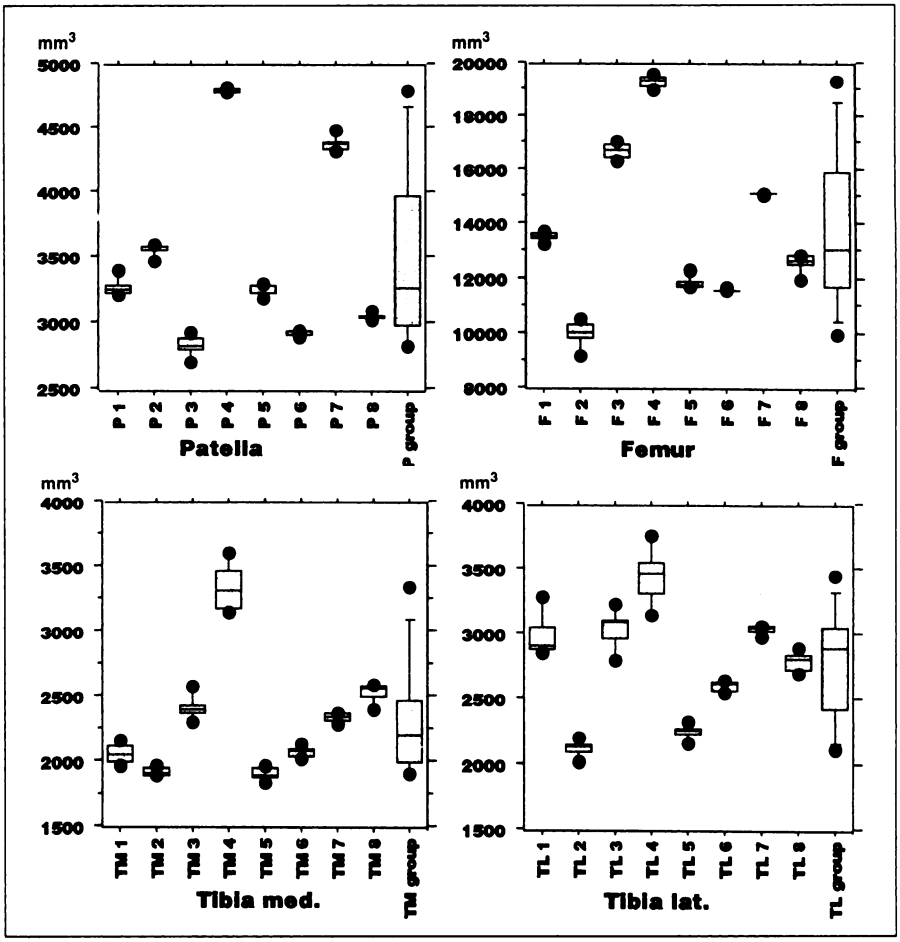

Fig. 2.—Box plots show variability of sixfold repeated volume measurements (mm^3) of knee joint cartilage in eight volunteers and variability of cartilage volumes in same group (P = patella, F = femur, TM = tibia medialis, TL = tibia lateralis, 1 = first volunteer, 2 = second volunteer..., 8 = eighth volunteer, med. = medialis, lat. = lateralis).

Discussion

Whereas previous studies dealt with the validation of MR imaging protocols for quantitative measurement of cartilage [5–21], our investigation focused on the in vivo reproducibility of MR imaging–based cartilage volume and thickness measurements in the knee joint of living subjects, and particularly on interscan reproducibility. This type of investigation is required for evaluating the potential of MR imaging to effectively discriminate between individuals with high or low cartilage volume and thickness and to reliably monitor changes in cartilage volume and thickness longitudinally in the same subject. Potentially useful clinical applications include the screening of individuals at high risk of cartilage loss (e.g., patients with cruciate ligament rupture) and the evaluation of the effectiveness of chondroprotective treatment strategies (e.g., drugs, surgical interventions, physiotherapy). Moreover, animal studies have suggested that cartilage thickness dynamically adapts to immobilization and exercise by atrophy and hypertrophy, respectively [25–29]. However, the functional adaptation of cartilage thickness to mechanical stimuli and the clinical relevance of this adaptation have not yet been analyzed in humans because of the lack of noninvasive measurement techniques.

A number of difficulties arise with such an analysis. One is that accurate delineation of articular cartilage depends on high contrast relative to the adjacent tissues. With conventional MR sequences the contrast-to-noise ratios may be unsatisfactory and various artifacts may distort the bone–cartilage interface. Therefore, a previously validated fat-suppressed gradient-echo sequence was selected in this study [5, 6, 10, 15–17, 19–21] to provide high tissue contrast and to eliminate chemical shift at the interface with the subchondral bone. A second difficulty is that for cartilage thickness measurements, the conventional in-plane resolution in the knee of 0.6 × 0.6 mm [5, 8–10] may not be sufficient because under these circumstances only a few pixels are available to delineate the cartilage layer. Therefore, a matrix of 512 × 512 pixels was chosen, resulting in an in-plane resolution of 0.31 × 0.31 mm. A third difficulty is that because the precise realignment of the section location and orientation in sequential measurements is problematic [5–8, 15–21], changes of cartilage thickness cannot be reliably quantified from serial images. We therefore used a method for determining the cartilage thickness throughout the entire joint rather than at specific locations [20, 21]. A fourth difficulty is that when cartilage thickness is determined in geometrically complex articular surfaces, the true normal or minimal surface distances may not lie in the imaging plane and the real thickness may be overestimated as a function of the out-of-plane devi-

TABLE 2 Reproducibility of Cartilage Volumes on MR Imaging[a]

Joint Surface	Min. (%)	Max. (%)	Mean (%)	ICC
Patella	0.4	2.7	1.3	.995
Femur	0.2	4.7	1.8	.993
Medial tibia	1.7	5.1	3.0	.965
Lateral tibia	1.2	6.2	3.4	.959

Note.—Min. = minimum, Max. = maximum, ICC = intraclass correlation coefficient [23, 24].

[a] Coefficient of variation in percent (SD / mean × 100) for sixfold determination.

ations of these distances. Because the section location and orientation may vary from examination to examination, 3D reconstruction and image processing are required, and we therefore performed the measurements independent of the original section plane.

In our study, the reproducibility of the volume measurements was slightly higher in the patella than in the femur, whereas in the tibial plateau reproducibility was somewhat less. These difficulties may be due to partial volume effects in the internal aspects of the tibial surfaces, which rise steeply to the intercondylar region. The reproducibility in these areas may be improved by reducing the section thickness, acquiring coronal (rather than sagittal) images, or both. However, the disadvantage is that in this case either the semiautomatic segmentation procedure becomes more time-consuming or the other joint surfaces of the knee cannot be reconstructed from the same data set. The reproducibility of our sequential volume measurements is in the same range as that found by Marshall et al. [9] in the medial femoral condyle but is higher than that reported by Pilch et al. [8] and Peterfy et al. [5] in the knee. This difference may be related to the higher in-plane resolution obtained in our study, but one must keep in mind that the cases investigated by Peterfy et al. included joints with cartilage lesions. In this context, our present analysis is valid for healthy cartilage. Future studies are required to establish the reproducibility of this technique in joints with moderate and severe osteoarthrosis and to what extent various imaging conditions (e.g., section orientation and thickness) affect the precision of the measurements in the different joint surfaces. In cases of cartilage damage, partial volume effects can be a problem and a lower section thickness may be required. However, with regard to the functional adaptation of normal cartilage, the screening of risk groups, and the staging of cartilage loss at its early phase, our data should provide a reasonable estimate of the current potential of MR imaging in sequential quantitative evaluation of articular cartilage.

The intraclass correlation coefficient of .959–.995 [23, 24] suggests that the method is highly reliable in the discrimination of individuals with high and low cartilage volumes in the population. The comparison of intra- and interobserver reproducibilities indicates that, owing to the high contrast that exists between the cartilage and surrounding tissues, different observers reach similar conclusions. Therefore, the measurements need not necessarily be made by the same person. On the basis of reasoning analogous to that of Cummings and Black [30], Peterfy et al. [5, 6] stated that the minimal difference of cartilage volume that may be reliably detected in a single individual (95% confidence level) is 2.8 times the CV% for the sequential determination. In our study this difference is equivalent to 4% in the patella, 5% in the femur, 8% in the medial tibia, and 10% in the lateral tibia. If several individuals are included in a study (e.g., to test the effectiveness of chondroprotective treatment strategies), these differences are of course considerably lower. However, these estimates are based on the single time point precision determined in this study.

Our study shows that not only the cartilage volume but also the 3D cartilage thickness

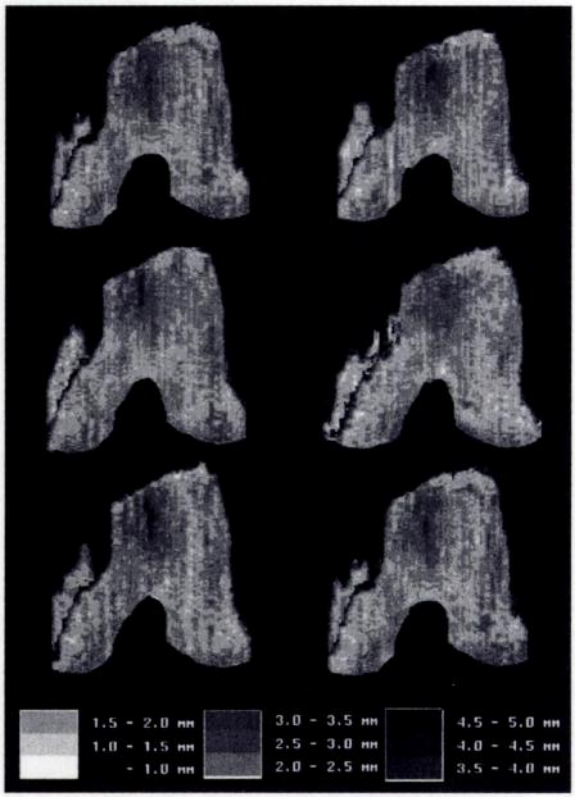

Fig. 3.—Sixfold evaluation of femoral cartilage thickness of 26-year-old healthy volunteer (anterior view of femoral trochlea; medial = left, lateral = right) as obtained with minimal-distance algorithm [20, 21] from MR images after three-dimensional (3D) reconstruction (Fig. 1). Thickness intervals of 0.5 mm have been projected onto 3D reconstructions of femoral cartilage. Knee joint has been deliberately repositioned in between six replicated acquisitions. For better clarity some thickness intervals have been grouped together in this image, but for evaluation of maximal cartilage thickness interval, we had color graphs that showed all 13 thickness intervals.

TABLE 3 Reproducibility of 3D Cartilage Thickness Measurements on MR Imaging

Joint Surface	Number of Deviations [a]			Mean Deviation [b]	
	0	1	2	Average Interval [c]	Worst-Case Interval [c]
Patella	71	43	6	0.3	0.9
Femoral trochlea	76	39	5	0.3	0.5
Medial femoral condyle	92	28	0	0.1	0.3
Lateral femoral condyle	81	36	3	0.2	0.5
Medial tibia	69	41	10	0.3	1.1
Lateral tibia	70	46	4	0.3	0.6

Note.—3D = three dimensional.

[a] Of the maximal thickness interval (0.5-mm steps) observed in 120 cases (15 paired comparisons in eight volunteers).

[b] Of the maximal thickness interval (0.5-mm steps) in the eight volunteers when comparing six replicated examinations.

[c] Of 0.5-mm cartilage thickness.

patterns are reproducible. The advantage of these reconstructions is that the cartilage thickness can be determined at specific joint regions, and this type of information is required for the calculation of cartilage material properties from arthroscopic indentation tests [1], the design of computer models of diarthrodial joints [2–4], and the evaluation of the functional adaptation of the cartilage thickness to mechanical stimuli [25–29]. Not only general but also regional changes of cartilage thickness may be analyzed. The benefit of the 3D technique is that the true (and not the apparent) cartilage thickness is determined and that its changes can be studied longitudinally because the measurements are not distorted by a nonidentical section orientation. Whereas the average deviation of the maximal cartilage thickness interval in replicated measurements of one individual was found to range from 0.1 to 0.3 intervals (of 0.5 mm), the maximal thickness in the group ranged from one (femoral condyles) to four (patella) intervals. These results suggest that regional changes of articular cartilage thickness can be suspected when they encompass more than one thickness interval (0.5 mm) and that they can be reliably determined when more than two intervals. Previous investigations indicate that cartilage lesions are accurately delineated by fat-suppressed gradient-echo sequences [31–33], and future studies must address the value of the 3D technique for quantifying local cartilage lesions and their progression in joint disease.

In conclusion, we have shown a high interscan reproducibility of MR imaging for the noninvasive quantification of cartilage volume and thickness in vivo, provided that a fat-suppressed gradient-echo sequence with adequate resolution and 3D concepts of digital image processing are used. On the basis of these methods, differences between individuals and changes in cartilage volume and thickness in the same individual over time, which cannot be directly determined from sectional images, may be evaluated with relatively high precision.

References

1. Lyyra T, Jurvelin J, Pitkänen P, Väätäinen U, Kiviranta I. Indentation instrument for the measurement of cartilage stiffness under arthroscopic control. *Med Eng Phys* **1995**;17:395–399
2. Blankevoort L, Kupier JH, Huiskes R, Grootenboer HJ. Articular contact in a three-dimensional model of the knee. *J Biomech* **1991**;24:1019–1031
3. Ateshian GA, Soslowsky LJ, Mow VC. Quantitation of articular surface topography and cartilage thickness in knee joints using stereophotogrammetry. *J Biomech* **1991**;24:761–776
4. Heegaard J, Leyvraz PF, Curnier A, Rakotomanana L, Huiskes R. The biomechanics of the human patella during passive knee flexion: ESB Research Award 1994. *J Biomech* **1995**;28:1265–1279
5. Peterfy CG, van Dijke DF, Janzen DL, et al. Quantification of articular cartilage in the knee with pulsed saturation transfer subtraction and fat-suppressed MR imaging: optimization and validation. *Radiology* **1994**;192:485–491
6. Peterfy CG, van Dijke DF, Lu Y, et al. Quantification of the volume of articular cartilage in the metacarpophalangeal joints of the hand: accuracy and precision of three-dimensional MR imaging. *AJR* **1995**;165:371–375
7. Eckstein F, Sittek H, Milz S, Putz R, Reiser M. The morphology of articular cartilage assessed by magnetic resonance imaging (MRI): reproducibility and anatomical correlation. *Surg Radiol Anat* **1994**;16:429–438
8. Pilch L, Stewart C, Gordon D, et al. Assessment of cartilage volume in the femorotibial joint with magnetic resonance imaging and 3D computer reconstruction. *J Rheumatol* **1994**;21:2307–2319
9. Marshall KW, Mikulius DJ, Guthrie JM. Quantitation of articular cartilage using magnetic resonance imaging and three-dimensional reconstruction. *J Orthop Res* **1995**;13:814–823
10. Piplani MA, Disler DG, Mc Cauley TR, Holmes TJ, Cousins JP. Articular cartilage volume in the knee: semiautomatic determination from three-dimensional reformations of MR images. *Radiology* **1996**;198:855–859
11. Chandnani VP, Ho C, Chu P, Trudell D, Resnick D. Knee hyaline cartilage evaluated with MR imaging: a cadaveric study involving multiple imaging sequences and intraarticular injection of gadolinium and saline solution. *Radiology* **1991**; 178:557–561
12. Hodler J, Trudell D, Pathria MN, Resnick D. Width of the articular cartilage of the hip: quantification by using fat-suppression spin-echo MR imaging in cadavers. *AJR* **1992**;159:351–359
13. Hodler J, Loredo RA, Longo C, Trudell D, Yu JS, Resnick D. Assessment of articular cartilage thickness of the humeral head: MR-anatomic correlation in cadavers. *AJR* **1995**;165:615–620
14. van Leersum MD, Schweitzer ME, Gannon F, Vinitski S, Finkel G, Mitchell DG. Thickness of patellofemoral articular cartilage as measured on MR imaging: sequence comparison of accuracy, reproducibility, and interobserver variation. *Skeletal Radiol* **1995**;24:431–435
15. Sittek H, Eckstein F, Gavazzeni A, et al. Assessment of normal patellar cartilage volume and thickness with MRI: an analysis of currently available pulse sequences. *Skeletal Radiol* **1996**;25:55–63
16. Eckstein F, Sittek H, Gavazzeni A, et al. Magnetic resonance chondro-crassometry (MR-CCM): a method for accurate determination of articular cartilage thickness? *Magn Reson Med* **1996**;35:89–96
17. Eckstein F, Adam C, Sittek H, et al. Non-invasive determination of cartilage thickness throughout joint surfaces using magnetic resonance imaging. *J Biomech* **1997**;30:285–289
18. Muensterer OJ, Eckstein F, Hahn D, Putz R. Computer-aided three-dimensional assessment of knee-joint cartilage with magnetic resonance imaging. *Clin Biomech* **1996**;11:260–266
19. Eckstein F, Gavazzeni A, Sittek H, et al. Determination of knee joint cartilage thickness using three dimensional magnetic resonance chondrocrassometry (3D MR-CCM). *Magn Reson Med* **1996**;36:256–265
20. Lösch A, Eckstein F, Haubner M, Englmeier K-H. A non-invasive technique for 3-dimensional assessment of articular cartilage thickness based on MRI. I. Development of a computational method. *Magn Reson Imaging* **1997**;15:795–804
21. Haubner M, Eckstein F, Lösch A, et al. A non-invasive technique for 3-dimensional assessment of articular cartilage thickness based on MRI. II. Validation with CT arthrography. *Magn Reson Imaging* **1997**;15:805–813
22. Englmeier K-H, Haubner M, Lösch A, et al. Hybrid rendering of multidimensional image data. *Methods Inf Med* **1997**;36:1–10
23. Fisher RA. *Statistical methods for research workers*, 14th ed. New York: Hafner, **1973**:213–249
24. Bartko JJ. The intraclass correlation coefficient as a measure of reliability. *Psychol Rep* **1966**;19:3–11
25. Jurvelin J, Kiviranta I, Tammi M, Helminen HJ. Softening of canine articular cartilage after immobilization of the knee joint. *Clin Orthop* **1986**;207:246–252
26. Helminen HJ, Jurvelin J, Kiviranta I, Paukkonen K, Säämänen AM, Tammi M. Joint loading effects on articular cartilage: a historical review. In: Helminen HJ, Kiviranta I, Tammi M, Säämänen AM, Paukkonen K, Jurvelin J, eds. *Joint loading: biology and health of articular structures*. Bristol, England: Wright, **1987**:1–46
27. Helminen HJ, Kiviranta I, Säämänen AM, et al. Effect of motion and load on articular cartilage in animal models. In: Kuettner KE, Schleyerbach P, Peyron JG, Hascall VC, eds. *Articular cartilage and osteoarthritis*. New York: Raven, **1992**:501–510
28. Kiviranta I, Tammi M, Jurvelin J, Säämänen AM, Helminen HJ. Moderate running exercise augments glycosaminoglycans and thickness of articular cartilage in the knee joint of young beagle dogs. *J Orthop Res* **1988**;6:188–195
29. Kiviranta I, Tammi M, Jurvelin J, Arosoki J, Säämänen AM, Helminen HJ. Articular cartilage thickness and glycosaminoglycan distribution in the young canine knee joint after remobilization of the immobilized limb. *J Orthop Res* **1994**;12:161–167
30. Cummings SR, Black D. Should perimenopausal women be screened for osteoporosis? *Ann Intern Med* **1986**;104:817–823
31. Recht MP, Kramer J, Marcelis S, et al. Abnormalities of articular cartilage in the knee: analysis of available MR techniques. *Radiology* **1993**;187:473–478
32. Disler DG, McCauley TR, Wirth CR, Fuchs MD. Detection of knee hyaline cartilage defects using fat-suppressed three-dimensional spoiled gradient-echo MR imaging: comparison with standard MR imaging and correlation with arthroscopy. *AJR* **1995**;165:377–382
33. Recht MP, Piraino DW, Paletta GA, Schils JP, Belhobek GH. Accuracy of fat-suppressed three-dimensional spoiled gradient-echo FLASH MR imaging in the detection of patellofemoral articular cartilage abnormalities. *Radiology* **1996**; 198:209–212