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Magnetic resonance imaging of the knee in chronic knee pain. A 2-year follow-up

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Summary

Objective: The aim of the study was to evaluate the change over time of cartilage defects, subchondral lesions and meniscal abnormalities of the knee using magnetic resonance (MR) imaging with a 2-year interval in patients with chronic knee pain.

Design: In the format of a prospective study of early osteoarthritis (OA), the signal knee (most painful at the inclusion in the study 1990) in 47 individuals, 25 women and 22 men (aged 41–57 years, median 50), with chronic knee pain, with or without radiographically determined knee OA, were examined using MR imaging on a 1.0 T imager with a 2-year interval (median 25 months, range 21–30). Cartilage defects, subchondral lesions and meniscal abnormalities were recorded and compared in blind between the examinations.

Results: Five new cartilage defects and eight subchondral lesions appeared during the 2-year interval. Seven defects and seven subchondral lesions disappeared during the same time. Thirty-two out of 93 cartilage defects (34%) and 19 out of 32 subchondral lesions (59%) displayed an increase or a decrease in size over time. A meniscal abnormality appeared in three locations, and disappeared in none. In 14 out of 54 locations (26%) with a meniscal abnormality an increase or a decrease of the abnormality was recorded over time and no abnormality decreased.

Conclusions: After the 2 years of observation it was possible to register, using MR imaging, the appearance, increase, decrease and disappearance of cartilage defects, subchondral lesions and meniscal abnormalities in middle-aged people with chronic knee pain. This has to be considered in studies of the natural course of knee OA as well as in studies of the intraarticular effect of pharmacological treatment aiming at cartilage repair or protection. © 2001 OsteoArthritis Research Society International

Key words: MR imaging, Osteoarthritis, Knee pain, Follow-up studies.

Introduction

Osteoarthritis (OA) is the most prevalent articular joint disease, but not much is known about the cause, the natural history and the progression of the disease[1]. Since OA is supposed to be a slowly progressive condition, it has up to now not been known exactly when in the pathophysiological process symptoms like pain are first noted by the patient.

It is important to develop methods that can detect less severe changes to learn more about the early pathophysiological processes. Arthroscopic evaluation is hampered because it is an invasive examination and has not yet been tested for interobserver reliability.

Magnetic resonance (MR) imaging is a non-invasive modality with multiplanar capability that allows direct visualization of articular cartilage and menisci, and also permits evaluation of subcortical bone marrow. These possibilities are of interest for monitoring the natural course of articular disorders and the response to treatment in patients with arthritis. Methods for measuring cartilage volume utilizing MR imaging with 3D digital image processing have been used[2,3] but we wanted to evaluate MR imaging as used in daily clinical practice and study the sensitivity of this method to detect changes of articular tissues over a two-year time period.

In an attempt to identify early signs of progress of knee OA, a prospective study on middle-aged people with chronic knee pain in southwest Sweden was initiated, 'the Spenshult cohort'[4]. The aim of the present study was to record any change in cartilage defects, subchondral lesions and meniscal abnormalities in the knee joint between MR studies with a 2-year interval in a random sample of people in this cohort.

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Methods

SUBJECTS

To create a cohort of individuals with chronic knee pain (duration >3 months at inclusion) for a prospective follow-up, an epidemiological survey was performed on 2000 individuals aged 35–54 years in a rural area in southern Sweden, 'the Spenshult cohort'[4]. Chronic knee pain was reported by 279 of 1853 people who completed the questionnaire and 204/279 consented to be examined clinically, biochemically and radiographically at baseline in

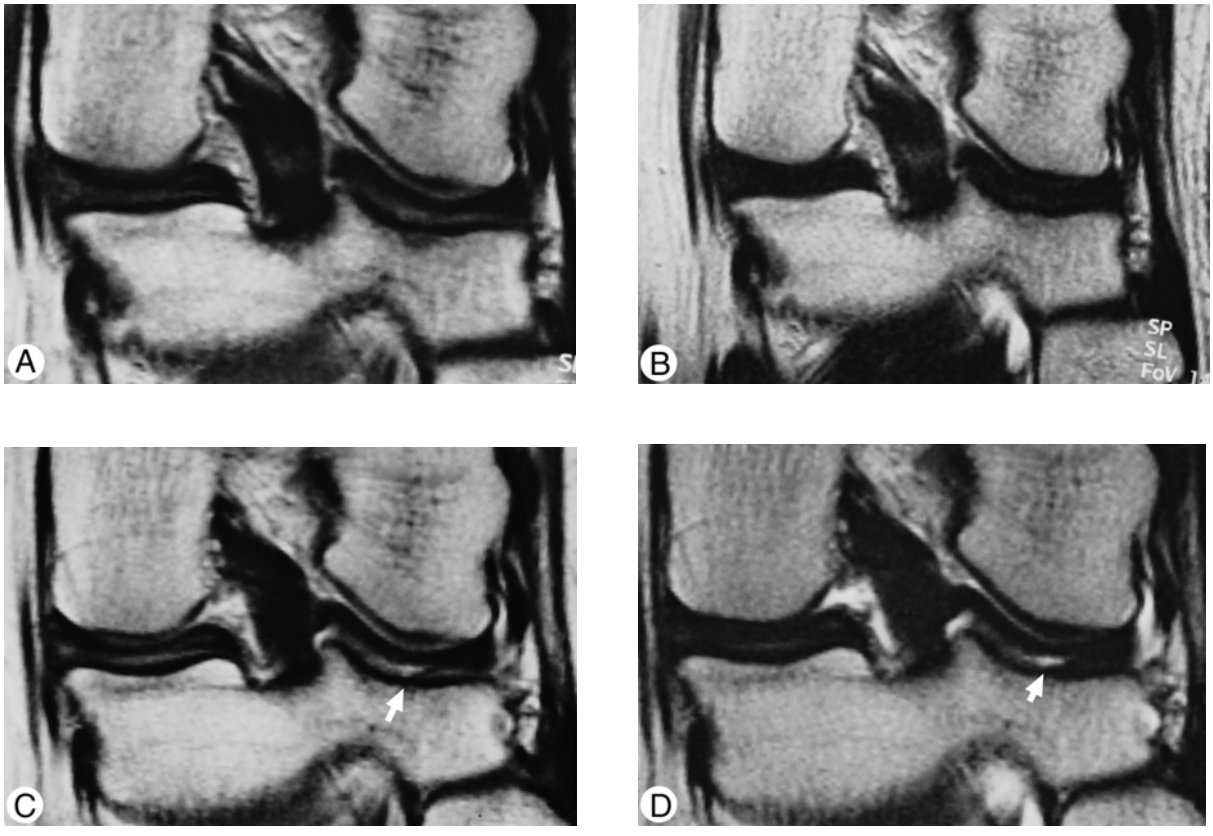

Fig. 1. Coronal (A) Pd- and (B) T2-weighted turbo spin–echo MR images show no cartilage defect at the baseline examination in this 57-year-old woman. The corresponding MR images after 25 months, (C) and (D), show that a grade 2 cartilage defect has appeared in the lateral tibial condyle (arrow).

1990–1991. Nineteen of the 204 subjects were excluded at this stage. Thirteen had arthritis other than OA and six had chronic knee pain resulting from a defined knee trauma. In the remaining 185 cases no obvious cause of chronic knee pain was found. Before the 3-year follow-up, another two persons were excluded, leaving 183 people. Due to misunderstanding, one of them was wrongly classified as suffering from chronic knee pain and the other one developed mild seronegative arthritis of the finger joints.

At the 3-year follow-up, a subgroup of 61 people (61/183) was chosen as a random sample from the initial cohort, after exclusion of those with severe radiographic OA with obliteration of the joint space or bone attrition at the baseline examination. The reason for the selection procedure was to ensure a follow-up of people with less severe disease in this obsevational study. All 61 subjects had a weight-bearing p.a. radiograph of tibiofemoral joint (TFJ), and an axial radiograph of patellofemoral joint (PFJ) in standing of the signal knee (the most painful at inclusion). MR imaging of the signal knee was performed in 60/61 people. One patient could not take part in the MR study because of claustrophobia. The MR examination was valid in all except one patient (59/60) due to trembling caused by Parkinson's disease.

At the 5-year follow-up all 59 people with a diagnostic MR study of the knee 2 years earlier were offered a second MR examination and 54 accepted. At the start of the 3-year follow-up (the baseline examination) the protocol of the MR studies was not definitely established and the intial eight patients in the study were not examined exactly according to the final protocol, which has been used since then. Seven of these initial eight patients were also examined at the 5-year follow-up and thus they did not have an identical MR examination regarding sequences at the 3-year follow-up and at the 5-year follow-up. Thus, in 47 people, the MR studies at the 3-year follow-up and at the 5-year follow-up were identical regarding sequences and only these were included in the study. There were 25 women (aged 42–57, median 50) and 22 men (aged 41–57 years, median 50). In these 47 people Kellgren & Lawrence[5] grade ≥2 was found in 15 signal knees at the 3-year follow-up. At the same examination, radiographic osteophytes were found in 36 of the TFJ and in 31 of the PFJ. In six knees only no osteophytes were found either in the TFJ or in the PFJ. A minimal joint space width <3 mm[6] in the TFJ was found in 10 of the knees and a minimal joint space width <5 mm[7] in the PFJ was found in 14 of the knees and joint space narrowing both in the TFJ and the PFJ was found in three knees. Two of the 47 people had undergone a high tibial osteotomy because of OA of the medial TFJ before the baseline MR study and were thus excluded concerning the TFJ. The median interval time between the MR studies was 25 months (range 21–30).

MR EXAMINATION

MR imaging of the signal knee was performed with a 1.0 T imager (Impact, Siemens) with a circular polarized surface coil. All people were examined with a proton density- and T2-weighted turbo spin–echo sequence (tSEPdT2) in the coronal, sagittal and axial views and with a turbo short

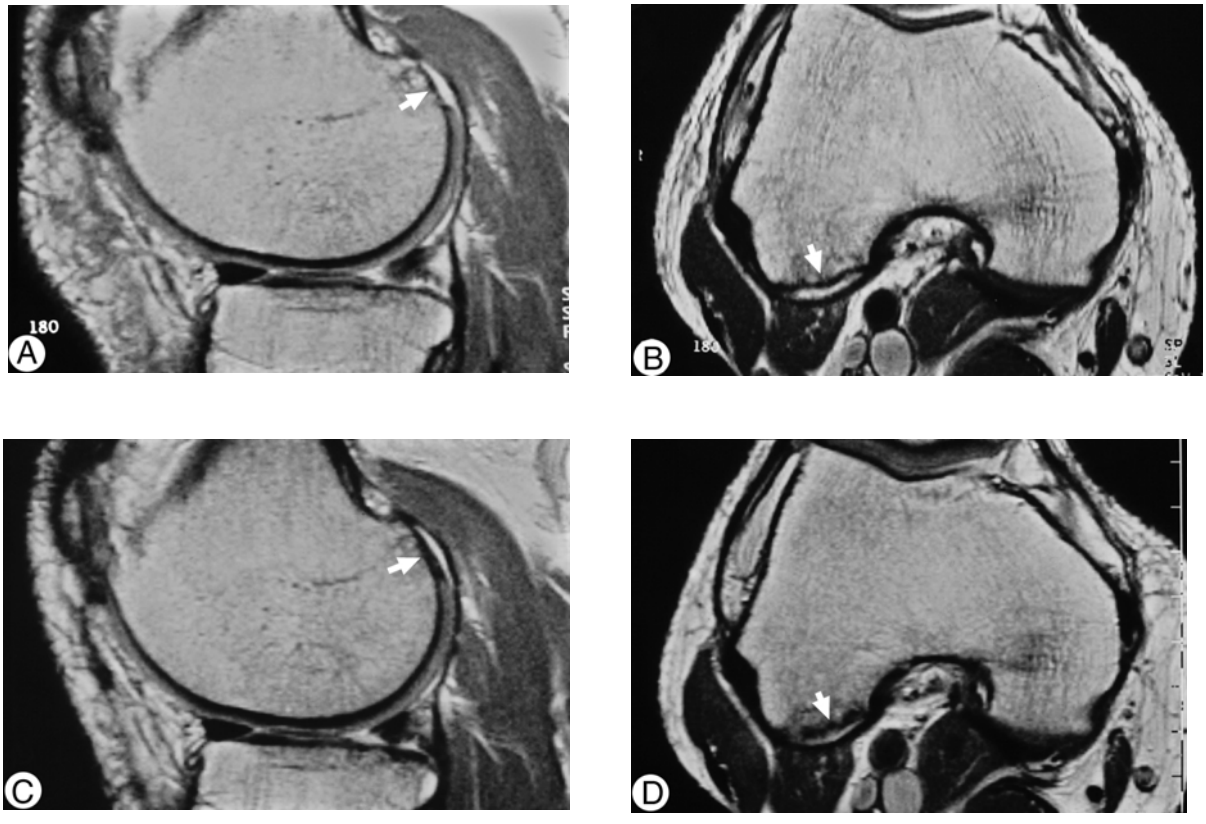

Fig. 2. (A) Sagittal and (B) axial Pd-weighted turbo–spin echo MR images showing a cartilage defect of grade 2 at the dorsal aspect of the lateral femoral condyle (arrow) in a 44-year-old man at the baseline examination. The corresponding MR images after 24 months, (C) and (D), show that the defect is partially filled in.

tau inversion recovery T2-weighted sequence (tSTIRT2) in the sagittal view. The sagittal sequence was perpendicular to a line connecting the dorsal aspect of the femoral condyles, the coronal sequence was parallel to that line and the axial sequence was perpendicular to the long axis of the patella. The sequence parameters for the tSEPdT2 was: TR/TE 4200/15-105 ms with two signals averaged, echo train length 7, FOV 145×145 mm, section thickness 3 mm with 0.3–0.6 mm intersection gap, matrix size 252×256 and acquisition time 5 min 8 s. The parameters for the tSTIRT2 were: TR/TE 4900/60 ms with two signals averaged, echo train length 11, TI 150 ms, FOV 200×200 mm, section thickness 4 mm, intersection gap 0.8 mm, matrix size 242×256 and acquisition time 3 min 40 s. The studies were printed on 35×43 cm films using a laser printer. The tSEPdT2 sequences were printed with 12 frames per film and the tSTIRT2 sequence with 20 frames per film. The window level and the window width chosen were not fixed between the studies and between the patients.

Cartilage defects in each of the articular surfaces of the TFJ and PFJ were classified as grade 1, ≤50% reduction of the cartilage thickness, as grade 2, >50% reduction of the cartilage thickness and as grade 3, cartilage defect with bone loss[4] (Figs 1 and 2). Signal changes of the cartilage with an intact surface were not registered.

Meniscal abnormalities such as full thickness tear[8] and deformity (post-operative, -traumatic, etc.) were recorded separately for the anterior, middle and posterior portion of each meniscus.

Subchondral lesions with increased signal in the tSTIRT2 sequence in the immediate vicinity of the joint cartilage in each articular surface (for instance the medial femoral condyle) were measured by a ruler and classified according to their greatest diameter as grade 1 (<1 cm), grade 2 (1–<2 cm) and grade 3 (≥2 cm)[9] (Fig. 3). If there were two or more lesions adjacent to the articular surface the largest lesion was measured.

In order to detect focal lesions, two of the authors (TB, OR), both experienced in musculoskeletal MR imaging, separately interpreted and compared the articular cartilage in and the subchondral bone adjacent to six joint surfaces as well as the three parts of each meniscus, in each patient, between the MR study at the 3-year follow-up and at the 5-year follow-up and then reached a consensus for a combined score. Whether a change was detected or not was registered for each tissue (articular cartilage, subchondral bone and meniscus) in every location. We used a semi-quantitative assessment of the lesions in which not only a difference in grades between the studies was noted but also a difference within a grade of a lesion was registered and, when necessary, a ruler was used. This method of composite analysis reflects daily clinical routine assessment.

The readers were blind regarding the time sequence of the MR studies and the name and the age of the patient. Furthermore, the time sequence was randomly chosen in the examinations. The same authors (TB, OR) have previously interpreted MR studies at the 3-year follow-up blindly and separately and then reached a consensus for a combined score[6,7,9]. Furthermore, 30 consecutive MR studies from the 5-year follow-up were reread twice by one observer (TB) 2 weeks apart and once by another observer

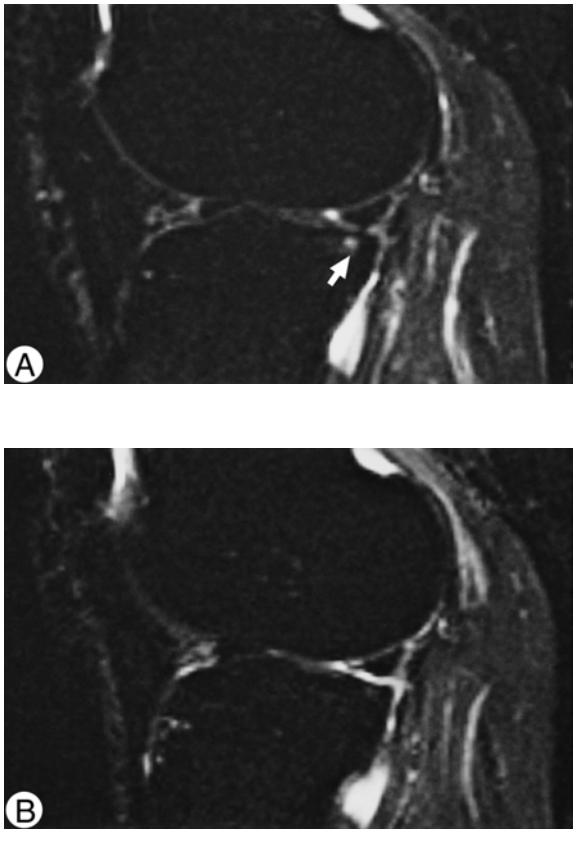

Fig. 3. (A) A sagittal T2-weighted turbo STIR MR image shows a grade 1 subchondral lesion (arrow) at the dorsal aspect of the lateral tibial condyle at the baseline examination in this 57-year-old woman. The corresponding MR image after 25 months, (B), shows that the lesion has disappeared.

(OR) for calculating the kappa values for intra- and inter-observer agreement for cartilage defects, subchondral lesions and meniscal abnormalities.

STATISTICAL METHODS

The measure used to assess intra- and interobserver agreement of grading cartilage defects, subchondral lesions, and meniscal abnormalities was kappa[10]. A kappa value of 1.00–0.81 was considered very good, 0.80–0.61 as good, 0.60–0.41 as moderate, 0.40–0.21 as fair, and 0.20–0.00 as poor. The differences in development patterns for the three types of tissue (i.e. articular cartilage, subchondral bone and menisci) were studied by means of a Chi-square analysis.

Table I
Number and grade (0–3) of MR-detected cartilage defects in the tibiofemoral joint of the signal knee in 45 people at the baseline examination

MR (grade)	Medial femur	Medial tibia	Lateral femur	Lateral tibia
0	27	36	37	38
1	7	5	3	2
2	10	3	5	4
3	1	1	—	1

Table II
Number and grade (0–3) of the MR-detected cartilage defects in the patellofemoral joint of the signal knee in 47 people at the baseline examination

MR (grade)	Patella	Femoral trochlea
0	16	27
1	14	13
2	17	7
3	—	—

ETHICAL APPROVAL

The MR studies were approved by the Ethics Committee of the Faculty of Medicine, University of Lund (ref. LU 248-93).

Results

The number and grade of MR-detected cartilage defects in the TFJ and in the PFJ at the baseline examination are shown in Tables I and II. During the 2 years of observation, a cartilage defect appeared (Fig. 1) in five articular surfaces and disappeared in five (Table III). An increase or decrease (Fig. 2) of a cartilage defect over time was recorded in 34 out of 93 articular surfaces with a defect. In 19 TFJ and 15 PFJ, the articular cartilage was normal.

The number and grade of MR-detected subchondral lesions in the TFJ and in the PFJ at the baseline examination are shown in Tables IV and V. Between the MR studies a subchondral lesion appeared adjacent to eight articular surfaces and disappeared (Fig. 3) adjacent to seven

Table III
Change of MR-detected cartilage defects in the tibiofemoral and the patellofemoral joint during 2 years of observation in the signal knee of 45 and 47 people respectively

Location	Cartilage defects				
	At baseline	Appearing	Increasing	Decreasing	Disappearing
Medial femur	18	2	5	1	1
Medial tibia	9	—	3	1	1
Lateral femur	8	1	1	1	—
Lateral tibia	7	1	3	1	—
Patella	31	1	4	3	4
Trochlea femur	20	—	3	6	1

Table IV
Number and grade (0–3) of MR-detected subchondral lesions in the tibiofemoral joint of the signal knee in 45 people at the baseline examination

MR (grade)	Medial femur	Medial tibia	Lateral femur	Lateral tibia
0	39	38	41	38
1	5	4	2	3
2	1	1	2	3
3	—	2	—	1

Table V
Number and grade (0–3) of MR-detected subchondral lesions in the patellofemoral joint of the signal knee in 47 people at the baseline examination

MR (grade)	Patella	Trochlea femur
0	42	44
1	4	1
2	1	2
3	—	—

(Table VI). An increase or decrease of a subchondral lesion over time was recorded adjacent to 19 out of 32 articular surfaces. In 32 TFJ and 39 PFJ, the subchondral bone marrow was normal.

The number and location of MR-detected meniscal abnormalities at the baseline examination are shown in Table VII. During the 2 years of observation a meniscal abnormality appeared in three locations (Table VII). A horizontal rupture appeared in the middle and posterior portion of one medial meniscus and a rupture of the same type appeared in the anterior horn of a lateral meniscus. No meniscal abnormality disappeared during the two years of observation. An increase or decrease of a meniscal abnormality was recorded in 16 out of 54 locations with an abnormality. The medial meniscus was normal in 23 knees and the lateral meniscus in 37 knees.

The intra-observer agreement regarding the grading of cartilage defects, subchondral lesions and meniscal abnormalities expressed as kappa values varied between 0.61–1.00. The inter-observer agreement for the corresponding grading varied between 0.39–1.00. The intra-observer percentage concordance varied between 83 and 100% and the inter-observer percentage concordance between 60 and 100%. The kappa values and the percentage concordance between the grading are given in Table VIII.

The development patterns for the three types of tissues (i.e. articular cartilage, subchondral bone and menisci) are presented in Table IX, and the differences in development patterns were studied by means of a Chi-square analysis. The test for Table IX was highly significant ($P<0.001$). The significance was due to differences between the development in articular cartilage and subchondral bone ($P<0.001$), between the development in articular cartilage and menisci ($P<0.001$) and between the development in subchondral bone and menisci ($P<0.013$). An analysis of the disease progression or the improvement of cartilage defects and subchondral lesions simultaneously on a patient level was performed and the course of OA in these two articular tissues was in general not parallel.

Table VI
Change of MR-detected subchondral lesions in the tibiofemoral and the patellofemoral joint during two years of observation in the signal knee of 45 and 47 people, respectively

Location	Subchondral lesions				
	At baseline	Appearing	Increasing	Decreasing	Disappearing
Medial femur	6	2	3	1	1
Medial tibia	7	—	2	1	2
Lateral femur	4	—	1	2	1
Lateral tibia	7	—	3	2	2
Patella	5	4	3	—	—
Trochlea femur	3	2	1	—	1

Table VII
Change of MR-detected meniscus abnormalities during two years of observation in the signal knee of 45 people

Location	Abnormality			
	At baseline	Appearing	Increasing	Decreasing
Anterior portion Medial meniscus	3	—	—	—
Middle portion Medial meniscus	15	1	6	—
Posterior portion Medial meniscus	22	1	8	—
Anterior portion Lateral meniscus	4	1	—	—
Middle portion Lateral meniscus	5	—	—	1
Posterior portion Lateral meniscus	5	—	—	1

Table VIII
Intra- and inter-observer agreement and percentage concordance of grading of MR-detected cartilage defects, subchondral lesions and meniscal abnormalities of the signal knee from the follow-up examination in 30 consecutive people

	Intra-observer agreement/ Percentage concordance	Inter-observer agreement/ Percentage concordance
Cartilage defect		
Medial femur	0.73/83%	0.70/83%
Medial tibia	0.91/97%	0.68/87%
Lateral femur	0.69/90%	0.40/77%
Lateral tibia	1.00/100%	0.39/79%
Patella	0.74/83%	0.39/60%
Trochlea femur	0.75/90%	0.40/77%
Subchondral lesion		
Medial femur	0.75/90%	0.52/80%
Medial tibia	0.61/87%	0.79/93%
Lateral femur	1.00/100%	0.65/97%
Lateral tibia	0.72/93%	0.75/93%
Patella	0.66/83%	0.51/80%
Trochlea femur	0.79/97%	1.00/1000%
Meniscal abnormality		
Medial	0.92/97%	0.86/93%
Lateral	0.91/97%	0.81/93%

Discussion

We have examined middle-aged people with long-standing knee pain with mild or moderate knee OA as only three patients had bone attrition in the TFJ and none in the PFJ. Two persons had undergone high tibial osteotomy because of OA of the medial TFJ before the baseline examination and were excluded concerning observations of the TFJ as the operation might have a significant influence on the OA disease in this articulation. However, two persons who underwent arthroscopy during the time of observation and had a partial meniscectomy of the lateral meniscus were not excluded as the operation was considered to have no or only minimal effect on the OA disease.

MR imaging is considered an accurate means of detecting and grading moderate and advanced cartilage lesions in the knee joint[11] and is thus useful in the evaluation of knee OA. The fast spin–echo 2D-sequences used in this study do not differ in this respect and have also been used by others[12,13]. According to recent results it appears that high resolution 3D gradient–echo sequences with the addition of fat suppression or magnetization transfer contrast are the best for depicting hyaline cartilage[2,14,15].

Meniscal abnormalities are mainly assessed by the Pd-weighted images of the conventional SEPdT2-sequence[8]. The diagnostic accuracy of turbo SEPdT2 regarding these abnormalities has been doubted[16], but this technique performs similarly to the conventional spin–echo sequence[17,18,19], something that is also in agreement with our clinical experience.

MR imaging is also a sensitive means for detecting bone marrow lesions and has rapidly become the preferred imaging technique to determine the presence and extent of these lesions[20]. T1-weighted, fat-saturation T2-weighted, and STIR sequences all provide a high degree of sensitivity for depiction of most types of bone marrow abnormalities[20]. We have used a tSTIRT2 sequence to depict subchondral lesions and in order to assess the presence and extent of subchondral bone involvement of the OA process. This sequence can provide STIR images much more rapidly than conventional sequences without compromising image quality or lesion detection[21,22,23]. The STIR sequence has been used by others[24] to detect subchondral lesions in knee OA.

An MR examination in our study consists of approximately 165 3–4 mm slices. Every study requires approximately 15–30 min of careful evaluation by each of the observers for detection and classification of (1) cartilage defects in six separate articular surfaces, (2) abnormalities in two menisci, and (3) subchondral lesions adjacent to six separate joint surfaces. Our technique to evaluate the primary and the follow-up MR study (approximately 330 slices) in each patient imply that the two examinations by each observer independently initially are compared slice by slice to detect any lesion and secondly to decide if any change of the lesion has happened. In case of disagreement between the observers, a second evaluation was performed to reach a consensus.

To our knowledge, hyaline cartilage, subchondral bone and menisci in MR studies of the knee are sometimes judged by a single observer but predominantly by two or more observers who work in conference. Due to the complexity of the MR study, every MR examination in our study required approximately 15–30 min of careful evaluation by each of the observers for detection and classification of the defects and abnormalities listed above. Therefore we believe that two or more observers who work in conference are necessary to avoid the possibility that some lesions might be overlooked and also that the lesions are thus judged more correctly than by a single observer even if our calculations of intra- and inter-observer agreement of cartilage defects, meniscal abnormalities and subchondral lesions in most locations were moderate, good or very good. However, the distribution of different grades of the

Table IX
The distribution of normal cartilage, subchondral bone and menisci as well as cartilage defects, subchondral lesions and meniscal abnormalities in MR imaging of tibiofemoral joint in the signal knee of 45 people during two years of observation

	Appeared/ increased	Not changed	Decreased/ disappeared	Normal	Total
Cartilage defects	16	24	6	134	180
	8.9%	13.3%	3.3%	74.4%	100%
Subchondral lesions	11	3	12	154	180
	6.1%	1.7%	6.7%	85.6%	100%
Meniscal abnormalities	12	23	0	55	90
	13.0%	26.0%	0%	61.0%	100%

lesions was in general skewed and under these circumstances, the kappa value tends to be low even if percentage concordance between the grading is high, as in our study.

In normal joints, degradation and synthesis of the articular cartilage and subchondral bone are balanced, while in OA the normal coupling between these processes is destabilized. Ultimately, OA leads to a softening, fibrillation, ulceration and loss of articular cartilage, sclerosis and eburnation of subchondral bone, osteophytes and subchondral cysts. But there is no evidence that the OA disease is a continuous degradation of the articular cartilage and of the subchondral bone. In some individuals, the OA process can probably remain static or even reverse. The latter phenomenon has been found after proximal tibial osteotomy for medial OA[25]. In others the progression of the OA process is slow and in yet another group of OA individuals the progress is rapid[26]. In our study we found examples that reflect these aspects of the disease. In the majority of cases no change was found during the two years of observation while cartilage defects during the same time appeared in some cases and disappeared in some. In several cases a pre-existing cartilage defect displayed either an increase or a decrease in size.

Subchondral lesions, as seen as areas with high signal in the tSTIRT2, reflect a replacement of the normal fatty bone marrow by a local increase in tissue water content, which could represent a synovial leak, underlying inflammation or the presence of fibrovascular tissue[24] and has been seen in knee OA and corresponds to a local scintigraphic uptake[9,24]. In middle-aged people with long-standing knee pain, the number of subchondral lesions was less than one third of the number of MR-detected cartilage defects[8]. It is possible that the subchondral lesions in these knees represent a more progressive OA disorder, as Dieppe *et al*.[27] found no radiographic progress during 5 years of observation in OA knees with normal scintigraphy at the baseline examination.

Horizontal meniscal tears are usually called degenerative tears and they increase in prevalence after 20 years of age, while bucket handle tears, flap tears and vertical tears decrease in prevalence after 20–30 years of age[28]. It is believed among knee arthroscopists that the degenerative process of the menisci is progressive and that these tears will not heal over time. These beliefs are supported by our findings that a meniscal abnormality appeared in three locations and increased in 14 locations while we recorded a decrease in only two locations and that happened in the same lateral meniscus, which was partially ectomized during the time of observation.

In the tibiofemoral joint we analyzed the distribution of joint surfaces with normal cartilage or cartilage defects that appeared/increased, were unchanged or decreased/disappeared during the time of observation, and of the corresponding numbers of normal subchondral bone marrow and subchondral lesions, and of normal menisci and meniscal abnormalities. Interestingly, we found that the distribution was uneven ($P<0.001$) and that was the result of an uneven distribution between the status of hyaline cartilage and bone marrow, between the status of hyaline cartilage, and menisci, and between the status of bone marrow and menisci. This supports the hypothesis that the course of the OA process in the hyaline cartilage, the subchondral bone marrow and the menisci is not parallel.

It has been shown that MR imaging can be used to determine cartilage volume and thickness in normal knee joints *in vivo*[3] and in osteoarthritic knee joints[2], with high precision, with fat-suppressed gradient–echo sequences and using 3D digital image processing. In this study we were not able to perform any cartilage volume measurements. For quantitation of subchondral lesions and meniscal abnormalities in the same way no such methods are yet available.

Some limitations in our study have to be pointed out. The two examinations in each patient were not printed with identical window-level and window-width on hard copies. This may influence the film reading and make the comparison between the examinations more uncertain. With the technique used, we were not able to evaluate the quality of newly formed cartilage in defects in which a decrease or a disappearance during the time of observation was recorded.

In conclusion, with MR imaging during 2 years of observation, we have been able to show the dynamic nature of the OA disorder in the knee joint with respect to cartilage defects, subchondral lesions and meniscal abnormalities. This has to be considered in studies of the natural course of OA as well as in studies of the intra-articular effect of pharmacological treatment aiming at cartilage repair or protection.

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