Clinical Imaging Assessments of Knee Osteoarthritis in the Elderly: A Mini-Review

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Key Words

Conventional X-ray · Imaging · Joint disease · Knee osteoarthritis · Magnetic resonance imaging · Radiology · Ultrasonography

Abstract

Knee osteoarthritis (OA) in the elderly is one of the most common degenerative age-related joint diseases leading to typical degradation of articular cartilage with severe pain and limitation of joint motion. Its increasing prevalence due to the demographic development of the society has major implications for individual and public healthcare with the increasing necessity for clinical imaging assessment in a high number of individuals. Although conventional X-ray radiographs are widely considered as gold standard for the assessment of knee OA, in clinical and scientific settings they increasingly bear significant limitations in situations when high resolution and detailed assessment of cartilage is demanded. New imaging modalities are broadening the possibilities in knee OA clinical practice and are offering new insights to help for a better understanding of the disease. X-ray analysis in OA of the knee is associated with many technical limitations and increasingly is replaced by high-quality assessment using magnetic resonance imaging or ultrasonography both in

clinical routine and scientific situations. These novel imaging modalities enable an in vivo visualization of the quality of the cartilaginous structure and bone as well as all articular and periarticular tissues. Therefore, the limitations of radiographs in knee OA assessment could be overcome by these techniques. This review article should provide an insight into the most important radiological features of knee OA and their systematic visualization with different imaging approaches that can be used in clinical routine.

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Introduction

Knee osteoarthritis (OA) is one of the most common chronic age-associated degenerative joint diseases leading to typical degradation of cartilage and reduced motion of the affected joints. It is the third most common reason for disease-related reduction in the quality of life, assessed on unemployed life-years [1]. Knee OA has been regarded as a disease of ‘wear and tear’ for a long time. However, recently and largely owing to the application of novel imaging techniques in large clinical studies, a change in paradigm has occurred in that a consensus has developed to perceive knee OA not simply as a disease of

Fig. 1. Posterior-anterior view of the knee joint in the 'Lyon position', i.e. a 10° caudal angulation for an optimal visualization of the joint space, of the left knee joint of a 71-year-old patient with definite knee OA. With a Kellgren-Lawrence score of 8 points the patient has knee OA grade 4. Large osteophyte formation (arrow-head) and the advanced narrowing of the medial joint space (arrow) with subcortical sclerosis and deformation of the joint surfaces (asterisk) are typical for the diagnosis of OA.

cartilage, but as a whole-joint disorder involving multiple joint tissues leading to joint failure [2].

The pathophysiology of knee OA is complex and the probability of developing this disease increases with age. The demographic development in Western industrialized countries prognosticates a dramatic increase of the incidences of knee OA during the coming decades [1]. Among 20-year-old individuals, the prevalence of knee OA is 9%, increasing to 30% in individuals older than 60 years, and 90% at the age between 70 and 74 [3]. Most commonly, OA develops in and affects the weight-bearing joints, such as the wrist, ankles, knees, hips, and vertebral joints [4]. The characteristic early symptoms for knee OA are motion-related pain and stiffness of the joint [5]. In contrast to the chronic inflammatory joint diseases, e.g. rheumatoid arthritis, these symptoms cannot be alleviated but increase with motion and joint use.

Conventional radiographic image analysis is still considered as the easiest and most cost-effective radiological modality for diagnosing and follow-up of knee OA.

The reduction of joint cartilage can indirectly be seen by an assessment of the reduction of joint space. Typically, joint space narrowing does not occur homogeneously over the entire width of the joint and is almost always accompanied by an increased subchondral sclerosis (fig. 1). Intra-articular free bony bodies and joint effusion are also typical features of an OA knee joint. In addition, the development of periarticular osteophytes and new bone formation as well as the occurrence of subcortical cysts with an intact bone margins are characteristic for the diagnosis of knee OA. If synovitis is present, the risk for the development of cortical bone lesions is high, and then called 'erosive OA'. These inflammatory changes in knee OA most likely develop as a secondary reaction to cartilage and bone destruction with dilution of the synovial fluid. There is a wide agreement that synovitis in the disease course of knee OA is not a passive expression of the structural degeneration, but that the inflammation is caused by the mechanic irritation due to debris of bone and cartilage destruction.

Erosive knee OA can mimic the picture of psoriatic arthritis and often only be distinguished to it by the psoriatic-typical distal joint involvement with the simultaneous appearance of erosions and bony osteo- and periosteal proliferations, joint space narrowing, 'pencil-cup' osteolyses, ankylosis and spondylitis [6].

Although X-ray analysis is still considered the gold standard in clinical and epidemiological settings, it is increasingly associated with several limitations: in clinical trials for the follow-up of the effect of disease-modifying drugs for the treatment of knee OA, a measurement of the joint cartilage is recommended [7]. Ideally, a valid (i.e. it really measures the cartilage) and reliable (i.e. the results are the same if measured under other circumstances) measurement of the joint cartilage should be performed which has a high sensitivity to change (i.e. the method allows to detect smallest anatomical changes). However, conventional X-ray image analysis does not fulfil these criteria. In addition, X-rays are summative two-dimensional projection images of the bone and intra- or extra-articular three-dimensional (3D) changes, such as cartilage erosions, free bone bodies, or intraosseous ganglion cysts cannot be seen without uncertainty.

Modern imaging modalities, especially magnetic resonance imaging (MRI) and ultrasonography, allow to overcome the above-mentioned weaknesses of X-ray radiography and for a detailed visualization of the knee

joint with all its bone, cartilaginous, ligamentous and soft-tissue structures to quantitatively assess the severity of knee OA [8, 9].

In 2011, as a result of a Delphi-based analysis, the working group 'Imaging' of the Osteoarthritis Research Society International (OARSI) published a novel MRI-based definition of knee OA: According to this publication, OA of the knee is diagnosed when both criteria A (1. presence of osteophytes, 2. loss of cartilage surface) or one criterion A and two criteria B (1. partial loss of cartilage surface, 2. menisci damage, 3. bone marrow edema, 4. subarticular defects) are present [10].

Intravital in vivo assessment of cartilage using special imaging modalities is increasingly being used for establishing the diagnosis and follow-up of OA of the knee and could, if brought into clinical practice, lead to a paradigmatic change in the treatment of cartilage damage in OA.

This review article should provide an insight into the most important radiological features of knee OA and their systematic visualization with different imaging approaches in clinical radiology practice.

Radiological Measurement of Knee OA

Conventional X-Ray Radiography

Conventional radiographic assessment is the most commonly used method to establish the diagnosis of knee OA and to measure the chronological course of the disease.

In 1957, Kellgren and Lawrence [4] developed the first and at present worldwide still considered as the most valid measuring method for a uniform graduation of knee OA by using X-rays. In 1961, the World Health Organization (WHO) accepted the Kellgren-Lawrence method as the standard method for graduating knee OA.

This method graduates the severity of knee OA as a sum score according to measurements of joint space width, deformation of joint surfaces, subchondral sclerosis, and the presence/absence of osteophytes (table 1). During the following decades after the publication of the Kellgren-Lawrence method, several other scores to individually graduate osteophytes, joint space narrowing, and subchondral sclerosis were also developed. However, these graduation techniques have frequently been questioned because of their crude classifications and both their low validity and low sensitivity in the assessment of disease progression. Moreover, the value of these methods were in doubt since they give osteophytes a central role in their scoring system, but the importance of osteophytes in the disease course of knee OA still remains un-

Table 1. Radiographic grading of knee OA according to the Kellgren-Lawrence score [4]

Osteophyte formation	none: 0 definite: 1 large: 2
Joint space width	normal: 0 narrowing: 1 advanced narrowing: 2
Subchondral sclerosis	gone: 3 none: 0 discrete: 1 discrete sclerosis with cyst formation: 2 severe sclerosis with cyst formation: 3
Deformation	none: 0 discrete: 1 strong: 2

Grade 0 = 0 points; grade 1 = 1–2 points; grade 2 = 3–4 points; grade 3 = 5–9 points; grade 4 = 10 points.

clear. It has been shown that the development of osteophytes in knee OA is associated with the presence but not the severity of knee pain and does not show a statistically significant correlation with disease progression [11]. However, some studies also revealed that the graduation of the course of the development of osteophytes had a better reproducibility than measurements of joint space width.

The radiographic assessment and measurements of joint space widths underlies the assumption that joint space narrowing during the chronic progressive course of knee OA directly correlates with a reduction in cartilage volume. However, this assumption is not necessarily correct since the radiographic joint space does not only consist of the cartilage but also other structures, such as the menisci, and an assessment of the latter is highly dependent on projection technique and/or inter-reader reliability [12]. In addition, conventional radiographic measurement of joint space width is relatively insensitive for the detection of changes over a short time period. In a 2-year observational study, Raynauld et al. [13] could demonstrate on prospectively collected follow-up images of conventional X-rays, which were taken in 6-month intervals, that no changes of joint space widths were measurable while on MRIs of these patients a significant loss of cartilage was seen.

At most radiology departments, a posterior-anterior view of the knee joint in the 'Lyon-position', i.e. a 10° caudal angulation for an optimal visualization of the joint space, is recommended (fig. 1).

Fig. 2. Standard T1-weighted coronal image on a clinical 1.5-T MRI demonstrates the asymmetric joint space narrowing due to loss of the integrity of the medial cartilage (brackets), subarticular bone abnormalities (asterisks), subarticular abrasion (arrow), marginal and central osteophytes (arrowheads) as well as intra-articular free bodies (broken arrow).

Magnetic Resonance Imaging

Non-invasive diagnostics of cartilage damage is pivotal for the understanding of the underlying disease mechanism and for the development, utilization, and follow-up of specific therapies. In the clinical radiological routine of the assessment of OA of the knee with MRI, several structures that are relevant for the functional integrity of the joint and that are considered to play a role during the development of OA as well as all anatomical structures can be visualized. Thus, MRI can assess the integrity of the cartilage, subarticular bone abnormalities, subchondral cysts, subarticular abrasion, marginal and central osteophytes, meniscus changes, the cruciate ligaments and collateral ligaments, synovitis and joint effusion as well as intra-articular free bodies, bursitis, and periarticular soft-tissue cysts (fig. 2). The role of MR arthrography, namely MRI assessment of the joint after intra-articular injection of MR contrast medium, for the diagnosis and assessment of knee OA is controversially discussed in the literature and MR arthrography is not routinely used in clinical practice [14]. However, in certain situations, such as postoperative assessment of the meniscus, uncertainty about the presence of chondral and osteochondral lesions and the presence of intra-articular bodies, MR arthrography might be used. Potential

future indications for MR arthrography might also be the evaluation of anterior cruciate ligament injuries and assessment of therapies under development such as autologous chondrocyte implants for the treatment of severe cartilage defects [14].

Due to their low signal-to-noise ratio and the only limited possibility of using a fat saturation technique, low-field MRIs (0.18–0.2 T) are clearly inferior to high-field MRIs (1.5 or 3.0 T) in context of image quality for the assessment of knee joint morphology. In several studies, 3.0-T MRIs have already proven their high potential for the assessment of the different composites of cartilage tissue [15].

In general, because of their wide range of contrast and their reduced chemical shift artifacts, fat suppression sequences are perfectly suited for the visualization of the hyaline articular cartilage. Their downside, however, is that they require longer acquisition times that can be cumbersome for elderly patients with knee and often back pain and have a high susceptibility for inhomogeneities of the magnetic field.

To assess the individual risk for the development of knee OA or the individual course of disease using a novel method, alternatively to measure joint space width with conventional radiography, cartilage thickness can be determined with MRI [16]. The great advantage of MRI is, as mentioned above, in the direct visualization of the joint cartilage rather than a crude estimation of the possible cartilage thickness by radiographic measurements of joint space widths. For such MRI measurements, T1-weighted fat-suppressed sequences are used with which the cartilage can directly be visualized. However, studies showed that a pure measurement of the cartilage thickness using MRI is associated with limitations and uncertainties, since the individual patient's cartilage thickness may vary depending on daytime of acquisition and long-term studies showed a low reproducibility of such measurements [17].

As a better method of cartilage quantification it is also possible to quantify the cartilage volume using MRI. This method has a high validity and MRI studies of cartilage volume measurements have shown a correlation coefficient of 0.98 between the calculations of MRI and the real cartilage volume of the surgery or postmortem specimen [18].

It has also been shown that the articular cartilage volume is a highly valid reference point for the clinical outcome of OA and for the probability of the later need for a therapy with knee endoprosthesis. The measurement of the cartilage volume has a good interindividual variability.

ity both in healthy and OA joints. In addition, measurements of the cartilage volume have a much higher sensitivity for volume changes than measurements of joint space width with radiography. Thus, it has been shown that changes of joint space widths in conventional X-rays are only perceptible when already 10–13% of the cartilage volume have already been used up [13].

A limitation of cartilage volume measurements is that individuals with large bones have a higher cartilage volume than individuals with small bones and, even after statistical correction, men have a larger joint surface than women which enhances the spectrum of possible pathological and physiological results. Another disadvantage of quantitative measurements is that they require special computer software and semiautomatic quantifications are very time-consuming.

Multiplane tomographic imaging and the possibility of 3D reconstructions with MRI allow to exactly visualize cartilage defects of the joint surface. Also, cartilage defects can be imaged with MRI earlier than changes can be seen on conventional X-rays [19]. Cartilage defects are defined as irregularities of the normally glassy cartilage that can be seen both with MRI or arthroscopy. However, since cartilage defects can be found in painless healthy individuals without radiographic OA as well as patients with diagnosed painful OA, their importance for the quantification and grading of OA is speculative [19, 20]. The presence of an MRI cartilage defect in asymptomatic individuals is statistically significantly associated with a reduction of the cartilage volume [9]. Whether MRI cartilage defects represent an early manifestation of knee OA has to date, however, not been clarified.

Nevertheless, in patients with definite knee OA, cartilage defects are prognosticators for faster cartilage loss, accelerated disease course, pain, physical limitations, and the necessity for the implantation of knee endoprosthesis [20].

The macromodular network of the hyaline articular cartilage mainly consists of collagen and proteoglycans. Under physiological conditions, this collagen network is highly organized in order to resist the shear force and pressure of mechanical stress. Glucosaminoglycans (GAGs) are recurring disaccharides with carboxyl and sulfate groups and substantial components of proteoglycans. GAGs are important structure components of the extracellular matrix and account for approximately 20% of cartilage volume. Cartilaginous collagen forms an iso-electric fiber network into GAGs as integral parts of proteoglycans are embedded. In the course of knee OA, typically a biochemical change in the substance of hyaline

cartilage occurs. Loss of GAGs and increased water content of the cartilage, while the collagenous components remain unchanged, are the first biochemical indicators of knee OA and generally accepted as early events of cartilage degradation. Already before the occurrence of osteoarthritic changes, the biochemical composition of the joint cartilage and its changes can already be visualized using several MRI techniques. All these methods are aiming at imaging the GAG component or the collagenous network of cartilage.

One of the most promising techniques for the visualization and quantification of the quality of cartilage is the ‘delayed gadolinium-enhanced MRI of cartilage’ (dGEMRIC) method [21]. This MRI technique, for an in vivo assessment of the cartilage’s GAG content and thus its quality, is established and validated. dGEMRIC can be performed on standard MRI machines. For this method, the routinely used anionic contrast medium gadopentate-dimeglumine is used which disaggregates after intravenous injection and one negatively charged gadopentate²⁻ (Gd-DTPA²⁻) accrues. The chemical principle of the dGEMRIC method is that GAGs are, because of their redundant carbon and sulfur groups, negatively charged and ionized in physiological pH. The anionic Gd-DTPA²⁻ distributes in the cartilage tissue in reciprocal proportion to the content of negatively charged GAGs. Therefore, the amount of Gd-DTPA²⁻ is low in healthy and, corresponding to reduced GAGs, high in damaged cartilage. Since Gd-DTPA²⁻ shortens the T1 relaxation time, it is possible to calculate the GAG content of cartilage via T1 analysis as the dGEMRIC index (fig. 3).

At several MRI centers, scientific prospective studies on the dGEMRIC technique in knee OA have already been performed. These studies could show that mechanical stress influences the biochemistry of cartilage and hence the dGEMRIC index of the joint. A decreased dGEMRIC index in the medial compared to the lateral knee joint compartment has been shown to be an early indicator of OA after medial meniscectomy [22].

The clarification of the nature of the chronic degradation of cartilage tissue stands in the center of most scientific studies about radiological imaging of knee OA. However, from the pathophysiological point of view, the subchondral bony structures are also considerably involved in the development and course of OA and often responsible for the severity of the disease. In this context, the radiological assessment of a bone marrow edema (BME) plays an outstanding role. Even if the presence of a BME can be considered a typical additional feature of knee OA and can be found in up to 38% of all patients with non-

Fig. 3. Sagittal high-resolution T1-weighted dGEMRIC MRI of the medial femoral condyle. Advanced signs of knee OA with osteophyte formation (arrows) and cartilage destruction. Pseudo-color T1 map of the cartilage after manual segmentation. Dark blue regions represent high GAG content of the cartilage (healthy cartilage), whereas green, yellow, and red regions correspond to low GAG content of the cartilage.

Fig. 4. Detailed visualization of osteophyte formation (arrow) and a rupture of the anterior cruciate ligament (arrowheads) in a 65-year-old patient with knee OA using the isotrope 3D proton-weighted TSE sequence PD SPACE (sampling perfection with application-optimized contrasts using different flip-angle evolutions) on a 3-T MRI machine.

radiographic OA (Kellgren-Lawrence score <2 on radiography but positive for cartilage defects on MRI), it is not very specific since it can also be found in up to 13% of healthy individuals [23]. Nevertheless, in patients with knee OA, the presence of BME is not only associated with a progression of joint space narrowing but can even predict it [24]. Moreover, there is a statistically significant relation between the severity of a 'baseline' BME and an increased cartilage loss in the course of the disease.

Special MRI sequences, e.g. turbo inversion recovery magnitude (TIRM), T2-weighted fat-saturated sequences (T2FS) and contrast medium-enhanced T1-weighted fat-saturated sequences (T1FS) can be used to detect BME (TIRM, T2FS) as well as bone inflammation (T1FS) of involved joints. The application of intravenous contrast medium is helpful in differentiating inflammation-induced BME from BME of other kinds, such as trauma. In a study comparing different MRI sequences, it has been shown that a fat-saturated water-sensitive fast spin echo sequence (e.g. a T2-weighted or proton-weighted sequence) is, in terms of sensitivity for the detection of

BME, superior to a gradient echo sequence (e.g. a dual echo steady state – DESS) [25].

The radiological assessment of the articular ligaments plays an important role in clinical MRI practice. It has been shown that OA changes can be found within 15–20 years in all patients after a complete rupture of the anterior cruciate ligament [26]. Moreover, a full rupture of the anterior cruciate ligament can be found in up to 23% of all patients with manifest painful knee OA. In addition, the above-mentioned BME often occurs concomitantly with chronic injuries of the anterior cruciate ligament in knee OA. The most accurate sequence for the assessment of articular ligaments on a 1.5-T MRI is the T2*-weighted gradient echo sequence MEDIC with fat saturation, whereas on a 3.0-T MRI it is the isotrope 3D proton-weighted (PD) turbo spin echo (TSE) sequence PD SPACE (sampling perfection with application-optimized contrasts using different flip-angle evolutions) (fig. 4).

MRI studies in patients with manifested knee OA have shown that ruptures in the menisci can be found in 91% of all cases in addition to bone, cartilaginous and liga-

Fig. 5. High-resolution color Doppler imaging of synovitis in the lateral knee compartment of a 71-year-old female patient with active knee OA. Early detection of a synovial activation is one of the advantages of ultrasonography using color Doppler imaging technique (arrowheads). F = Femur; T = tibia.

mentous changes [27]. Ruptures of the menisci in knee OA are significantly associated with the presence of cartilage defects and a rapid progression of cartilage loss. In addition, the same risk factors associated with the development of knee OA, namely age, body mass index, female gender, and genetics are applicable for the occurrence of ruptures of the menisci. Therefore, in MRI of patients with a suspicion for knee OA, a detailed assessment of the menisci using appropriate sequences should be included in the study protocol.

Ultrasonography

In several clinical situations of arthropathies of the elderly, ultrasonography can be used for image-guided interventions, e.g. intra-articular injections or biopsies. For radiological assessment of knee OA, ultrasonography plays only a minor role both in clinical routine as well as scientific settings. However, ultrasonographic assessment still represents a good and rapidly available method to judge acute inflammatory changes in knee OA, even in outpatients. Periarticular soft-tissue swelling and a suprapatellar joint effusion can be well diagnosed with ultrasonography. Moreover, the use of the Doppler technique allows, without high costs, real-time visualization and quantification of an inflammatory reaction and thus follow-up of the disease course during therapy. Radiological detection of a synovial activation in case of an inflammation can already be achieved at an early stage with color or power Doppler ultrasonography (PDUS) (fig. 5). However, the PDUS technique is sometimes limited in the de-

Fig. 6. Sagittal high-resolution ultrasonography imaging of a large popliteal Baker cyst in a 69-year-old male patient with recent-onset knee OA.

Fig. 7. Ultrasonographic visualization of the medial femoro-tibial (F/T) joint structures in a 65-year-old female patient with incipient knee OA shows the severe protrusion of the medial meniscus (asterisk) with the development of a large meniscus cyst (arrowheads).

tection of slow flow and flow in small vessels of neoangiogenesis present in synovial inflammation [28]. Therefore, contrast-enhanced ultrasound in knee OA with the use of specific intravenously injected microbubbles can be used and has been shown to improve the detection of vascularity in joints of patients with OA when compared with PDUS. Moreover, contrast-enhanced ultrasound has even been reported to have a higher sensitivity in the de-

tection of vascularity in comparison to contrast-enhanced MRI in patients with knee OA [29].

Hence, articular cartilaginous and periarticular soft-tissue structures can also partially be visualized with ultrasonography, a technique that represents a useful and helpful method to detect early knee OA already in the absence of clear radiographic signs or clinical symptoms. Even bony changes such as periarticular osteophyte formation or calcifications of the soft tissue can be assessed by ultrasonography without X-ray radiation. Even the femoro-tibial joint (the anterior weight-bearing joint surface and Hoffa's fat pad), the medial and lateral joint structures (including peripheral parts of the menisci) as well as a possible presence of a Baker cyst can be assessed (fig. 6, 7) [30]. The main weakness of ultrasonography lies in the impossibility to look at deeper structures as the latter mentioned and that ultrasound has a limited reproducibility due to its dependency on examiner and experi-

ence. Therefore, ultrasonography is more of a good in vivo imaging method in addition to conventional radiography and MR tomography than an independent standalone diagnostic modality.

In conclusion, the demographic development in Western industrialized countries with an increasing proportion of elderly individuals in our population predicts an increase of ageing-related OA of the knee for the next decades. A systematic clinical radiological evaluation of elderly patients with knee OA includes the assessment of the periarticular soft tissue, the cartilaginous thickness, the cartilage volume, possible cartilage defects, the macromolecular network of the hyaline cartilage, BME, menisci, and articular ligaments. Modern imaging modalities, such as MRI and ultrasonography, allow overcoming the limitations of conventional radiography and visualizing the knee structures in great detail to quantitatively assess the severity of knee OA.

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