



Imaging of knee osteoarthritis: a review of multimodal diagnostic approach

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Abstract: Knee osteoarthritis (KOA) is a common chronic condition among the elderly population that significantly affects the quality of life. Imaging is crucial in the diagnosis, evaluation, and management of KOA. This manuscript reviews the various imaging modalities available until now, with a little focus on the recent developments with Artificial Intelligence. Currently, radiography is the first-line imaging modality recommended for the diagnosis of KOA, owing to its wide availability, affordability, and ability to provide a clear view of bony components of the knee. Although radiography is useful in assessing joint space narrowing (JSN), osteophytes and subchondral sclerosis, it has limited effectiveness in detecting early cartilage damage, soft tissue abnormalities and synovial inflammation. Ultrasound is a safe and affordable imaging technique that can provide information on cartilage thickness, synovial fluid, JSN and osteophytes, though its ability to evaluate deep structures such as subchondral bone is limited. Magnetic resonance imaging (MRI) represents the optimal imaging modality to assess soft tissue structures. New MRI techniques are able to detect early cartilage damage measuring the T1ρ and T2 relaxation time of knee cartilage. Delayed gadolinium-enhanced MRI of cartilage, by injecting a contrast agent to enhance the visibility of the cartilage on MRI scans, can provide information about its integrity. Despite these techniques can provide valuable information about the biochemical composition of knee cartilage and can help detect early signs of osteoarthritis (OA), they may not be widely available. Computed tomography (CT) has restricted utility in evaluating OA; nonetheless, weight-bearing CT imaging, using the joint space mapping technique, exhibits potential in quantifying knee joint space width and detecting structural joint ailments. PET-MRI is a hybrid imaging technique able to combine morphological information on bone and soft tissue alterations with the biochemical changes, but more research is needed to justify its high cost and time involved. The new tools of artificial intelligence, including machine learning models, can assist in detecting patterns and correlations in KOA that may be useful in the diagnosis, grading, predicting the need for arthroplasty, and improving surgical accuracy.

Keywords: Knee; magnetic resonance imaging (MRI); ultrasound; radiography; degenerative

Submitted Dec 15, 2022. Accepted for publication Mar 22, 2023. Published online Apr 07, 2023.

doi: 10.21037/qims-22-1392

View this article at: <https://dx.doi.org/10.21037/qims-22-1392>

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Introduction

One of the most common chronic conditions involving the knee is osteoarthritis (KOA), affecting predominantly people at advanced age, more frequently observed in women (1).

Clinical presentation usually manifests with a typical symptomatic triad that includes gradual onset of pain that is worsened with exercise and decreases with rest, rigidity in the morning or after daytime inactivity, and progressive limitation on functional ability, resulting in a significant impact on the quality of life.

This is a slowly progressive multifactorial process with multi-compartmental and multi-tissue alterations, recognized as a disorder of the whole articulation. Aetiology is multifactorial and includes individual risk factors and genetic susceptibility. It seems to be related to the imbalance between catabolic and anabolic changes in the joint tissue, leading to tissue destruction, pain, and physical as well as psychological distress (2).

Various imaging techniques, including radiography, magnetic resonance imaging (MRI), computed tomography (CT), and ultrasound, have been widely used in the assessment of KOA. Each technique has its advantages and limitations, and the optimal approach depends on the clinical scenario and the specific question being asked.

In view of the many existing imaging modalities and most recent developments in the field, the purpose of this review is to summarize the main imaging findings of KOA and the potential role of new tools in the diagnosis and assessment of KOA, to aid in the early detection of these degenerative phenomena.

Radiography

Radiography should be the first-line imaging modality for the diagnosis of osteoarthritis (OA) of the knee, according to the European Alliance of Associations for Rheumatology (EULAR) (3) and the American College of Radiology (ACR) (4). It is considered the gold standard because of its high specificity, wide availability, and low cost. It can directly evaluate the joint space narrowing (JSN), a very specific sign for cartilage loss. Several studies used X-rays to identify risk factors for OA and its progression (2,5).

The most frequent radiographic abnormalities are symmetric JSN, osteophyte formation, subchondral sclerosis, bone remodelling and subluxation, with joint involvement that can be unicompartmental (most frequently

medial tibio-femoral joint), bicompartamental (which may involve the medial tibiofemoral and patellofemoral joints or the lateral tibiofemoral and patellofemoral joints), or tricompartmental (2). Intra-articular free bony bodies and joint effusion are also typical for OA. There are several radiographic classification systems used to evaluate KOA and to measure the chronological course of the disease. The best-known systems are the Kellgren and Lawrence (K/L) one and Osteoarthritis Research Society International (OARSI) atlas criteria. The K/L system, first described in 1957, provides 4 grades of OA severity, from 0 (no evidence of X-ray changes), to 4 (characterized by large osteophytes, marked narrowing of joint space, severe sclerosis and definite deformity of bone ends) (6-9). In 1961 the World Health Organization indicated the K/L method as the standard for grading KOA.

The OARSI atlas are publications about radiographic features of OA in different joints, providing a grading scheme for those features illustrated by imaging examples. In the evaluation of the knee, the OARSI atlas uses semi-quantitative separate scoring for osteophytes (0 to 3) and medial and lateral compartment JSN (0 to 3).

A 2014 review compared the K/L system and OARSI atlas criteria, showing that radiographic tibiofemoral OA was almost twice as common using OARSI atlas criteria compared with the K/L system (10).

After the publication of the K/L method, many other scores tried to grade KOA, giving osteophytes a central role in disease progression. Studies demonstrated that osteophytes are associated with knee pain but not with its severity.

In order to correctly make a differential diagnosis between inflammatory and degenerative conditions when JSN is found on radiography, the literature proposed some diagnostic algorithms. In particular, the presence of bone erosions, osteopenia and soft tissue swelling should suggest an inflammatory process, whereas the presence of osteophytes, bone sclerosis, and subchondral cysts with intact bone margins should suggest a degenerative process (11-14). Furthermore, in degenerative joint disease, the finding of marginal osteophytes is typically used to detect OA, while the findings of JSN, bone sclerosis, and subchondral cysts are used to assess severity. When synovitis is present, cortical bone lesions may occur, thus leading to erosive OA. It seems to be related to an inflammatory trigger causing cartilage and bone destruction with synovial fluid dilution.

Erosive OA may mimic psoriatic arthritis, which

differs from OA because of erosions and bony osteo - and periosteal proliferations, JSN and ankylosis and spondylitis.

Radiography has several drawbacks, such as its inability to directly visualize soft tissues changes: the measurement of JSN has low sensitivity for soft tissue alterations and the presence of subchondral sclerosis, cysts, and osteophytes have low sensitivity for cartilage degeneration; inability to recognize signs of early stage, because when secondary changes occur (cartilage loss, osteophyte formation and meniscal extrusion), the disease is at a late stage; the discordance between radiographic findings and the severity of OA, related to the differences in pathophysiology of distinct OA phenotypes (15,16).

Ultrasound (US)

US is a safe and inexpensive examination, able to visualize several structural knee abnormalities, but requires a skilled operator. EULAR, in 2001, developed guidelines for musculoskeletal US (17) and ACR, in 2012, published recommendations on the use of US in clinical practice (18). US can evaluate several structures involved in the pathophysiology of KOA, such as the bone surface, menisci, synovium. It is therefore possible to visualize synovial inflammation and hypertrophy, extrusions of the menisci, osteophytes and superficial components of the joint cartilage using both grey scale and power Doppler technique (19). The most common ultrasonography findings observed in the KOA are:

- ❖ Joint effusion, which is an increased articular fluid in the joint cavity, widely associated in literature to knee pain in patient with KOA (20,21).
- ❖ Popliteal cysts, a cystic formation between semimembranosus muscles and medial gastrocnemius;
- ❖ Quadriceps tendinopathy, visualized as increased hypoechogenicity, thickening and neo-vascularization of the tendon, which has a greater cross-sectional diameter (22). Studies have also shown that decreased quadriceps tendon thickness appears to be a risk factor for knee pain in KOA (23);
- ❖ Patellar tendinopathy, with thickening of the patellar tendon;
- ❖ Pes anserinus bursitis, an inflammation of the pes anserinus bursa, which appears thickened and hypogenic (24);
- ❖ Other bursitis of the superficial bursae, including prepatellar and infrapatellar ones (25).

In a cross-sectional observational study Kandemirli

et al. evaluated the ultrasound features of KOA and their associations with knee pain, with the evidence of a correlation between Baker's cyst and severity of the pain and functional status scores (26). Thus, considering the discordance between radiographic severity and pain in KOA widely debated in the literature (27), the visualization of soft tissue structures with US could provide more information and explain factors related to pain in OA of the knee. To support this hypothesis, a further study showed that US recognition of synovitis was an important predictive factor for pain in patients with equal radiographic grades of KOA (28).

It has been reported that US has a higher sensitivity than physical examination and similar to histology and MRI in the detection of synovitis and joint effusion (sensitivity of 97%) (19). Moreover, US has a high positive predictive value (ranging from 88% to 100%) for detecting cartilage degeneration, indicating its potential role in the screening setting (29).

However, the limitations of US are mainly its strong dependence on the operator and its inability to evaluate subchondral cysts and bone marrow lesions (30).

Although radiography is the primary method for assessing joint space width, it has poor sensitivity to change over to determine longitudinal progression; a large multicenter study highlighted US role in measuring the joint space width. The authors demonstrated US feasibility in accurately evaluate the joint space width with a negative correlation with age and body mass index and positive with height (31,32).

Currently, US is not recommended as first-line imaging for the diagnosis of KOA, however, it may be helpful as a second-line modality after negative radiographic findings or radiographic joint effusion (17). It has also an important role in guiding therapeutic procedures, such as helping to assess correct needle position in the joint during intra-articular injections.

MRI

MRI currently is not routinely used for diagnosis and management of KOA because of its limited availability, high costs, long scanning time and contraindications in some patients (e.g., pacemaker or other non-compatible MRI implants and devices). However, it is considered the most accurate imaging modality technique for diagnosing knee pathologies for its excellent spatial resolution and its ability to optimally visualize all joint structures, such as the articular

cartilage, synovium, menisci, ligaments, bone, muscles, and tendons, without the use of ionizing radiation (33).

Since conventional MRI sequence protocols allow a morphologic assessment of the changes typical of advanced stages of KOA, the rising of new MRI techniques that investigate objective, quantifiable biomarkers, could identify the cartilage biochemical changes occurring in the early stages, before any morphologic changes.

Articular cartilage lesions

MRI allows an excellent direct evaluation of cartilage and subchondral bone degeneration, closely related to the progression of OA, providing information on morphological changes of cartilage, commonly using two-dimensional intermediate fast spin-echo (2D FSE) or turbo spin-echo sequences, which can accurately depict chondral surface, while Fat saturation images recognize bone marrow alterations (34). On the other hand, it can provide information on biochemical changes, using T2 mapping, T1 ρ , delayed gadolinium enhanced MR of cartilage (dGEMRIC), sodium MR and diffusion-weighted imaging (DWI) sequences (33-35).

Fat suppression sequences are the most commonly used for the visualization of hyaline cartilage because of their wide range of contrast and their low chemical shift artifact, nevertheless they require long acquisition times causing inhomogeneities of magnetic field.

From a morphological point of view the cartilage damage usually occurs in association with degenerative bone marrow lesions, which are subchondral areas of hyperintensity on proton density (PD) sequences and hypointensity on T1 sequences, with a non-cystic aspect; the signal depends mainly on the presence of bone marrow necrosis, fibrosis and only a few on edema. They can increase or decrease over time, and this fluctuation is associated with cartilage loss (36,37). These lesions often occur at the insertions of anterior cruciate ligament (ACL), defined as traction bone marrow lesions, which don't have any correlation with cartilage loss, but with ACL tears. Furthermore, some studies demonstrated that patients with radiographically proven OA and pain were more likely to have these alterations than patients without pain (38), and that fluctuant lesions were seen more commonly in patients with pain (39).

The pathophysiology of the cartilage lesion is characterized by increased permeability of the cartilage matrix, allowing increased fluid content and mobility.

Thus, there is an elevation in hydrodynamic fluid pressure and more stress throughout the matrix, resulting in degeneration of the proteoglycan-collagen matrix and loss of cartilage tissue. Consequently, since the transverse relaxation time (T2) is sensitive to the amount of water and the amount and orientation of the proteoglycan-collagen matrix in the articular cartilage, several studies have shown that T2 relaxation times are correlated to matrix changes in early stages of the OA process (35,40,41).

There are several methods to evaluate the MRI features of KOA, especially the three-dimensional morphology of cartilage. Quantitative methods mostly measure the volume, surface area of cartilage and thickness, with good correlation with clinical symptoms and providing information in predicting the need for total knee arthroplasty (42). In particular, MR can assess the cartilage thickness on T1-weighted fat suppressed images, although this method has some drawbacks because cartilage thickness may vary depending on daytime of acquisition, with a low reproducibility (43) (*Figure 1*). A more precise method, which demonstrated to have a strong correlation with cartilage volume at surgery, is quantifying the volume. This method demonstrated to be a good predictor for clinical outcome and for the need for endoprosthesis (44), and is more sensitive to volume changes than quantification of joint space width with X-ray.

The earliest events in the development of cartilage degeneration in KOA include alterations in the biochemical composition of the extracellular matrix of articular cartilage, which are not adequately detectable by conventional MRI, such as decrease in the size of proteoglycans and glycosaminoglycan (GAG) content and increase in water content and mobility. Thus, early identification of prestructural cartilage damage is essential to understand the development of cartilage degeneration. New emerging MRI sequences are able to show biochemical changes, such as T1 ρ and T2 mapping, which can accurately distinguish between mild OA and healthy cartilage based on differences in cartilage composition that develop even before morphological changes (35).

T1 ρ mapping technique, for instance, based on generation of T1 ρ relaxation time maps, uses a T1 ρ parameter sensitive to low-frequency, slow-motion interactions between motion-restricted water and macromolecules in the extracellular matrix showing great sensitivity to detect the presence of GAG and water content (45-47). A higher T1 ρ value may be determined by depletion of GAG content, which is one of the earliest signs of damaged lesion (48-50). Several studies

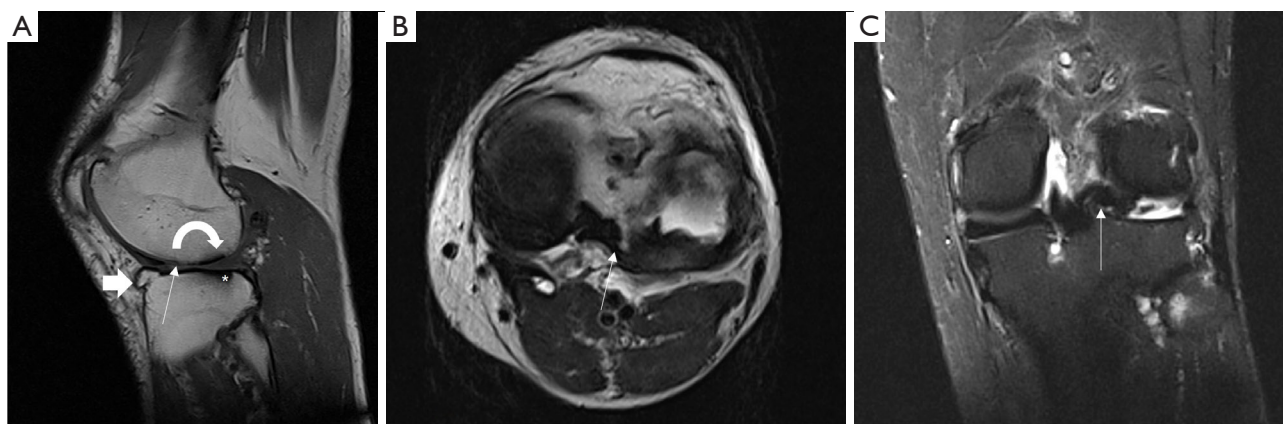


Figure 1 Magnetic resonance images showing advanced degenerative abnormalities. (A) Sagittal T1-weighted image shows loss of the integrity of the external cartilage (straight arrow), subarticular bone abnormalities (asterisk), subarticular abrasion (curved arrow), marginal osteophytes (thick arrow). (B) Axial T2-weighted image shows flap tear of the lateral meniscus posterior horn (arrow). (C) Coronal PD FS sequence shows the meniscal flap in the intercondylar notch (straight arrow) and bone marrow lesion adjacent to ACL distal insertion. PD, proton density; FS, fat saturation; ACL, anterior cruciate ligament.

have also shown that there is a positive correlation between high $T1\rho$ values and the severity of OA, with higher values in advanced stages.

T2 Mapping, using $T2^*$ relaxation times to assess water mobility and organization of macromolecules in cartilage, has been described in several studies for its potential role in detecting pre-morphological changes that occur in the early stages of KOA (51,52).

Another available method of indirectly measuring GAG content in cartilage is Delayed Gadolinium-Enhanced MRI of cartilage (dGEMRIC), based on maps of $T1$ values aimed to evaluate the concentration of gadolinium-based contrast agents (GBCAs), which accumulates, by diffusion, in areas of low GAG concentration (53). Drawbacks include long acquisition times and the use of intravenous injection of GBCAs.

Meniscus and ligament damage

In predisposed individuals (e.g., knee malalignment, obesity, and occupational risks) chronic abnormal biomechanical stress may lead to pathological response of joint tissues, and finally to meniscal damage and extrusion. Knee trauma can also trigger a meniscal damage. Loss of meniscus function can then result in a reduction in cartilage proportion, bone changes including changes in trabecular bone, increased bone mineral density, development of subchondral bone marrow lesions, and

increased malalignment. Meniscal damage is visible by MRI, with sensitivity and specificity in detection of meniscal tear reported in the range of 82–96% (54).

Several studies have shown that meniscal tears in asymptomatic knees are more common than previously thought and that the prevalence of meniscal tears in the knee increases with age, ranging from 19% in women aged 50–59 years to more than 50% in men aged 70–90 years.

These so-called degenerative meniscal tears are typically horizontal cleavage lesions or tears of the body or posterior horn of the medial meniscus and they may be associated with severe meniscal destruction. Degenerative meniscal tears could act as key factors in the early development of KOA, although they are often not directly related to knee pain (55,56). The sagittal plane is the most used for meniscal pathology evaluation; conventional sagittal spin-echo and fast spin-echo PD sequences demonstrated to have almost the same sensitivity and specificity for meniscal tear arthroscopically confirmed (57) (Figure 2).

Modern MRI techniques using delayed gadolinium-enhanced, $T1\rho$ and T2 mapping techniques will hopefully improve our understanding of the significance of early-stage intra-meniscal changes in OA. In particular $T1\rho$ and T2 mapping correlate with OA clinical findings and regional variation of $T1\rho$ in degenerated menisci strongly correlated with water content and moderately with mechanical alterations (58). In a study involving pre-radiographic OA, posterior root/horn radial tears

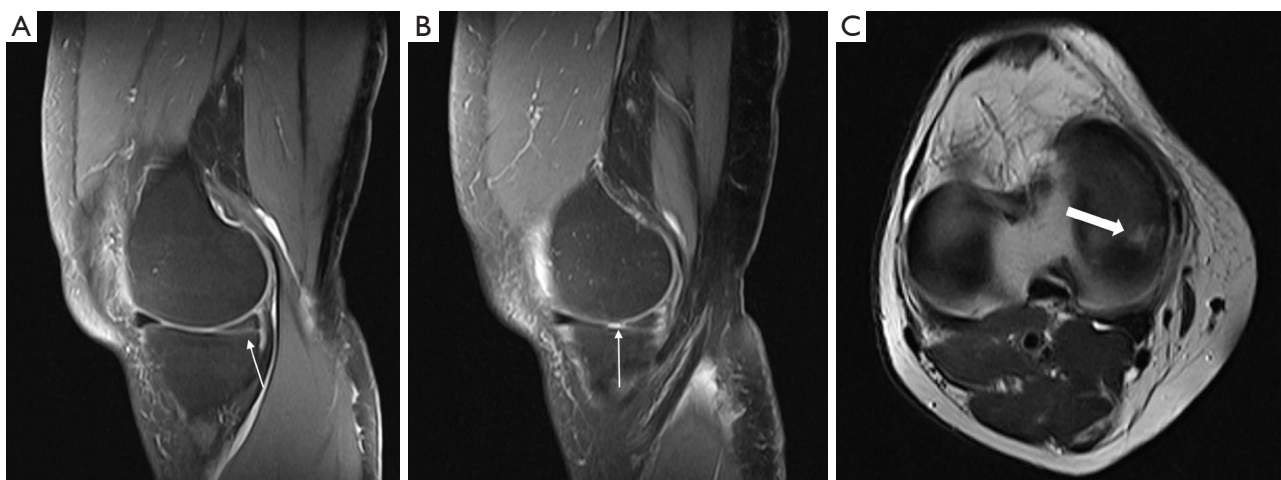


Figure 2 Degeneration of the posterior horn and a radial tear of the medial meniscus. (A) Sagittal PD-Fat sat image shows degeneration of the posterior horn of the medial meniscus (white arrow). (B) Sagittal PD-Fat sat and (C) axial T2-weighted images show a radial tear of the medial meniscus (white arrow). PD, proton density.

of medial meniscus were independent risk factors for an increase of T1 ρ values of medial compartment cartilage, suggesting its potential to recognize early-stage OA (59). In a longitudinal 4-year study, a significant medial meniscal extrusion predicted incident radiographic OA; a greater medial meniscal extrusion at baseline correlated with an earlier onset of OA (60). Meniscal tear appears as a high-intensity signal clearly disrupting the articular surface of the meniscus; on the other hand, if a high intensity signal approaches the articular surface without reaching it, it is not a tear, but an intra-meniscal degenerative process or myxoid degeneration. This clear distinction is only possible in 90% of cases. In the remaining 10% of cases, integration with the physical examination is essential. It is possible that myxoid degeneration is related to aging or normal wear and tear of the joint, but its real cause is currently unknown. In order to preserve meniscal tissue as much as possible, partial meniscectomy has become the preferred surgical procedure for patients with meniscal damage, and the concept of meniscal repair has been taken up and refined, with the introduction of arthroscopic surgical techniques (61,62).

Ligament damage

Ligament injury is a predisposing factor for developing OA, in particular anterior cruciate ligament tears (ACL).

Incidental ACL tears occur in about 20–40% in patients affected by KOA, and seem to be secondary to mechanical impact on notch osteophytes with fibers degeneration,

alterations in notch width and depth.

ACL tears cause alteration in knee biomechanical imbalance, leading to medial loading, increasing the risk of medial KOA; furthermore, ACL is the main restraint against anterior tibial translation.

Traction bone marrow lesions at proximal and distal ACL insertion strongly correlate with ACL pathology (63).

An ACL ganglion cyst is a cystic formation found within the ligament, which is able to stretch it because of an accumulation of mucinous fluid. It's bounded by pseudomembrane and appears fusiform or rounded, with a clear boundary extending along the course of the ACL. The ACL fibers are normally present, but appear thinned due to the mass effect caused by the cyst.

The patients are usually asymptomatic without signs of articular instability at physical examination. In the sagittal plan images, the ACL has a drumstick appearance, while in the coronal and axial plans ACL shows internal signals similar to those of fluids. Differential diagnosis with an ACL lesion or tumour is required.

ACL mucoid degeneration is an uncommon pathological condition; the pathogenesis, prevalence, and association with other intra-articular knee structural damage is not fully understood. The main MRI features suggestive of ACL mucoid degeneration are abnormally thickened and an ill-defined, bulky ACL, increased intra-ligamentous signals (intermediate signal intensity on T1-weighted images, high signal intensity on T2-weighted images, and proton density weighted images) on all sequences interspersed among

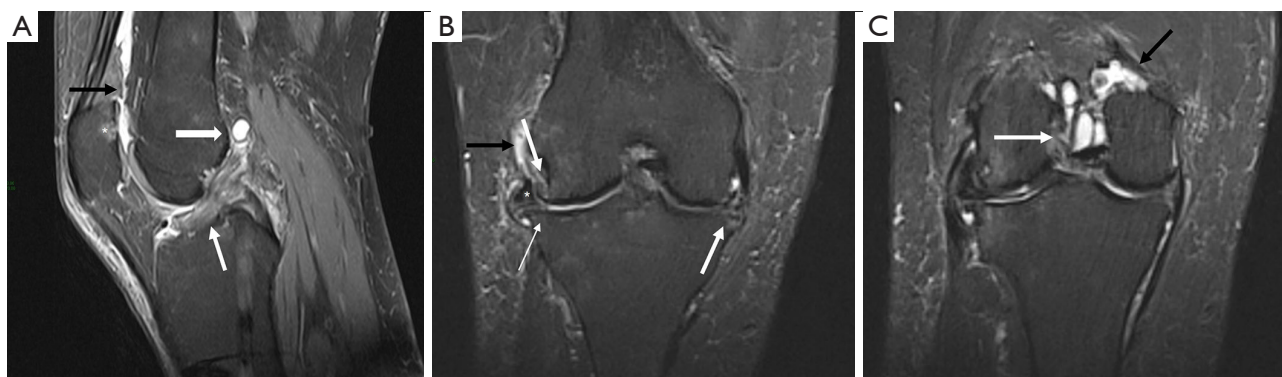


Figure 3 Mucoïd degeneration with a ganglion cyst. (A) Sagittal PD-Fat sat shows a thickened ACL with mucoïd degeneration (white arrow) with a ganglion cyst at the proximal insertion (thick arrow), synovial hypertrophy (black arrow) and full thickness chondral loss with bone marrow lesion (head arrow). (B) The coronal PD-FS plane shows marginal osteophytes production (white arrows), meniscal extrusion (asterisk) and synovial hypertrophy (black arrow). (C) A more posterior coronal PD-FS plane shows multiloculated joint effusion (white arrow) with ganglion cyst (black arrow). PD, proton density; ACL, anterior cruciate ligament; FS, fat saturation.

visible intact fibres and preserved normal ACL orientation and continuity (64) (*Figure 3*). The presence of an ACL tear at baseline increased the risk for cartilage loss in the medial compartment at 30-month follow-up. When adjustment for medial meniscal damage was performed, however, this effect was diluted. In another cohort of 245 elderly individuals (aged 70 to 79 years), a good correlation between any ligament tear in the knee and cartilage loss was found (65).

The posterior cruciate ligament (PCL) plays a role in the kinematics of the knee, mainly for the medial compartment, and a tear with a subsequent deficiency may increase the incidence of KOA.

Synovitis

Progressive OA involves all tissues of the knee joint, including synovia. In fact, several US and MRI studies have shown the presence of synovitis in OA, hardly detected by radiography or clinical examination in the early stages.

The cause of inflammation of the synovium in OA is probably multifactorial. It could be induced by the release of cartilage fragments that activate synovial lining cell, or by calcium phosphate or calcium pyrophosphate dihydrate crystals inciting low-grade inflammatory changes in chronic OA. The production of mediators in synovial tissue leads to the activation of chondrocytes, which produce catabolic factors, and, at the same time, stimulate production of other cytokines, which promotes angiogenesis, perpetuating the cascade of cartilage destruction. Synovitis has been correlated with pain and

associated with disease progression and severity (66,67). In the OA synovitis is not usually randomly distributed, but has a predilection for cartilage-pannus junction. Evaluation of synovial tissue by MRI is usually performed with either non-contrast MRI or after gadolinium administration. In non-contrast MRI a hypointense signal intensity can be found in Hoffa's fat pad in T1-weighted SE sequences, which can be related to synovitis (*Figure 4*). Nevertheless, contrast-enhanced (CE) MRI better differentiates synovitis from joint effusion by increasing the signal intensity of synovitis; in fact, as Loeuille and colleagues demonstrated by comparing three scoring systems for synovitis, only scoring of contrast-enhanced T1-weighted images correlated with microscopically proven synovitis (66). Synovitis can play a role in progression of cartilage loss and in knee pain (68-70).

Most recently a study demonstrated that synovitis may be independent of joint effusion because it was present in 96% of patients with OA and effusion and in 70% of knee without effusion (71).

Computed tomography (CT)

Due to its inability to depicting soft tissue abnormalities, computed tomography has currently limited application in the assessment of OA; however, it plays a role in the visualization of mineralized articular and periarticular structures, useful in the differential diagnosis between calcium pyrophosphate dehydrate deposition disease and other crystal arthropathies, like gout, by identifying typical

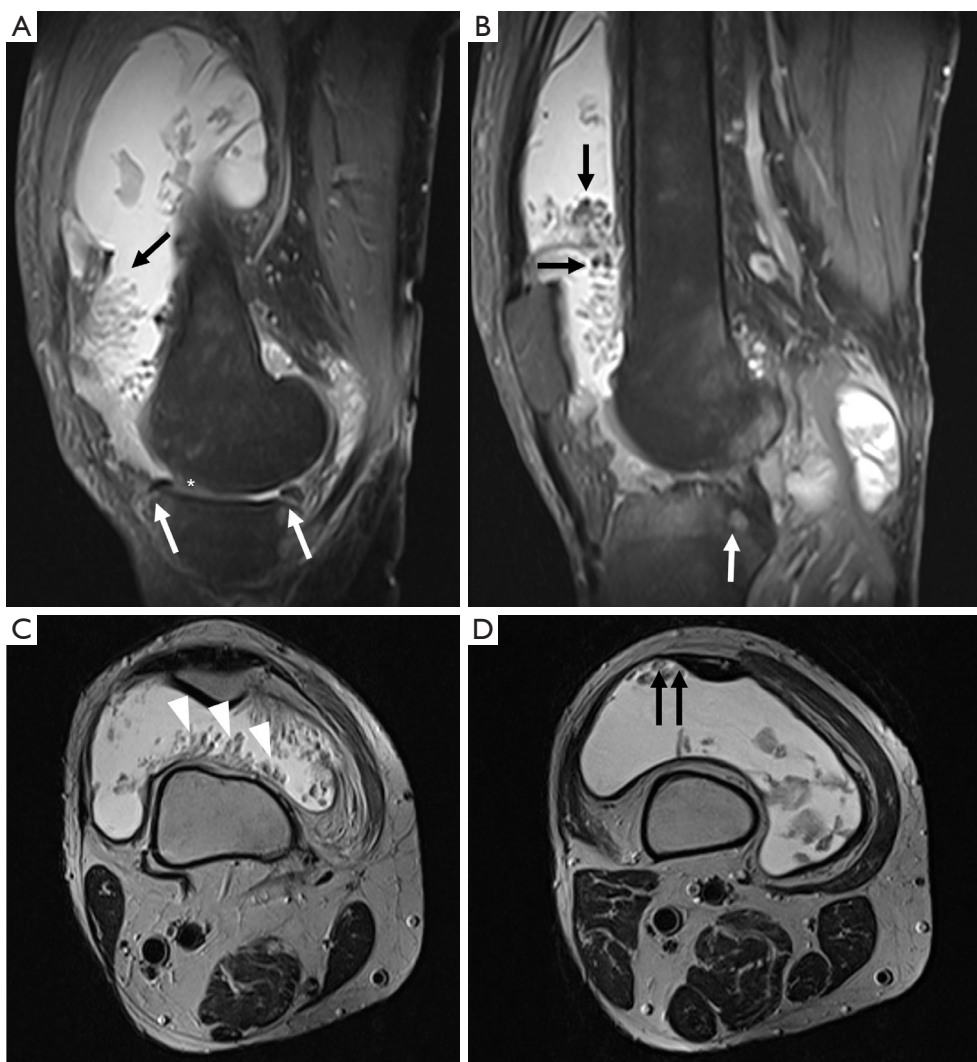


Figure 4 Femorotibial osteoarthritis, large effusion and hypertrophic synovium. (A) Sagittal PD-FS sequence shows advanced femorotibial osteoarthritis, with full thickness cartilage loss (asterisk), large effusion and significant synovial thickening (black arrow). Note also the luxation of medial meniscus and osteophyte formation (white arrows). (B) An inner slice shows also free loose bodies within the joint effusion (black arrows) as also bone marrow lesion on the posterior aspect of the tibial plateau (white arrow). (C) Axial T2 weighted sequence shows the hypertrophic synovium (arrowhead) and (D) free loose bodies (black arrows). PD, proton density; FS, fat saturation.

calcifications. In a similar way to conventional radiography, the presence of subchondral bone cysts, subchondral sclerosis, and osteophyte formations on CT may suggest the early signs of OA.

Furthermore, a technique called “joint space mapping” is able to measure the knee joint space width in in the three dimensions from weight-bearing computed tomography imaging (WB-CT), acquiring images of the standing knee (72). This new technique, easily reproducible, showed a relationship between the three-dimensional distribution

of joint space and structural joint disease.

A recent study compared WB-CT with non-WB-CT and WB-radiography in the three-dimensional analysis for quantification of KJS width, with the evidence of detailed joint space quantification and increased sensitivity in visualizing bone-on-bone appositions, underestimated or undetectable on non-WB-CT and WB-radiography (73).

In recent years, it was also described how dual-layer detector computed tomography is able to offer information regarding the assessment of knee cartilage using a

technique called “calcium-suppressed (CaSupp)” (74). This technology, by removing the calcium component from the images, is able to provide information about the presence of bone marrow edema. It was observed that CaSupp images were able to distinctly identify defect and cartilage thinning, sub-acute bone marrow edema or infrapatellar fat pad edema similarly to the images derived from MRI, in patients with KOA.

Currently, in clinical practice, EULAR recommended CT investigation as a second-line imaging modality for detailed imaging of bone in atypical cases (3).

Positron emission tomography (PET)-MRI

PET, using 2-¹⁸F-fluoro-2-deoxy-D-glucose (¹⁸F-FDG) or fluorine-18-sodium fluoride (¹⁸F-NaF) and reflecting glucose metabolism, is able to identify malignant tumors, inflammation and infection.

Since the cartilage matrix is composed of glycosaminoglycan and chondrocytes use glucose for their metabolism, PET examination may detect cartilage metabolism changes, as it might occur in KOA, with the evidence of periarticular uptake with a SUV significantly higher than those in young and healthy patients, suggesting the presence of synovitis (75).

Currently, several studies have investigated the role of an integrated investigation with PET and MRI, combining the morphological information on bone marrow and soft tissue alteration from MRI, and the biochemical change detected through PET images.

The finding of increased bone blood flow and remodelling proved that subchondral bone changes are present before and during the development of KOA, and this data is helpful on one hand to understand the pathophysiology of OA, on the other hand to guide in the early diagnosis of KOA, leading to improve treatment planning. The great potential of PET-MRI is to match the capability of detect molecular activity with the high resolution of MRI to localize the pathological process. Furthermore, is it possible, for instance, to detect metabolic abnormalities in subchondral bone that appears normal on MRI investigation (76,77). In fact, Kogan *et al.* showed that 37% of subchondral uptake regions at PET actually had a normal appearance on MRI (78).

Furthermore, a cross-sectional study reported, using hybrid PET-MRI technique, that synovitis appear more intense when adjacent to peripheral bone regions with increased metabolic activity (79).

The potential role of PET-MRI in detection of periprosthetic joint infections was investigated in a 2022 prospective study by Henkelmann *et al.*, with the evidence of sensitivity and specificity for periprosthetic infections higher in the soft tissue (100% and 100%) and decreased values for 57% and 50% in the periprosthetic bone margin (57% and 50%) and bone marrow (75% and 33%); however, these first results, while promising, may not justify the high cost and time involved (80).

Artificial intelligence (AI) and machine learning

AI is an emerging technique that uses computers to imitate cognitive function of the human brain. This technology is growing rapidly and is increasing its applications, including in the radiology and orthopedic fields. In the OA of the knee, promising results have been described regarding automatic classification of radiographs for diagnosis of KOA, in predicting the need for total knee arthroplasty (TKA) and in postoperative outcomes, mainly through machine learning (ML) models (81). ML refers to a branch of AI that uses special algorithms that allow the machine to auto-learn from empiric data, in order to achieve improved accuracy during the training phase (82). Various ML models, based on the Kellgren-Lawrence classification system, have been developed for the diagnosis and grading of KOA (83-86). Furthermore, latest available studies and reviews suggest that ML models may be potentially useful in improving surgical accuracy and reducing the cost of manual labor: in fact, some ML algorithms could also be applied to develop models for pre-TKA planning or, for example, prediction of implant dimensions, or 3-D reconstruction of the lower limb to facilitate robotic-assisted TKA.

However, as there are often mismatches between radiological and clinical severity on KOA, these ML algorithms are limited in clinical decision-making, because the decision of surgery is more dependent on the severity of symptoms. Thus, new studies will be needed to include more clinical parameters and overcome these limitations.

More recently, some studies analysed the role of deep learning models for clinical MR in patients affected by KOA; they demonstrated that a transfer learning model is able to automatically segment knee cartilage, with performance comparable to human, using MR images with a small training data size, facilitating the clinical application of quantitative MRI techniques and other prediction models for improved patient treatment planning (83).

Conclusions

To date, conventional radiography is still considered the first-line imaging modality for the evaluation of KOA for its high specificity, wide accessibility, and low cost. MRI, for his high sensitivity and excellent spatial resolution of the soft tissue, remain the mainstay of imaging in assessing disease extent and severity, evaluating all the joint tissues involved in the process and understanding the pathologic changes. Ultrasound may be used as a valuable tool for the evaluation of joint effusion, popliteal cysts and superficial bursae and tendons for the patients who cannot undergo MRI. Important information may also be provided by CT, for instance using weight-bearing CT. New imaging and AI techniques are constantly being developed for the diagnosis and management of KOA. AI techniques have the potential to improve the accuracy of diagnosis, monitor disease progression, and guide treatment decisions. However, further research is needed to validate the effectiveness of these techniques in clinical practice.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: With the arrangement by the Guest Editor and the editorial office, this article has been reviewed by external peers.

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://qims.amegroups.com/article/view/10.21037/qims-22-1392/coif>). The special issue “Imaging of Aging and Age-Related Disorders” was commissioned by the editorial office without any funding or sponsorship. CAM served as the unpaid Guest Editor of the issue and serves as an unpaid editorial board member of *Quantitative Imaging in Medicine and Surgery*. The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Cite this article as: Piccolo CL, Mallio CA, Vaccarino F, Grasso RF, Zobel BB. Imaging of knee osteoarthritis: a review of multimodal diagnostic approach. *Quant Imaging Med Surg* 2023;13(11):7582-7595. doi: 10.21037/qims-22-1392