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Mechanisms of Osteoarthritis in the Knee: MR Imaging Appearance

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Abstract

Osteoarthritis has grown to become a widely prevalent disease that has major implications in both individual and public health. Although originally considered to be a degenerative disease driven by “wear and tear” of the articular cartilage, recent evidence has led to a consensus that osteoarthritis pathophysiology should be perceived in the context of the entire joint and multiple tissues. MRI is becoming an increasingly more important modality for imaging osteoarthritis, due to its excellent soft tissue contrast and ability to acquire morphological and biochemical data. This review will describe the pathophysiology of osteoarthritis as it is associated with various tissue types, highlight several promising MR imaging techniques for osteoarthritis and illustrate the expected appearance of osteoarthritis with each technique.

Keywords

magnetic resonance imaging; osteoarthritis; knee

Osteoarthritis (OA) has become an enormous clinical burden as its impact upon the aging population has become increasingly apparent. OA, characterized as the slow progressive loss of joint function, affects over 27 million adults in the United States alone (1) and has become the most prevalent chronic disease of the elderly (2, 3). Although OA affects various joints throughout the body, including the hip, spine and hand, this review will focus on OA in the context of the knee joint as the vast majority of OA research and imaging is conducted upon the knee joint due to its clinical importance and convenient accessibility.

Although OA was conventionally deemed to be a degenerative disease driven by articular cartilage “wear and tear,” recent evidence has led to a new view that OA pathophysiology should be perceived in the context of the entire joint with involvement of several tissues (4,

5). OA is now understood to be the result of an imbalance between catabolic and anabolic activities in joint tissue, eventually leading to permanent tissue degradation, pain, physical disability and psychological distress (5–7). Tissues of interest associated with OA, in the context of the knee joint, include the articular cartilage, synovium, menisci, ligaments, bone, muscles, and tendons (Fig. 1). Because of the different characteristics of these tissues and their responses to OA, advanced imaging methods sensitive to various types of tissues are needed to properly evaluate OA.

Despite the high prevalence of OA, there are currently no therapies to prevent, cure, or stop its progression. Existing therapeutic approaches are symptomatic and focus upon alleviating pain and maintaining joint function. Nonpharmacologic treatments include physical therapy, bracing, shoe insoles, massage, acupuncture, or for overweight patients, weight loss (8). Pharmacologic treatment options include Aspirin, nonsteroidal anti-inflammatory drugs (NSAIDs), Acetaminophen or joint injections with steroid or hyaluronic acid (8). Surgical interventions include osteochondral fragment pinning or grafting, microfracture, chondrocyte transplantation, unicondylar knee arthroplasty, and at most advanced stages, total knee arthroplasty.

The problem here becomes twofold and circular. Drug development is needed to prevent, cure, or stop the progression of the disease before it reaches irreversible stages; however, the conventional methods often cannot detect OA until it has progressed considerably and can only detect gross morphological changes that occur over long periods. To develop treatments to prevent the progression of OA, we need to understand what subtle changes occur in early-stage OA and how to detect them. More sensitive tests would be instrumental in implementing earlier diagnosis protocols and providing reliable methods for describing the disease process.

Several imaging modalities are currently available to diagnose and evaluate OA. Conventional radiography, which is easily applicable and relatively low in cost, is currently considered to be the “gold standard.” However, it can only detect secondary changes such as osteophyte formation (3, 9), cartilage loss, and meniscal extrusion indirectly, demonstrated through joint space narrowing (10–12). Additionally, clinically significant radiographic changes are often not apparent with conventional radiography for at least one or even two years (13, 14). Standard and power Doppler ultrasound can be used to evaluate inflammation and vascularization; however, ultrasound is user-dependent, and the role of vascularization evaluation is uncertain in OA diagnosis and evaluation (4). Arthrography or combined computed tomography (CT) arthrography can show cartilage surface irregularities, meniscal tears, osteophytes, and subchondral cysts and bodies, but they are invasive by nature and require radiation exposure (3, 4, 15, 16). Digital tomo-synthesis, a technique that acquires an arbitrary number of cross-sectional images from one pass of an X-ray tube, uses multiple acquisition angles but fewer angles than a conventional CT scan. Interest in the application of digital tomosynthesis for musculoskeletal purposes has increased due to its lower dose and potentially lower cost in comparison to CT. Digital tomosynthesis has also demonstrated greater sensitivity and similar specificity in the detection of osteophytes and subchondral cysts to that of conventional radiography; however, some studies have reported that

osteophytes depicted with conventional radiography were more strongly associated with pain overall than those depicted with digital tomosynthesis (17).

Due to its excellent soft tissue contrast and ability to acquire morphological and biochemical data, the importance of MRI in OA imaging is becoming more apparent (5). Advances in MRI technology have improved its ability to detect bone marrow lesions, joint fluid changes, ligamentous and meniscal damage, osteophyte formation, cartilage morphology, as well as macromolecular changes, which often precede morphological changes. Additionally, various semi-quantitative, morphologic MR scoring systems have been developed to reliably evaluate OA in the context of the whole knee joint (7, 18–20).

Early detection and thorough evaluation of OA are critical for understanding the progression of OA. Such methods will contribute to the development of new drugs to prevent, slow or halt OA progression and guide clinical decision-making. This review will describe the pathophysiology of OA associated with various tissue types, highlight several promising MR imaging techniques with which to image OA and illustrate the expected appearance of each technique important to the evaluation of OA.

ARTICULAR CARTILAGE

MR imaging of the articular cartilage is particularly important, as articular cartilage degeneration is often cited as the structural hallmark of OA progression. Conventional MR techniques have typically shown morphological changes, which most likely represent advanced stages of OA. Morphological changes, such as structural degradation and tissue loss, however, are thought to be preceded by biochemical changes of the extracellular matrix (3, 9, 10) stressing the importance of both morphological and biochemical evaluation of the articular cartilage. Commonly used sequences for morphological MR imaging include original and fast or three-dimensional (3D) variations of spin-echo (SE) and gradient-recalled echo (GRE). Physiological imaging techniques that can be used to evaluate biochemical changes in the articular cartilage include T2 mapping, T1ρ, delayed gadolinium enhanced MR of cartilage, sodium MR and diffusion-weighted imaging (DWI).

Morphological MR Imaging

For clinical detection of cartilage lesions, two-dimensional intermediate fast spin-echo (2D FSE) or turbo spin-echo MRI is frequently used. This method results in excellent depiction of the chondral surface outlined by bright fluid. Fat suppression is useful for detection of subchondral bone marrow lesions. However, 2D FSE imaging is limited for quantitation of cartilage thinning due to thick slices and slice gaps.

One method for morphological MR imaging of cartilage that lends itself to segmentation and quantitative analysis is three-dimensional spoiled gradient recalled echo imaging (3D-SPGR) imaging with fat suppression (21, 22). Obtained by spoiling the transverse steady state with semirandom radiofrequency (RF) phase alterations, 3D-SPGR acquires high-resolution images with contrast similar to that of T1-weighted sequences. Disadvantages of 3D-SPGR methods include the long acquisition time and lack of reliable contrast between cartilage and fluid (3, 9). In attempt to overcome these drawbacks, several techniques have

been developed, including driven equilibrium Fourier transport (DEFT), 3D dual-echo steady state (3D DESS), balanced steady-state free precession (bSSFP) with fat suppression and a few of its derivatives such as vastly interpolated projection reconstruction (VIPR) and fluctuating equilibrium MR (FEMR). DEFT imaging preserves signal from cartilage while increasing that of synovial fluid, allowing for a high cartilage signal-to-noise ratio (SNR), high synovial fluid signal with a short TR and improved full cartilage thickness imaging. DEFT imaging exploits the T2/T1 tissue ratio by returning the magnetization to the z-axis with a 90-degree pulse, resulting in signal enhancement of tissues with long T1 relaxation times (23).

Recently, many large studies including the Osteoarthritis Initiative, have used 3D DESS as the standard method for cartilage morphology, segmentation, and quantitation. The 3D DESS imaging acquires images with nearly isotropic resolution, high SNR and high cartilage-to-fluid contrast at a reduced scan time (24, 25). The 3D DESS images are obtained by acquiring two or more gradient echoes, separating them with a refocusing pulse and combining the image data to obtain higher T2* weighting (26).

bSSFP, which is also known as true fast imaging with steady-state precession (true FISP), fast imaging employing steady-state acquisition (FIESTA) or balanced fast field echo imaging with its variants VIPR and FEMR, is another group of techniques that acquires images with great fluid-to-cartilage contrast by increasing signal intensity of fluid while preserving that of cartilage.

By combining bSSFP imaging with 3D-radial k-space acquisition and using T2/T1 weighted contrast and isotropic resolution, VIPR produces images with high tissue contrast and reduced artifact at shorter scanning times (27). FEMR generates images with high SNR and high synovial fluid signal intensity while maintaining high cartilage signal intensity based upon the T1/T2 ratio in the tissues (27). The 3D fast spin echo (FSE) (GE Healthcare: Cube, Philips: VISTA, Siemens: SPACE) acquires isotropic images that have increased SNR and SNR efficiency with proton density (PD) or T2-weighted contrast. The 3D-FSE images are acquired by using a restoring pulse and variable flip-angle RF pulses applied along an echo train length producing a pseudo steady state (28–31).

Ultrashort TE (uTE) imaging uses microsecond TEs to allow visualization of tissues with short T2 relaxation times. By using echo times (TE) that are 20–50 times shorter than those applied in conventional T2 sequences, uTE can obtain high signal from traditionally low signal tissues. This advantage has allowed the separate cartilage layers and meniscal zones to be visualized (32–34). Additionally, studies have shown that uTE-T2* values are correlated with indices sensitive to collagen microstructure, suggesting that mapping of articular cartilage with uTE-T2* may be sensitive to matrix degeneration (35).

Table 1 gives an overview of the advantages and disadvantages of various sequences used for morphological imaging. Although these morphological imaging techniques have advantages in terms of resolution, contrast and acquisition time, they are limited in their lack of biochemical data acquisition.

Physiological MR Imaging

Advancements in MR imaging have allowed for more reliable information regarding the macromolecular changes that accompany the OA process, often occurring before morphological changes. The cartilage degradation that occurs with OA is characterized by an increase in permeability of the cartilage matrix, which allows for greater water content and mobility. These changes result in increased hydrodynamic fluid pressure and an increased stress throughout the matrix, leading to proteoglycan-collagen matrix degeneration and cartilage tissue loss (9, 36).

Transverse relaxation time (T2) has been shown to be sensitive to the quantity of water and the quantity and orientation of the proteoglycan-collagen matrix in articular cartilage (37, 38). T2 relaxation values have also been correlated with cartilage damage, which allows for the creation of T2 maps to detect early biochemical changes (39). T2 mapping is accomplished with a multiecho multispin sequence to decrease exam time while signal levels are fitted to mono or multiple decaying exponentials, depending upon the number of components of the tissue that are expected to have different T2 relaxation times (40). Various promising studies have demonstrated that T2 relaxation times are correlated to both water and proteoglycan-collagen matrix changes in early stages of the OA process (41–46) (Fig. 2).

T1 ρ , or spin lattice relaxation in the rotating frame, has also been suggested to be a promising method in the detection of early OA changes (45, 46). T1 ρ is accomplished by tipping the magnetization into the transverse plane and “spin-locking” it with a constant RF field. It is sensitive to the interactions between motion-restricted water molecules and the surrounding macromolecules, such as proteoglycan in cartilage (47, 48). With cartilage degeneration, proteoglycan decreases, affecting this physiochemical interaction, and T1 ρ has been regarded as an effective tool with which to evaluate early OA development (47, 48) (Fig. 3).

Delayed gadolinium-enhanced MR imaging (dGEMRIC), similar to T1 ρ , exploits the ability to detect proteoglycan depletion associated with early OA. dGEMRIC imaging is made possible by exploiting the negative fixed charged density associated within the extracellular matrix of cartilage. dGEMRIC acquires a reflection of the proteoglycan content of the cartilage upon the principle that the gadolinium ions injected into the matrix are distributed relative to the negatively charged proteoglycan concentration. Negatively charged Gd(DTPA)₂ are repelled from regions of high proteoglycan concentration while they aggregate in regions of proteoglycan depletion. The application of T1, 3D SPGR with variable flip angles or bSSFP sequences following the Gd(DTPA)₂ administration results in an indirect measure of proteoglycan concentration. The dGEMRIC index refers to the T1 measurements generated, with a low dGEMRIC index corresponding to a low T1 signal intensity, indicating a high Gd(DTPA)₂ concentration and proteoglycan depletion (49, 50) (Fig. 4).

Sodium imaging, like dGEMRIC, has demonstrated potential in detecting proteoglycan depletion by exploiting the negative fixed charged density within the extracellular matrix of cartilage. As positively charged sodium ions associate with negatively charged

proteoglycans, proteoglycan depletion is reflected as a decrease in sodium signal (51–53). For these reasons, sodium imaging has demonstrated to be sensitive to small changes in proteoglycan depletion and provides a promising technique for evaluating early stage OA (54) (Fig. 5). However, due to the low sodium concentration compared with hydrogen and the low gyromagnetic ratio, sodium imaging is best done at a high field (3 Tesla [T] or 7T) to improve SNR and resolution.

Diffusion-weighted imaging (DWI) is another method with which to image OA progression. DWI provides valuable information regarding the structure and organization of cartilage by applying multiple diffusion-sensitive gradients to evaluate water molecule orientation. Recent studies with diffusion imaging have shown that the apparent diffusion coefficient (ADC), a quantitative measurement that varies according to the structure and physiological state of the tissues, correlates with the proteoglycan content in cartilage (55, 56). Staroswiecki et al were able to simultaneously estimate the ADC and the T2 relaxation times of cartilage from two acquisitions by modifying the spoiler gradient area and flip angle of the DESS sequence, renamed 3D quantitative DESS (3D qDESS) (24). From these images with different diffusion weightings, they were able to create high-resolution T2 and ADC maps without blurring or distortion from a scan with reasonable time (Fig. 6) (24).

SYNOVIUM

Although often regarded as secondary to cartilage degradation, recent evidence shows an increasingly integrated role of synovial tissue in OA (57, 58). Inflammation of the synovium, or synovitis, has been well correlated with pain in OA (59, 60) and has also been associated with OA progression (61) and severity (62, 63). Evaluation of the synovial tissue with MR imaging is primarily accomplished with non-contrast-enhanced (CE) MR imaging and gadolinium (Gd)-based CE MR imaging. Non-CE MR imaging such as T1-weighted SE sequences has been used to correlate synovitis with hypointense signal intensity in Hoffa's fat pad (64). In fat-suppressed PD or T2-weighted SE sequences, hyperintense signal intensity changes in Hoffa's fat pad have been demonstrated to be surrogate markers for joint-wide synovitis (65, 66). However, CE MRI better differentiates synovitis from joint effusion. By enhancing synovium signal intensity and maintaining the hypointensity of effusion with the administration of Gd, CE-MR imaging is better able to differentiate between the two pathologies than non-CE MR imaging, in which synovitis and joint effusion are both represented as hyperintense signals (Fig. 7). Loeuille et al recently demonstrated that microscopic synovitis is not correlated with non-CE MRI (67), while Roemer et al. showed that signal intensity changes in Hoffa's fat pad on non-CE MR imaging were less specific for peripatellar synovitis than changes seen with CE sequences (68). Additionally, other studies have demonstrated the correlation between CE-MR detected synovitis and histology (63, 67). Most recently and using both CE-MR and non-CE MR, Roemer et al showed that, in patients with OA, synovitis was present in 96.3% of knee joints with effusion and in 70% of those knees without an effusion (69). This finding may indicate that synovial pathology may be independent of joint effusion and a more reliable predictor of pathology. Administration of contrast agents, however, is associated with increased cost and scan time, risk of nephrogenic systemic fibrosis and possible allergic

reactions. Such disadvantages of CE MR imaging highlight the need for research into more sensitive and specific non-CE MR imaging methods.

MENISCI

The menisci are fibrocartilagenous structures that serve to provide shock absorption and load transmission between the femur and tibia in both the medial and lateral compartments of the knee joint (70, 71). Meniscal injuries are largely thought to be a predisposing factor to OA, and it has been shown that partial and total meniscectomies increase the strain on articular cartilage, resulting in dynamic deformation in the knee joint (72, 73).

The sagittal plane is most frequently used for meniscal pathology evaluation with MR imaging, but the coronal (74, 75) and axial (76, 77) planes have also been demonstrated to improve the diagnosis of specific types of meniscal tears. Although several different MR imaging sequences can be used to evaluate meniscal pathology, it is important to keep echo times short to improve the SNR, decrease susceptibility and artifact, acquire more slices per scan and keep scan time to a minimum (78). In comparing conventional sagittal spin-echo and fast spin-echo PD sequences, they were found to be not statistically different in their sensitivity and specificity of evaluating arthroscopically confirmed meniscal tears. The sensitivity and specificity of the spin-echo sequence was reported to have a sensitivity of 90% and specificity of 90% while the fast spin echo had a sensitivity of 84% and specificity of 94% specificity (79).

Several technological advancements in MR imaging have greatly improved the visualization and diagnosis of meniscal pathology. Imaging at higher field strengths (1.5 and 3.0T) has increased the SNR achievable while maintaining comparable sensitivity and specificity values (80–82). Parallel imaging techniques have also enabled drastic reduction in scan time without loss to sensitivity, specificity, and accuracy, by exploiting the spatially-varying sensitivity profiles of phased array coil elements and extending the image field of view (FOV) with multiple channels (83, 84). Imaging with uTE, as previously mentioned, has provided great value to the assessment of the menisci and other tissues with short T2 relaxation times by allowing the visualization meniscal infrastructure (34, 35, 39) (Fig. 8). Additionally, recent studies have demonstrated that uTE-T2* mapping of the meniscus provides the ability to detect meniscal tears and may be sensitive to subclinical meniscal damage subsequent to joint injury (85).

T1 ρ and T2 measurements have shown to correlate with clinical OA findings (86), and regional variations of T1 ρ and T2 in degenerated menisci have been found to strongly correlate with water content and moderately correlate with mechanical properties (87, 88). Such information can be instrumental in OA diagnosis as it can be related to the physiological properties of the meniscus. These findings help to further elucidate the role menisci play in OA and indicate that degenerative, biochemical changes in the menisci may be detectable using MRI.

LIGAMENTS

Ligament injury is often regarded as a predisposing factor for OA. Damage to ligaments, especially the anterior cruciate ligament (ACL), can predispose patients to early development of OA (89, 90). Additionally, knee range of motion deficits, regardless of meniscal status, are thought to be ligament-related and have been correlated with a higher radiographic OA prevalence after ACL reconstruction (91). While MR imaging allows for great visualization of the ACL and posterior cruciate ligament (PCL), the acquired images may be obscured by intra-articular pathologies. Similarly, the imaging of the lateral collateral ligament (LCL) and the medial collateral ligament (MCL), while also important, can be limited by the complex anatomy of the posterolateral and posteromedial corners. Despite these limitations, MR imaging is still the modality of choice for the evaluation of ligaments because of its flexibility and excellent soft tissue contrast.

CONCLUSION

The importance of diagnosing, treating, and preventing OA is becoming increasingly clear as its prevalence continues to grow. Research continues to support the notion that OA is a complex disease that involves the entire joint, indicating that the assessment of various tissue structures is most ideal for evaluation. Although supplemental modalities may be implicated to further assess OA, MR imaging, with its excellent soft tissue contrast and ability to acquire morphological and biochemical data, is a promising technique with which to comprehensively evaluate an osteoarthritic joint and to inform a patient's treatment regimen. While further investigation is needed to fully comprehend the mechanisms of OA and its MR imaging appearance, the morphological and biochemical imaging methods presented in this review reveal significant understanding of the progression of the disease.

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REFERENCES

1. Lawrence RC, Felson DT, Helmick CG, et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. Part II. *Arthritis Rheum.* 2008; 58:26–35. [PubMed: 18163497]
2. Felson DT, Zhang Y, Hannan MT, et al. The incidence and natural history of knee osteoarthritis in the elderly. The Framingham Osteoarthritis Study. *Arthritis Rheum.* 1995; 38:1500–1505. [PubMed: 7575700]
3. Choi JA, Gold GE. MR imaging of articular cartilage physiology. *Magn Reson Imaging Clin N Am.* 2011; 19:249–282. [PubMed: 21665090]
4. Bijlsma JW, Berenbaum F, Lafeber FP. Osteoarthritis: an update with relevance for clinical practice. *Lancet.* 2011; 377:2115–2126. [PubMed: 21684382]
5. Roemer FW, Crema MD, Trattnig S, Guermazi A. Advances in imaging of osteoarthritis and cartilage. *Radiology.* 2011; 260:332–354. [PubMed: 21778451]
6. Eyre DR. Collagens and cartilage matrix homeostasis. *Clin Orthop Relat Res.* 2004; (Suppl):S118–S122. [PubMed: 15480053]

7. Felson DT, Niu J, Guermazi A, et al. Correlation of the development of knee pain with enlarging bone marrow lesions on magnetic resonance imaging. *Arthritis Rheum.* 2007; 56:2986–2992. [PubMed: 17763427]
8. Zhang W, Moskowitz RW, Nuki G, et al. OARSI recommendations for the management of hip and knee osteoarthritis, Part II: OARSI evidence-based, expert consensus guidelines. *Osteoarthritis Cartilage.* 2008; 16:137–162. [PubMed: 18279766]
9. Bruno, MA.; Gold, GE.; Mosher, TJ. *Arthritis in color: advanced imaging of arthritis.* Philadelphia: Elsevier Saunders; 2009. Technical considerations for clinical MRI of arthritis; p. 153-192.
10. Boegard T, Rudling O, Petersson I, Jonsson K. Correlation between radiographically diagnosed osteophytes and magnetic resonance detected cartilage defects in the tibiofemoral joint. *Ann Rheum Dis.* 1998; 57:401–407. [PubMed: 9797566]
11. Boegard T, Jonsson K. Radiography in osteoarthritis of the knee. *Skeletal Radiol.* 1999; 28:605–615. [PubMed: 10591922]
12. Hunter DJ. Imaging insights on the epidemiology and pathophysiology of osteoarthritis. *Rheum Dis Clin North Am.* 2009; 35:447–463. [PubMed: 19931798]
13. Boegard TL, Rudling O, Petersson IF, Jonsson K. Joint space width of the tibiofemoral and of the patellofemoral joint in chronic knee pain with or without radiographic osteoarthritis: a 2-year follow-up. *Osteoarthritis Cartilage.* 2003; 11:370–376. [PubMed: 12744943]
14. Vignon E, Conrozier T, Hellio Le Graverand MP. Advances in radiographic imaging of progression of hip and knee osteoarthritis. *J Rheumatol.* 2005; 32:1143–1145. [PubMed: 15977349]
15. Gold GE, Burstein D, Dardzinski B, Lang P, Boada F, Mosher T. MRI of articular cartilage in OA: novel pulse sequences and compositional/ functional markers. *Osteoarthritis Cartilage.* 2006; (Suppl A):A76–A86. [PubMed: 16716605]
16. Coumas JM, Palmer WE. Knee arthrography. Evolution and current status. *Radiol Clin North Am.* 1998; 36:703–728. [PubMed: 9673648]
17. Hayashi D, Xu L, Roemer FW, et al. Detection of osteophytes and subchondral cysts in the knee with use of tomosynthesis. *Radiology.* 2012; 263:206–215. [PubMed: 22438445]
18. Hunter DJ, Lo GH, Gale D, Grainger AJ, Guermazi A, Conaghan PG. The reliability of a new scoring system for knee osteoarthritis MRI and the validity of bone marrow lesion assessment: BLOKS (Boston Leeds Osteoarthritis Knee Score). *Ann Rheum Dis.* 2008; 67:206–211. [PubMed: 17472995]
19. Kornaat PR, Ceulemans RY, Kroon HM, et al. MRI assessment of knee osteoarthritis: Knee Osteoarthritis Scoring System (KOSS)—inter-observer and intra-observer reproducibility of a compartment-based scoring system. *Skeletal Radiol.* 2005; 34:95–102. [PubMed: 15480649]
20. Peterfy CG, Guermazi A, Zaim S, et al. Whole-Organ Magnetic Resonance Imaging Score (WORMS) of the knee in osteoarthritis. *Osteoarthritis Cartilage.* 2004; 12:177–190. [PubMed: 14972335]
21. Cicuttini F, Forbes A, Asbeutah A, Morris K, Stuckey S. Comparison and reproducibility of fast and conventional spoiled gradient-echo magnetic resonance sequences in the determination of knee cartilage volume. *J Orthop Res.* 2000; 18:580–584. [PubMed: 11052494]
22. Eckstein F, Westhoff J, Sittek H, et al. In vivo reproducibility of three-dimensional cartilage volume and thickness measurements with MR imaging. *AJR Am J Roentgenol.* 1998; 170:593–597. [PubMed: 9490936]
23. Gold GE, Fuller SE, Hargreaves BA, Stevens KJ, Beaulieu CF. Driven equilibrium magnetic resonance imaging of articular cartilage: initial clinical experience. *J Magn Reson Imaging.* 2005; 21:476–481. [PubMed: 15779031]
24. Staroswiecki E, Granlund KL, Alley MT, Gold GE, Hargreaves BA. Simultaneous estimation of T(2) and apparent diffusion coefficient in human articular cartilage in vivo with a modified three-dimensional double echo steady state (DESS) sequence at 3 T. *Magn Reson Med.* 2012; 67:1086–1096. [PubMed: 22179942]
25. Hardy PA, Recht MP, Piraino D, Thomasson D. Optimization of a dual echo in the steady state (DESS) free-precession sequence for imaging cartilage. *J Magn Reson Imaging.* 1996; 6:329–335. [PubMed: 9132098]

26. Eckstein F, Hudelmaier M, Wirth W, et al. Double echo steady state magnetic resonance imaging of knee articular cartilage at 3 Tesla: a pilot study for the Osteoarthritis Initiative. *Ann Rheum Dis*. 2006; 65:433–441. [PubMed: 16126797]
27. Kijowski R, Blankenbaker DG, Klaers JL, Shinki K, De Smet AA, Block WF. Vastly undersampled isotropic projection steady-state free precession imaging of the knee: diagnostic performance compared with conventional MR. *Radiology*. 2009; 251:185–194. [PubMed: 19221057]
28. Gold GE, Busse RF, Beehler C, et al. Isotropic MRI of the knee with 3D fast spin-echo extended echo-train acquisition (XETA): initial experience. *AJR Am J Roentgenol*. 2007; 188:1287–1293. [PubMed: 17449772]
29. Friedrich KM, Reiter G, Kaiser B, et al. High-resolution cartilage imaging of the knee at 3T: basic evaluation of modern isotropic 3D MR-sequences. *Eur J Radiol*. 2011; 78:398–405. [PubMed: 20138723]
30. Stevens KJ, Busse RF, Han E, et al. Ankle: isotropic MR imaging with 3D-FSE-cube—initial experience in healthy volunteers. *Radiology*. 2008; 249:1026–1033. [PubMed: 19011194]
31. Stevens KJ, Wallace CG, Chen W, Rosenberg JK, Gold GE. Imaging of the wrist at 1.5 Tesla using isotropic three-dimensional fast spin echo cube. *J Magn Reson Imaging*. 2011; 33:908–915. [PubMed: 21448957]
32. Gatehouse PD, He T, Puri BK, Thomas RD, Resnick D, Bydder GM. Contrast-enhanced MRI of the menisci of the knee using ultrashort echo time (UTE) pulse sequences: imaging of the red and white zones. *Br J Radiol*. 2004; 77:641–647. [PubMed: 15326040]
33. Gold GE, Bergman AG, Pauly JM, et al. Magnetic resonance imaging of knee cartilage repair. *Top Magn Reson Imaging*. 1998; 9:377–392. [PubMed: 9894740]
34. Robson MD, Gatehouse PD, Bydder M, Bydder GM. Magnetic resonance: an introduction to ultrashort TE (UTE) imaging. *J Comput Assist Tomogr*. 2003; 27:825–846. [PubMed: 14600447]
35. Williams A, Qian Y, Bear D, Chu CR. Assessing degeneration of human articular cartilage with ultra-short echo time (UTE) T2* mapping. *Osteoarthritis Cartilage*. 2010; 18:539–546. [PubMed: 20170769]
36. Borthakur A, Mellon E, Niyogi S, Witschey W, Kneeland JB, Reddy R. Sodium and T1rho MRI for molecular and diagnostic imaging of articular cartilage. *NMR Biomed*. 2006; 19:781–821. [PubMed: 17075961]
37. Nieminen MT, Rieppo J, Toyraas J, et al. T2 relaxation reveals spatial collagen architecture in articular cartilage: a comparative quantitative MRI and polarized light microscopic study. *J Magn Reson Imaging*. 2001; 46:487–493.
38. Luske S, Claassen H, Gehrke T, et al. Evaluation of water content by spatially resolved transverse relaxation times of human articular cartilage. *Magn Reson Imaging*. 2000; 18:423–430. [PubMed: 10788720]
39. Nishioka H, Hirose J, Nakamura E, et al. T1rho and T2 mapping reveal the in vivo extracellular matrix of articular cartilage. *J Magn Reson Imaging*. 2012; 35:147–155. [PubMed: 21990043]
40. Smith HE, Mosher TJ, Dardzinski BJ, et al. Spatial variation in cartilage T2 of the knee. *J Magn Reson Imaging*. 2001; 14:50–55. [PubMed: 11436214]
41. Dardzinski BJ, Mosher TJ, Li S, Van Slyke MA, Smith MB. Spatial variation of T2 in human articular cartilage. *Radiology*. 1997; 205:546–550. [PubMed: 9356643]
42. Mosher TJ, Dardzinski BJ, Smith MB. Human articular cartilage: influence of aging and early symptomatic degeneration on the spatial variation of T2—preliminary findings at 3 T. *Radiology*. 2000; 214:259–266. [PubMed: 10644134]
43. Mosher TJ, Smith H, Dardzinski BJ, Schmithorst VJ, Smith MB. MR imaging and T2 mapping of femoral cartilage: in vivo determination of the magic angle effect. *AJR Am J Roentgenol*. 2001; 177:665–669. [PubMed: 11517068]
44. Poon CS, Henkelman RM. Practical T2 quantitation for clinical applications. *J Magn Reson Imaging*. 1992; 2:541–553. [PubMed: 1392247]
45. Mosher TJ, Zhang Z, Reddy R, et al. Knee articular cartilage damage in osteoarthritis: analysis of MR image biomarker reproducibility in ACRIN-PA 4001 multicenter trial. *Radiology*. 2011; 258:832–842. [PubMed: 21212364]

46. Wheaton AJ, Casey FL, Gougoutas AJ, et al. Correlation of T1rho with fixed charge density in cartilage. *J Magn Reson Imaging*. 2004; 20:519–525. [PubMed: 15332262]
47. Akella SV, Regatte RR, Gougoutas AJ, et al. Proteoglycan-induced changes in T1rho-relaxation of articular cartilage at 4T. *Magn Reson Imaging*. 2001; 46:419–423.
48. Li X, Han ET, Ma CB, Link TM, Newitt DC, Majumdar S. In vivo 3T spiral imaging based multi-slice T(1rho) mapping of knee cartilage in osteoarthritis. *Magn Reson Imaging*. 2005; 54:929–936.
49. Filidoro L, Dietrich O, Weber J, et al. High-resolution diffusion tensor imaging of human patellar cartilage: feasibility and preliminary findings. *Magn Reson Imaging*. 2005; 53:993–998.
50. Stanisiz GJ, Henkelman RM. Gd-DTPA relaxivity depends on macromolecular content. *Magn Reson Imaging*. 2000; 44:665–667.
51. Borthakur A, Shapiro EM, Beers J, Kudchodkar S, Kneeland JB, Reddy R. Sensitivity of MRI to proteoglycan depletion in cartilage: comparison of sodium and proton MRI. *Osteoarthritis Cartilage*. 2000; 8:288–293. [PubMed: 10903883]
52. Wheaton AJ, Borthakur A, Shapiro EM, et al. Proteoglycan loss in human knee cartilage: quantitation with sodium MR imaging—feasibility study. *Radiology*. 2004; 231:900–905. [PubMed: 15163825]
53. Wang L, Wu Y, Chang G, et al. Rapid isotropic 3D-sodium MRI of the knee joint in vivo at 7T. *J Magn Reson Imaging*. 2009; 30:606–614. [PubMed: 19711406]
54. Gold, GE.; Koo, S.; Staroswiecki, E.; Watkins, R.; Hargreaves, B.; Bangerter, NK. Proceedings of the 17th Annual Meeting of ISMRM. Honolulu, Hawai'i: 2009. In vivo sodium MRI at 3.0T of patients with previous ACL injury.
55. Raya JG, Arnoldi AP, Weber DL, et al. Ultra-high field diffusion tensor imaging of articular cartilage correlated with histology and scanning electron microscopy. *MAGMA*. 2011; 24:247–258. [PubMed: 21630094]
56. Raya JG, Melkus G, Adam-Neumair S, et al. Change of diffusion tensor imaging parameters in articular cartilage with progressive proteoglycan extraction. *Invest Radiol*. 2011; 46:401–409. [PubMed: 21427593]
57. Sellam J, Berenbaum F. The role of synovitis in pathophysiology and clinical symptoms of osteoarthritis. *Nat Rev Rheumatol*. 2010; 6:625–635. [PubMed: 20924410]
58. Hayashi D, Roemer FW, Katur A, et al. Imaging of synovitis in osteoarthritis: current status and outlook. *Semin Arthritis Rheum*. 2011; 41:116–130. [PubMed: 21295331]
59. Brandt KD, Dieppe P, Radin E. Etiopathogenesis of osteoarthritis. *Med Clin North Am*. 2009; 93:1–24. xv. [PubMed: 19059018]
60. Myers SL, Brandt KD, Ehlich JW, et al. Synovial inflammation in patients with early osteoarthritis of the knee. *J Rheumatol*. 1990; 17:1662–1669. [PubMed: 2084242]
61. Ledingham J, Regan M, Jones A, Doherty M. Factors affecting radiographic progression of knee osteoarthritis. *Ann Rheum Dis*. 1995; 54:53–58. [PubMed: 7880123]
62. Smith MD, Triantafillou S, Parker A, Youssef PP, Coleman M. Synovial membrane inflammation and cytokine production in patients with early osteoarthritis. *J Rheumatol*. 1997; 24:365–371. [PubMed: 9034998]
63. Loeuille D, Chary-Valckenaere I, Champigneulle J, et al. Macroscopic and microscopic features of synovial membrane inflammation in the osteoarthritic knee: correlating magnetic resonance imaging findings with disease severity. *Arthritis Rheum*. 2005; 52:3492–3501. [PubMed: 16255041]
64. Fernandez-Madrid F, Karvonen RL, Teitge RA, Miller PR, An T, Negendank WG. Synovial thickening detected by MR imaging in osteoarthritis of the knee confirmed by biopsy as synovitis. *Magn Reson Imaging*. 1995; 13:177–183. [PubMed: 7739358]
65. Hill CL, Gale DG, Chaisson CE, et al. Knee effusions, popliteal cysts, and synovial thickening: association with knee pain in osteoarthritis. *J Rheumatol*. 2001; 28:1330–1337. [PubMed: 11409127]
66. Hill CL, Hunter DJ, Niu J, et al. Synovitis detected on magnetic resonance imaging and its relation to pain and cartilage loss in knee osteoarthritis. *Ann Rheum Dis*. 2007; 66:1599–1603. [PubMed: 17491096]

67. Loeuille D, Rat AC, Goebel JC, et al. Magnetic resonance imaging in osteoarthritis: which method best reflects synovial membrane inflammation? Correlations with clinical, macroscopic and microscopic features. *Osteoarthritis Cartilage*. 2009; 17:1186–1192. [PubMed: 19332177]
68. Roemer F, Guermazi A, Zhang Y, et al. Hoffa's fat pad: evaluation on unenhanced MR images as a measure of patellofemoral synovitis in osteoarthritis. *AJR Am J Roentgenol*. 2009; 192:1696–1700. [PubMed: 19457837]
69. Roemer FW, Kassim Javaid M, Guermazi A, et al. Anatomical distribution of synovitis in knee osteoarthritis and its association with joint effusion assessed on non-enhanced and contrast-enhanced MRI. *Osteoarthritis Cartilage*. 2010; 18:1269–1274. [PubMed: 20691796]
70. Messner K, Gao J. The menisci of the knee joint. Anatomical and functional characteristics, and a rationale for clinical treatment. *J Anat*. 1998; 193:161–178. [PubMed: 9827632]
71. McDevitt CA, Webber RJ. The ultrastructure and biochemistry of meniscal cartilage. *Clin Orthop Relat Res*. 1990;8–18. [PubMed: 2406077]
72. Song Y, Greve JM, Carter DR, Giori NJ. Meniscectomy alters the dynamic deformational behavior and cumulative strain of tibial articular cartilage in knee joints subjected to cyclic loads. *Osteoarthritis Cartilage*. 2008; 16:1545–1554. [PubMed: 18514552]
73. Song Y, Greve JM, Carter DR, Koo S, Giori NJ. Articular cartilage MR imaging and thickness mapping of a loaded knee joint before and after meniscectomy. *Osteoarthritis Cartilage*. 2006; 14:728–737. [PubMed: 16533610]
74. Magee T, Williams D. Detection of meniscal tears and marrow lesions using coronal MRI. *AJR Am J Roentgenol*. 2004; 183:1469–1473. [PubMed: 15505322]
75. Magee TH, Hinson GW. MRI of meniscal bucket-handle tears. *Skeletal Radiol*. 1998; 27:495–499. [PubMed: 9809878]
76. Lee JH, Singh TT, Bolton G. Axial fat-saturated FSE imaging of knee: appearance of meniscal tears. *Skeletal Radiol*. 2002; 31:384–395. [PubMed: 12107571]
77. Tarhan NC, Chung CB, Mohana-Borges AV, Hughes T, Resnick D. Meniscal tears: role of axial MRI alone and in combination with other imaging planes. *AJR Am J Roentgenol*. 2004; 183:9–15. [PubMed: 15208100]
78. Helms CA. The meniscus: recent advances in MR imaging of the knee. *AJR Am J Roentgenol*. 2002; 179:1115–1122. [PubMed: 12388483]
79. Hopper MA, Robinson P, Grainger AJ. Meniscal tear evaluation. Comparison of a conventional spin-echo proton density sequence with a fast spin-echo sequence utilizing a 512×358 matrix size. *Clin Radiol*. 2011; 66:329–333. [PubMed: 21356395]
80. Craig JG, Go L, Blechinger J, et al. Three-tesla imaging of the knee: initial experience. *Skeletal Radiol*. 2005; 34:453–461. [PubMed: 15968554]
81. Magee T, Williams D. 3.0-T MRI of meniscal tears. *AJR Am J Roentgenol*. 2006; 187:371–375. [PubMed: 16861540]
82. Ramnath RR, Magee T, Wasudev N, Murrah R. Accuracy of 3-T MRI using fast spin-echo technique to detect meniscal tears of the knee. *AJR Am J Roentgenol*. 2006; 187:221–225. [PubMed: 16794180]
83. Niitsu M, Ikeda K. Routine MR examination of the knee using parallel imaging. *Clin Radiol*. 2003; 58:801–807. [PubMed: 14521891]
84. Kreitner KF, Romaneeshen B, Krummenauer F, Oberholzer K, Muller LP, Duber C. Fast magnetic resonance imaging of the knee using a parallel acquisition technique (mSENSE): a prospective performance evaluation. *Eur Radiol*. 2006; 16:1659–1666. [PubMed: 16733683]
85. Williams A, Qian Y, Golla S, Chu CR. UTE-T2 * mapping detects sub-clinical meniscus injury after anterior cruciate ligament tear. *Osteoarthritis Cartilage*. 2012; 20:486–494. [PubMed: 22306000]
86. Rauscher I, Stahl R, Cheng J, et al. Meniscal measurements of T1rho and T2 at MR imaging in healthy subjects and patients with osteoarthritis. *Radiology*. 2008; 249:591–600. [PubMed: 18936315]
87. Son M, Goodman SB, Chen W, Hargreaves BA, Gold GE, Levenston ME. Regional variation in T1rho and T2 times in osteoarthritic human menisci: correlation with mechanical properties and matrix composition. *Osteoarthritis Cartilage*. 2013; 21:796–805. [PubMed: 23499673]

88. Wang L, Chang G, Xu J, et al. T1rho MRI of menisci and cartilage in patients with osteoarthritis at 3T. *Eur Radiol.* 2012; 81:2329–2336.
89. Lohmander LS, Ostenberg A, Englund M, Roos H. High prevalence of knee osteoarthritis, pain, and functional limitations in female soccer players twelve years after anterior cruciate ligament injury. *Arthritis Rheum.* 2004; 50:3145–3152. [PubMed: 15476248]
90. Lohmander LS, Englund PM, Dahl LL, Roos EM. The long-term consequence of anterior cruciate ligament and meniscus injuries: osteoarthritis. *Am J Sports Med.* 2007; 35:1756–1769. [PubMed: 17761605]
91. Shelbourne KD, Urch SE, Gray T, Freeman H. Loss of normal knee motion after anterior cruciate ligament reconstruction is associated with radiographic arthritic changes after surgery. *Am J Sports Med.* 2012; 40:108–113. [PubMed: 21989129]

Figure 1. Schematic drawing of a normal (left) and osteoarthritic (right) knee. OA pathophysiology should be perceived in the context of the whole joint with the articular cartilage, synovium, menisci, ligaments, bone, muscles and tendons all involved. (Reproduced from Hunter DJ, Felson DT. Osteoarthritis. *BMJ* 2006;18:639–642, with permission of BMJ Publishing Group Ltd.)

Figure 2.

Cartilage lesions depicted in proton density weighted images (left) and T2 relaxation maps (right). Cartilage lesions often appear larger on T2 mapping images than with proton density weighted images (a–d). T2 mapping also has the ability to detect lesions that are not visible on proton density weighted images (a,b). (Reproduced from Hannila I, Nieminen MT, Rauvala E, Tervonen O, Ojala R. Patellar cartilage lesions: comparison of magnetic resonance imaging and T2 relaxation-time mapping. *Acta Radiol* 2007;48:444–448, with permission of Informa Healthcare.)

Figure 3.

T1 ρ maps obtained in the knee of a healthy volunteer (a) and a patient with severe osteoarthritis (OA) (b). T1 ρ values are elevated in the cartilage of the patient with OA as compared to the healthy volunteer. (Reproduced with permission from Crema MD, Roemer FW, Marra MD, Burstein D, Gold GE, Eckstein F, et al. Articular cartilage in the knee: current MR imaging techniques and applications in clinical practice and research. *Radiographics* 2011;31:37–61.)

Figure 4.

Medial compartments of the tibia and femur in an injured (a) and uninjured knee (b). dGEMRIC indices can be calculated, allowing for quantitative evaluation of the cartilage. The red regions, present in the injured knee, denote regions of low GAG concentration while the blue regions, more prevalent in the uninjured knee, signify regions of high GAG concentration. (Reproduced from Fleming BC, Oksendahl HL, Mehan WA, Portnoy R, Fadale PD, Hulstyn MJ, et al. Delayed gadolinium-enhanced MR imaging of cartilage (dGEMRIC) following ACL injury. *Osteoarthritis Cartilage* 2010;18:662–667, with permission of Elsevier.)

Figure 5.

Sagittal sodium maps overlaid onto proton images obtained from a healthy patient (a) and a patient with OA (b). Regions in which the sodium concentration is reduced, as evident in B, indicate decreased proteoglycan content (Reproduced from Braun HJ, Gold GE. Diagnosis of osteoarthritis: Imaging. *Bone* 2012;51:278–288, with permission of Elsevier.)

Figure 6.

High-resolution 3D qDESS images of the knee in vivo. The different diffusion weightings, lower diffusion weighting (**a**) and higher diffusion weighting (**b**), result in different contrasts between cartilage (solid arrow) and fluid (dashed arrow). Expected T2 variation within cartilage is demonstrated on both the 3D qDESS T2 map (**c**) and the fast spin-echo (FSE) T2 map (**d**). Overlaying the 3D qDESS ADC map (**e**) on (**b**) does not show any distortion or blurring, while the spin-echo diffusion weighted image ADC map (**f**) overlaid on a source FSE T2-weighted image clearly shows distortion. (Reproduced Starswiecki E, Granlund KL, Alley MT, Gold GE, Hargreaves BA. Simultaneous estimation of T2 and apparent diffusion coefficient in human articular cartilage in vivo with a modified three-dimensional double

echo steady state (DESS) sequence at 3T. Magn Reson Med 2011 doi: 10.1002/mrm.23090, with permission of Wiley-Liss, Inc., a subsidiary of John Wiley & Sons, Inc.)

Figure 7. T1-weighted fat suppressed images with intravenous gadolinium contrast Magnetic resonance images depicting synovitis in the medial (**a**) and lateral (**b**) compartments of the knee (arrows). (Images courtesy of Hillary Braun, Stanford University.)

Figure 8.

Sagittal uTE images of menisci with various echo times. Signal can be obtained from the meniscus with uTE, which allows for evaluation of the meniscal infrastructure. (Reproduced from Omoumi P, Bydder G, Znamirowski MR, Du J, Statum SS, Chung CB. Infrastructure of menisci with MR imaging. In: Proceedings of the 18th Annual Meeting of ISMRM, Stockholm, Montreal, Canada, 2010 (Abstract 3180), with permission.)

Table 1

Overview of the Advantages and Disadvantages of Various Sequences Used for Morphological Imaging

	Advantages	Disadvantages
3D-SPGR	High resolution, thin slices, reformatting ability	Long scan times, lack of reliable contrast between cartilage and fluid
DEFT	High cartilage SNR	
3D DESS	High resolution, good contrast between cartilage and fluid	
bSSFP	Good contrast between cartilage and fluid	Low resolution
3D-FSE	Isotropic voxels, thin sections, reformatting ability, good contrast between cartilage and fluid	Low in plane resolution
uTE	Ability to visualize signal in tissues with short TE	