Review Article

Advances in Magnetic Resonance Imaging of Articular Cartilage

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Abstract

The pathology, assessment, and management of articular cartilage lesions of the hip and knee have been the subject of considerable attention in the recent orthopaedic literature. MRI has long been an important tool in the diagnosis and management of articular cartilage pathology, but detecting and interpreting early cartilaginous degeneration with this technology has been difficult. Biochemical-based MRI has been advocated to detect early cartilaginous degenerative changes and assess cartilage repair. Techniques such as T2 mapping, T1rho (ie, T1 in the rotating frame), sodium MRI, and delayed gadolinium-enhanced MRI of cartilage (dGEMRIC) take advantage of changes in the complex biochemical composition of articular cartilage and may help detect morphologic cartilaginous changes earlier than does conventional MRI. Although the newer modalities have been used primarily in the research setting, their ability to assess the microstructure of articular cartilage may eventually enhance the diagnosis and management of osteoarthritis.

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Dr. Jazrawi or an immediate family member is a member of a speakers' bureau or has made paid presentations on behalf of Smith & Nephew and serves as a paid consultant to Ferring Pharmaceuticals and Core Essence Orthopaedics. Dr. Recht or an immediate family member serves as an unpaid consultant to Siemens Musculoskeletal Advisory Committee and serves as a committee member of the International Skeletal Society and the Society of Skeletal Radiology. None of the following authors or any immediate family member has received anything of value from or owns stock in a commercial company or institution related directly or indirectly to the subject of this article: Dr. Alaia, Dr. Chang, and Dr. FitzGerald.

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Imaging is essential in the diagnosis and management of pathology. The advent of MRI has enhanced our ability to diagnose pathology related to soft tissue, bone, and cartilage. Recently, there has been increased interest in the imaging of articular cartilage in the fields of orthopaedics and radiology. Morphologic assessment of articular cartilage via specialized MRI sequences has enhanced our ability to detect pathology and to distinguish between soft-tissue structures in joints.

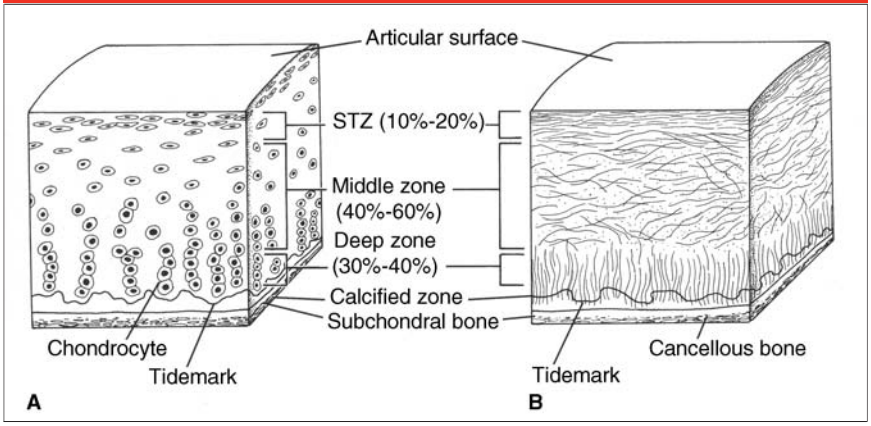
New biochemical imaging techniques, such as T2 mapping, T1rho (ie, spin-lattice relaxation in the rotating frame) imaging, sodium MRI, and delayed gadolinium-enhanced MRI of cartilage (dGEMRIC), have been used to directly assess articular cartilage, with the presumption that early detection and management of articular cartilage lesions may assist in preventing the progression of degenerative arthritis. These modalities have been used primarily for research purposes to date, with a focus mainly on the hip and knee. Evidence has begun to be presented in support of their use in the clinical setting.

Articular Cartilage

Structure and Function

An understanding of the structure and function of articular cartilage is critical because each biochemical imaging modality targets a different component. Articular cartilage encompasses an intricate balance of water, chondrocytes, and a rich extracellular matrix (ECM) composed of collagen fibers and proteoglycan

Figure 1



Illustrations demonstrating articular cartilage morphology. **A,** Schematic image demonstrating chondrocyte organization in the three main zones of uncalcified cartilage (ie, superficial tangential zone [STZ], middle, deep), the tidemark, and the subchondral bone. **B,** Sagittal cross-sectional illustration of collagen fiber architecture demonstrating the three salient zones of articular cartilage. Note the changes in collagen orientation from the superficial to the deep zone. Chondrocyte orientation also changes from the superficial zone (densely packed, flat) to the deep zone (columnar orientation perpendicular to the surface). The tidemark represents a relative change from the deep zone to the zone of calcified cartilage. (Reproduced from Buckwalter JA, Mow VC, Ratcliffe A: Restoration of injured or degenerated articular cartilage. *J Am Acad Orthop Surg* 1994;2[4]:192-201.)

molecules. Water makes up between 65% and 80% of the total weight.[1] The remainder of the wet weight is made up mainly of collagen, of which 90% to 95% is type II, and proteoglycans, particularly glycosaminoglycan (GAG). The characteristic proteoglycan molecule, aggrecan, houses approximately 160 GAG chains. Each chain contains chondroitin sulfate and keratin sulfate, which are highly negatively charged. These proteoglycans help disperse load throughout a joint and endow cartilage with a high compressive strength. Their cumulative large negative charge increases the osmolality of the tissue and attracts water molecules into its substrate. Swelling is prevented by the highly organized collagen fibers in the ECM.

Cartilage is divided into zones based on its structure and function[1] (Figure 1). The superficial zone forms a smooth gliding surface. This zone is composed of collagen fibers oriented parallel to the articular surface. The superficial zone contains a low proteoglycan concentration and a high concentration of collagen. Water content is highest in this zone. The intermediate (ie, middle or transitional) zone consists of obliquely oriented collagen fibers. This level has a high proteoglycan content but a lower concentration of water and collagen than that of the superficial zone. The deep zone contains dense collagen fibers oriented perpendicular to the articular surface. This zone has the highest concentration of proteoglycans and the lowest concentration of water. The underlying zone of calcified cartilage is a smaller layer, consisting of radially oriented collagen fibers embedded in a calcified matrix. This layer separates the overlying deep zone from the subchondral bone.[1] Here, collagen fibers traverse into the tidemark, which represents a relative change from the deep zone to the zone of calcified cartilage.

Morphologic Imaging

Sequences dedicated to the morphologic assessment of articular cartilage are currently the standard of care in MRI of articular cartilage. These include pulse sequences that are specifically designed to assess articular cartilage and that have the capability to discern articular cartilage from subchondral bone, meniscus, and fibrocartilage.

One of the initially accepted sequences was fat-suppressed T1-weighted gradient-echo imaging, in which the low signal of suppressed fat in the subchondral bone contrasts with the high signal intensity of articular cartilage. This method was shown to have >90% sensitivity and specificity for the detection of morphologic cartilage defects, using arthroscopy as the standard of care.[2] However, the fat-suppressed technique is associated with rapid signal degradation in the setting of instrumentation and metallic debris, increased scan times, and difficulty in distinguishing articular cartilage from surrounding soft tissues.[3]

Intermediate-weighted fast spin-echo (FSE) MRI, which takes advantage of the water content of articular cartilage, offers the advantage of shorter imaging times than those of spin-echo sequences and uses echo times in the range of 30 to 35 msec. Intermediate-weighted FSE MRI also demonstrates excellent contrast between articular cartilage and surrounding structures such as the labrum and meniscus. On FSE sequences, articular cartilage, which has structure even though it contains water, demonstrates intermediate signal intensity; free water demonstrates high signal intensity; and the

highly organized fibrocartilage meniscus demonstrates low signal intensity. FSE MRI also provides reduced susceptibility artifact, and fat suppression may be added to more readily distinguish between cartilage, synovium, and joint fluid. It can also visualize gray-scale anatomy, that is, it can differentiate signals based on the water content and collagenous organization of the various zones of articular cartilage. Scan times are relatively short, taking only a few minutes to complete. Potter et al[4] evaluated 616 articular surfaces using FSE compared with arthroscopy. They found FSE MRI to have 87% sensitivity, 94% specificity, and 95% negative predictive value. Interobserver agreement was almost perfect, with a kappa value of 0.93.

Overview of Biochemical Imaging

Several modalities have been introduced in recent years for assessing the biochemical integrity of articular cartilage, including T1rho, T2 mapping, sodium MRI, and dGEMRIC. All have been studied at high-field MRI (eg, 1.5 or 3.0 tesla [T]). T2 mapping and dGEMRIC have received a significant amount of recent attention in the literature, and these modalities may become the most routinely used biochemical MRI sequences in the clinical setting. Both modalities can be performed at conventional-field strength, such as 1.5 and 3.0 T. Neither requires intricate pulse sequences or offline reconstruction. Additionally, these techniques have short scanning times, so they can be added to routine MRI without a notable increase in total scanning time. Although the other techniques have shown promise, more research is required to establish definitive clinical uses for them.

T2 Mapping

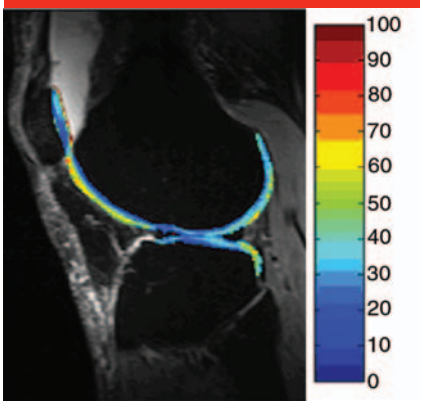
T2 mapping measures the collagen component cartilage ECM by assessing the changing interactions between water and collagen molecules (Figure 2). It can detect zonal variations in articular cartilage, as well. With T2 mapping, scanning times are short (approximately 6 minutes), contrast administration is not needed, and three-dimensional imaging can be performed.

T2 maps are strongly influenced by the orientation of collagen molecules and dipole-dipole interaction anisotropy.[5] The collagen matrix in articular cartilage is, at baseline, a highly organized microstructure. The deep layer of articular cartilage is densely packed with collagen fibers, and the high anisotropy of this layer is reflected in low T2-signal intensity. In the transitional layer, there is less anisotropy, more disorganization in the collagen matrix, and an increase in T2 signal. Thus, T2 mapping values increase from deep to transitional layers in healthy articular cartilage. Disturbances in this structure caused by cartilage injury/degeneration lead to an increased amount of free water and, therefore, increased T2-signal intensity.

There are limitations to T2 mapping. First, it is susceptible to bone-cartilage interface artifact as well as postoperative metallic particles that may make it difficult to accurately measure T2 values.[6] Second, the superficial zone of articular cartilage, which has a highly ordered collagen structure and therefore a shortened T2 value, is below the resolution of T2 relaxation mapping and cannot be adequately assessed at this time.

T2 mapping may be particularly useful in the evaluation of articular cartilage after reparative procedures because it can indicate whether the expected normal zonal variations in healthy articular cartilage have been restored. However, T2 mapping of cartilage has little or no relation to the proteoglycan depletion of cartilage.

Figure 2

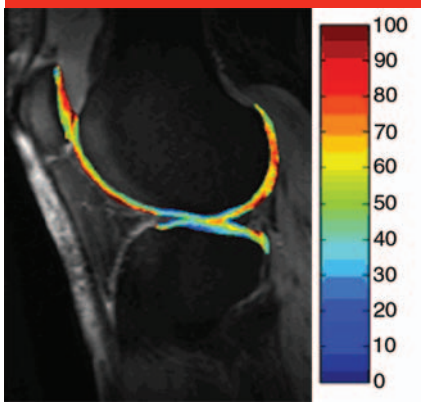


Sagittal fat-suppressed 3-tesla two-dimensional multi-echo spin-echo (MESE) sequence magnetic resonance image of the knee in a healthy volunteer, demonstrating T2 mapping. In a T2-weighted MESE sequence, the T2 relaxation value of cartilage is determined by repeating a sequence with the same repetition time (TR) but varying echo times (TE), usually in the range of 15 to 100 msec. For this image, the following parameters were chosen: TR/TE = 4,000 msec/TE = 16.5, 33, 49.5, 66, and 82.5 msec. Reconvoxel size = 0.586 mm × 0.586 mm. Slice thickness = 1.5 mm. In the setting of cartilage degeneration, collagen damage and increased hydration in the extracellular matrix can increase T2 values. The color bar reflects the T2 values of cartilage (msec), which can be spatially "mapped" on the anatomic image of cartilage.

T1rho

Proteoglycan loss is believed to be one of the primary events in the pathologic cascade of osteoarthritis (OA).[7] Several techniques have been developed that target these molecules, with the assumption that early detection of changes in GAG may allow early intervention. T1rho MRI is used to assess low-frequency interactions between hydrogen and macro-

Figure 3



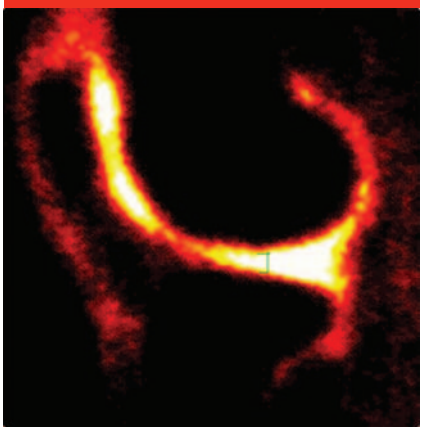
Sagittal 3-tesla T1rho magnetic resonance image of the knee in a healthy volunteer obtained with a three-dimensional spin lock gradient-echo sequence (TR/TE = 175/2.04 msec, spin-lock frequency = 300 Hz, time of spin lock = 2/10/20/30 msec, slice thickness = 3 mm, matrix = 128 × 256, field of view = 15 cm). In the setting of cartilage degeneration, proteoglycan loss in the extracellular matrix may be reflected in elevated T1rho values. The color bar on the right reflects the T1rho values of cartilage (msec), which can be spatially mapped on the anatomic image of cartilage.

molecules in free water (Figure 3). T1rho values have been shown to correlate with proteoglycan content and fixed-charge density in enzymatically degraded bovine specimens and in clinical osteoarthritic specimens. T1rho values increase as proteoglycan content decreases in articular cartilage.[8]

Sodium MRI

Sodium MRI was first described in the early 1990s[9] (Figure 4). Similar to dGEMRIC, this modality takes advantage of the highly negative fixed charge of GAG in articular cartilage. Sodium has a positive ionic charge, and it is found in higher concentrations in the interstitium than in the synovial fluid secondary to its attraction to the anionic GAG charge.

Figure 4



Sagittal 7-tesla sodium magnetic resonance image of the knee in a healthy 42-year-old male volunteer. The image was obtained with a three-dimensional gradient ultrashort-echo time sequence (TR/TE = 20 msec/0.160 msec, 1.5-mm isotropic spatial resolution). The articular cartilage of the femorotibial compartment is demarcated by the green bracket.

Therefore, within cartilage, higher sodium concentrations are found in areas of high GAG concentration. Intravenous contrast administration is not needed for sodium MRI. However, this modality requires specialized hardware and has a suboptimal signal-to-noise ratio in comparison with proton imaging.[10] This suboptimal ratio is problematic at field strengths used in clinical imaging. Because of these limitations, to date proteoglycan-directed imaging has focused more on dGEMRIC imaging than on sodium MRI. The use of higher field strength (eg, 7 T) may increase the utility of sodium imaging. However, such high-field magnets are available at only a limited amount of academic centers, and they are used mostly in research.

Delayed Gadolinium-enhanced MRI of Cartilage

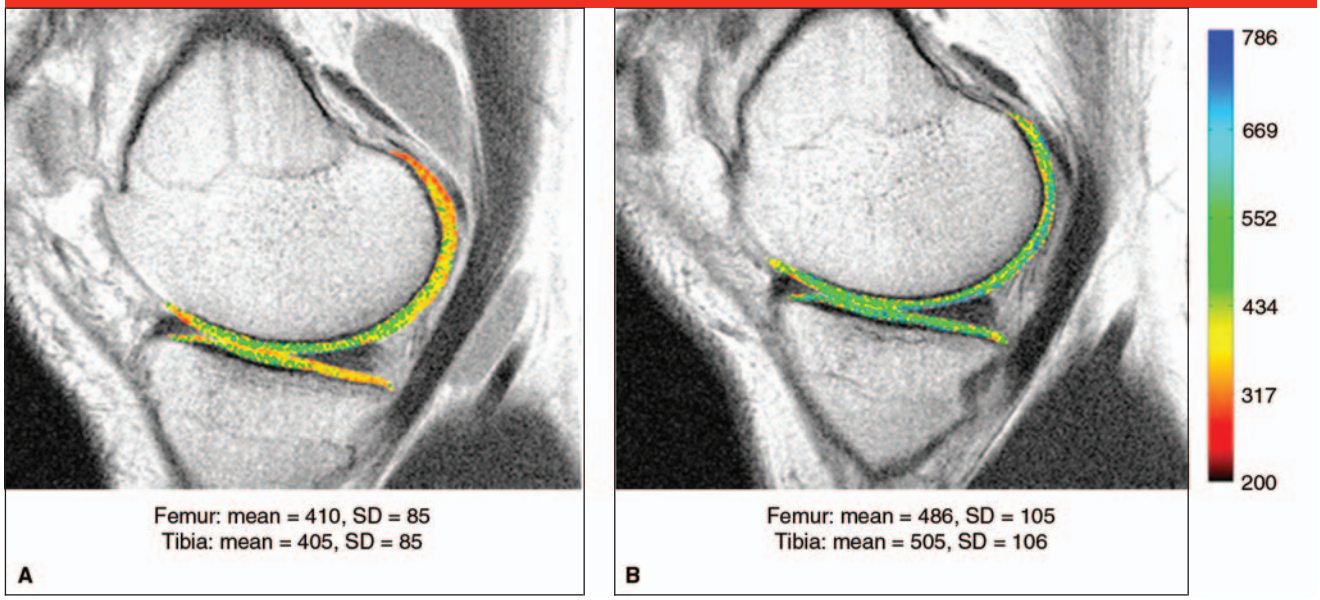
dGEMRIC is a proteoglycan-based imaging technique that has been validated in several reports[11-13] (Figure 5). It is designed to assess biochemical properties of articular cartilage by taking advantage of the highly negative charge of GAG molecules.[11,12] Early changes in OA include a reduction in GAG concentration.[7] In dGEMRIC, the patient is injected with intravenous contrast at 0.2 to 0.3 mmol/kg or 0.4 to 0.6 mL/kg,[14-16] which is two to three times the standard dose used in gadolinium-enhanced MRI. At our institution, we routinely use double-dose gadolinium at a rate of 0.4 mL/kg. The patient must complete a short course of exercise (eg, stairs, walking) at his or her own pace to disperse gadolinium throughout the joint prior to imaging. Gadopentetate dimeglumine disperses inversely with the amount of GAG in cartilage; thus, normal articular cartilage should have a low concentration, and damaged cartilage should have a high concentration.

One disadvantage of dGEMRIC is the requirement of higher doses of intravenous gadolinium, with all of its attendant risks. Patients with poor renal function should not undergo dGEMRIC because of the risk of nephrogenic systemic fibrosis, a rare and sometimes fatal syndrome. Although some believe that precontrast imaging is necessary, other studies have shown otherwise.[17]

Neither the precise amount of exercise required after injection nor the time from injection to imaging has been fully delineated. Most authors agree that patients need between 10 and 15 minutes of light exercise following injection and that 45 and 90 minutes should elapse from injection to imaging; however, there have been reports that shorter time from injection to imaging may be adequate for evaluation of the hip.[18]

A recent study highlighted the importance of biochemical imaging and assessed the association between dGEMRIC findings and the eventual

Figure 5



The delayed gadolinium-enhanced MRI of cartilage (dGEMRIC) technique as used to generate sagittal T1 maps of the medial compartment of a knee with acute anterior cruciate ligament injury (**A**) and of the contralateral uninjured knee (**B**). The blue areas indicate high concentrations of glycosaminoglycan, and the red areas indicate low concentrations. The scale to the right reflects the dGEMRIC index, with higher values corresponding to increased glycosaminoglycan concentration. SD = standard deviation. (Reproduced with permission from Fleming BC, Oksendahl HL, Mehan WA, et al: Delayed gadolinium-enhanced MR imaging of cartilage [dGEMRIC] following ACL injury. *Osteoarthritis Cartilage* 2010;18[5]:662-667.)

development of knee OA. Owman et al[19] used dGEMRIC to evaluate patients with knee pain and normal radiographs. At average 6-year follow-up, 9 of 16 knees showed radiographic osteoarthritic changes, and two patients required total knee arthroplasty. In the patients with radiographic OA at follow-up, the dGEMRIC index at baseline was lower than in the knees that did not develop radiographic changes.

The reproducibility and reliability of dGEMRIC have been validated by several reports on the hip and knee.[20-22] GAG mapping on MRI has been compared with histologic specimens from human osteochondral samples stained with toluidine blue.[18] A close correspondence was found between the dGEMRIC maps and the histologic specimen, which supports the idea that mapping on MRI is a valid method of measuring GAG. Bittersohl et al[20] assessed 10 hips with no evidence of prior cartilage injury clinically and on standard MRI at 4-week intervals. Differences in the scans were not statistically significant, and inter- and intraobserver analyses proved a high agreement for T1(Gd [gadolinium]) assessment. Multanen et al[21] found good reproducibility at superficial, deep, and full-thickness regions of interest in 10 asymptomatic volunteers who were scanned three times at 1.5 T. In one study, the knees of 12 healthy volunteers were evaluated by six different observers with different skill sets.[22] Low inter- and intraobserver variability was found for both tibial and femoral regions of interest. Investigator experience did not affect variability.

Most studies to date have focused on high-field imaging; however, ultrahigh-field imaging (ie, 7 T) has gained attention recently.[23] This modality has shown promise for dGEMRIC and T2 mapping. Protocol optimization, the introduction of new coils, and investment in ultrahigh-field imaging could lead to advances in imaging and increased use of this modality in the orthopaedic setting.

Adaptability of Articular Cartilage

Biochemical imaging of articular cartilage also enables study of the adaptability of articular cartilage. In a cross-sectional dGEMRIC study of age-matched healthy volunteers, Tiderius et al[15] found increased T1 relaxation time in the medial and lateral compartments of persons with increased activity level, which indicates that GAG content and cartilage health may be positively affected by exercise. Lesser gadolinium accumulation in cartilage leads to a longer

T1 relaxation time and is equated with increased GAG. Roos and Dahlberg[14] noted a similar finding in a study examining the effect of moderate exercise on patient status after meniscectomy. Patients were randomized to either a program of moderate exercise or a nonintervention control group. Baseline T1 dGEMRIC values and thus, GAG content, were similar in both groups before the intervention. However, after 4 months, the experimental group showed a significant increase in GAG content compared with the control group (+15 msec and −15 msec, respectively; $P = 0.036$). This finding underscores the potential importance of physiologic loading on the health of articular cartilage. These improvements correlated with better clinical outcome scores. These studies provide initial evidence that early preventative measures may in the future play a role in the management of early OA.

Clinical Applications of Biochemical Imaging

Femoroacetabular Impingement

Jessel et al[24] assessed 37 hips with radiographic evidence of femoroacetabular impingement (FAI). Most hips had cam lesions or combined cam and pincer lesions. Average patient age was 25 years at the time of imaging. dGEMRIC scans of patients with low-grade OA were obtained. Despite minimal radiographic evidence of osteoarthritic changes, the average dGEMRIC indices were significantly lower than indices of morphologically normal hips ($P < 0.0001$). A lower index is indicative of low proteoglycan concentration. In this study, no correlations were found between Tönnis grade or joint space narrowing and pain. However, the dGEMRIC index significantly correlated with pain on a Western Ontario and McMaster Universities index. Significantly lower dGEMRIC indices were noted in patients with larger α angles (60° to 70°) than in patients with α angles of 50° to 60° ($P < 0.05$), which suggests that worse femoral deformity correlates with a greater degree of articular cartilage damage on MRI. These results underscore the idea that pain may typically precede radiographic changes and that FAI may be a possible pathomechanism for early hip arthritis, which emphasizes the importance of early intervention in these patients.

Bittersohl et al[25] provided further evidence to support these inferences. They used dGEMRIC and three-dimensional T1 mapping (ie, color map reflecting T1 relaxation times) to study FAI in 26 patients with cam or pincer impingement as well as 10 asymptomatic volunteers. All patients with FAI had evidence of GAG damage compared with their healthy counterparts. Distribution of T1 dGEMRIC values were in accordance with the specific type of impingement, with cam impingement showing a more anterosuperior pattern of cartilage damage, and pincer impingement showing a generalized circumferential decrease in dGEMRIC values and a more global detrimental effect on cartilage. These results emphasize the potential for these imaging modalities in evaluating cartilage in young patients with hip pain.

Bittersohl et al[6] were among the first to describe the clinical relevance of T2* mapping, a variation of T2 mapping with a shorter acquisition time. They used it to assess hip articular cartilage in healthy volunteers and in patients with FAI. T2* values changed significantly with various grades of articular cartilage damage; however, the authors of the study concluded that dGEMRIC indices had greater sensitivity in measuring damage.

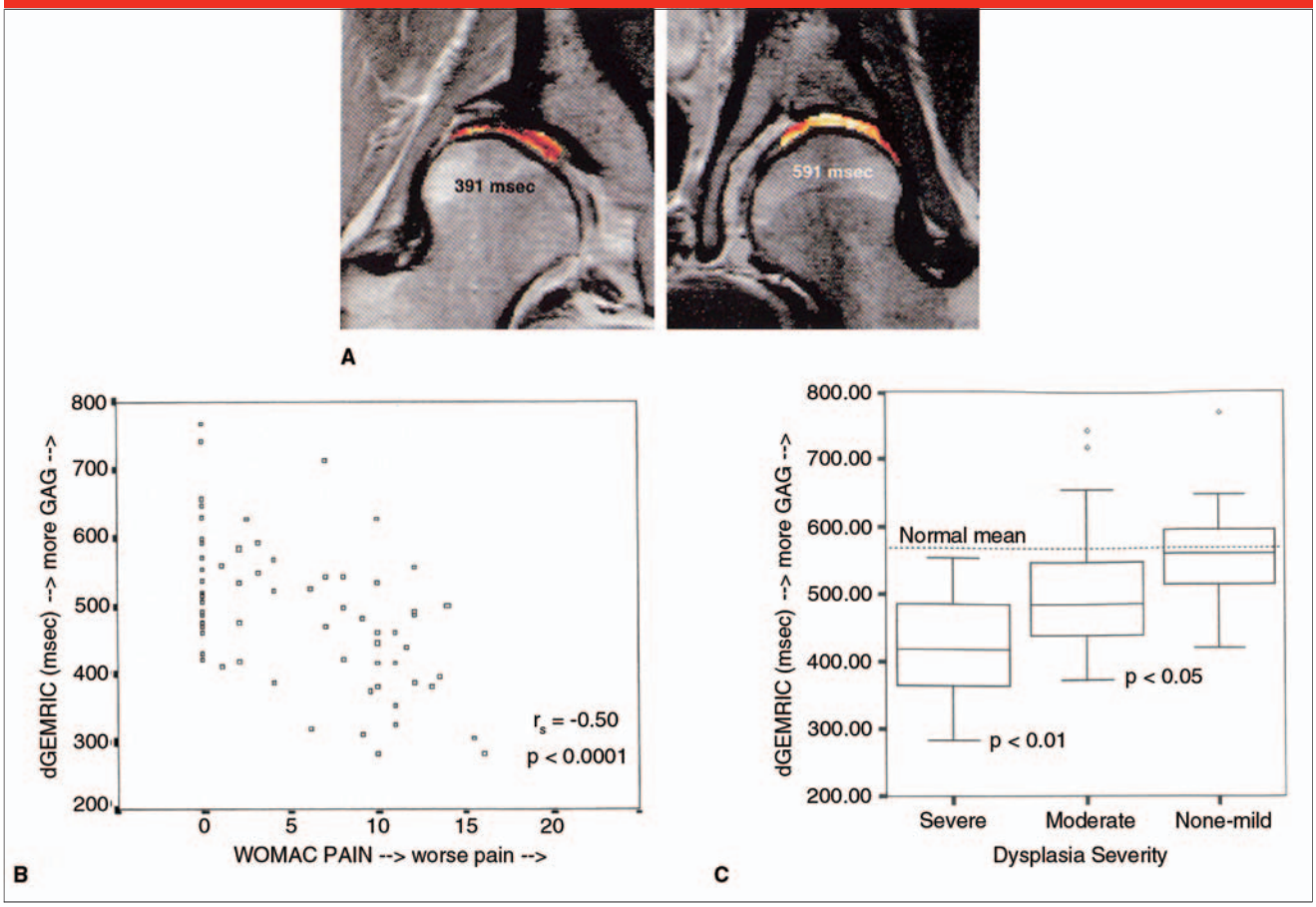
Childhood Hip Disorders

Advances in MRI of cartilage have also played a role in furthering our understanding of developmental dysplasia of the hip. Jessel et al[26] found age, center-edge angles, and the presence of a labral tear to be good independent risk factors for the development of arthritis in persons with hip dysplasia. The cartilaginous changes in dGEMRIC scans became more pronounced as age increased and center-edge angles decreased. Nishii et al[27] compared normal hips, prearthritic hips, and hips with early arthritic changes using standard 3-T MRI and T2 mapping. They found that the frequency of the gradient T2 pattern, that is, increased T2 signal from deep cartilage layers to superficial cartilage layers in healthy cartilage, was significantly lower for dysplastic hips than for normal hips in both the acetabular and femoral cartilage ($P < 0.05$). The authors concluded that T2 mapping could be a useful adjunct in determining early cartilaginous changes. Moreover, in their study, no patient with early arthritic changes had a normal gradient appearance of the superior femoral or acetabular cartilage.

Kim et al[16] studied 68 hips (43 patients) and found a significant correlation between dGEMRIC score and pain ($P < 0.0001$) as well as dysplasia severity (ie, mild, moderate, severe; $P < 0.0001$). The joint space width did not differ significantly among those with mild, moderate, or severe dysplasia (Figure 6). The authors concluded that dGEMRIC could be a useful indicator of cartilage health in patients with developmental dysplasia.

Cunningham et al[28] studied patients treated with Bernese periacetabular osteotomy for the management of hip

Figure 6

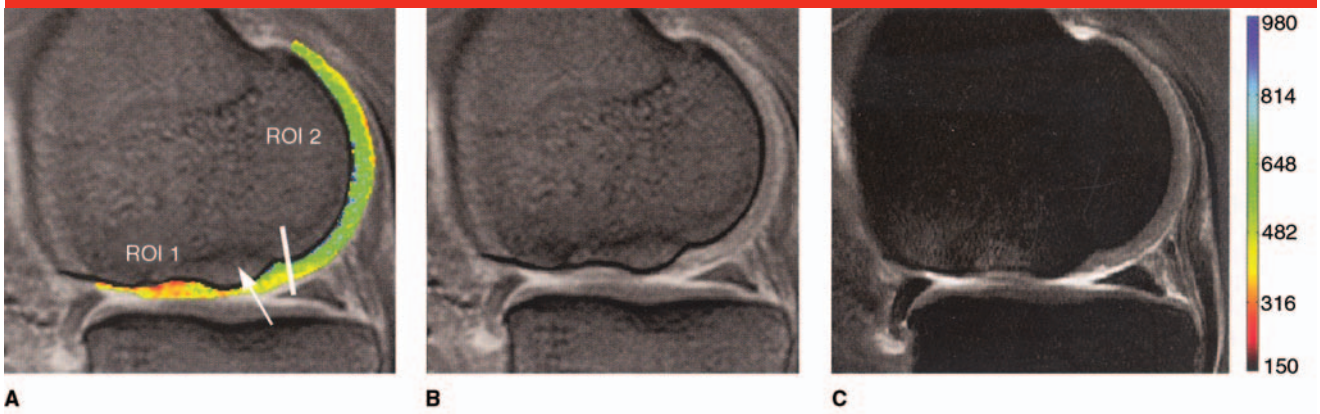


A, Coronal delayed gadolinium-enhanced MRI of cartilage (dGEMRIC) images in a patient with hip dysplasia. The image on the left demonstrates a symptomatic hip, indicated by the low dGEMRIC index, which corresponds to glycosaminoglycan (GAG) degeneration. The opposite side (left) was morphologically normal and asymptomatic. Five hundred seventy milliseconds is considered to be approximately normal. **B,** Scatter plot demonstrating a significant negative correlation between the dGEMRIC indices and the Western Ontario and McMaster Universities (WOMAC) pain score in a study of 43 patients (68 hips) ($P < 0.0001$).[16] **C,** Box plot demonstrating the correlation between dGEMRIC indices and severity of hip dysplasia. Statistical significance was noted between the none-mild and the moderate group ($P < 0.05$) and between the moderate and the severe group ($P < 0.01$) as determined with the Mann-Whitney test. (Reproduced with permission from Kim YJ, Jaramillo D, Millis MB, Gray ML, Burstein D: Assessment of early osteoarthritis in hip dysplasia with delayed gadolinium-enhanced magnetic resonance imaging of cartilage. *J Bone Joint Surg Am* 2003;85[10]:1987-1992.)

dysplasia. Patients with a lower dGEMRIC index (ie, average T1 dGEMRIC values of the acetabular and femoral head cartilages in the weight-bearing zones across coronal slices) and thus, greater evidence of cartilage damage, were significantly more likely to experience clinical failure postoperatively. The dGEMRIC index was found to be the most important predictor of failed osteotomy, more so than Tönnis grade or the presence of radiographic subluxation.

Biochemical imaging has recently been applied to the long-term study of cartilage in patients with documented hip pathology in childhood. Zilkens et al[29] reported that at a mean of 24.5 years following diagnosis of Legg-Calvé-Perthes disease in childhood, hip joint cartilage showed significant GAG loss in the medial compartment ($P = 0.018$). Reduction in GAG was less apparent centrally and laterally. This reduction was not evident on initial radiographic examination, which underscores the potential need for further evaluation of this childhood disease process. In a different study, Zilkens et al[30] reported on the midterm follow-up of patients treated for mild to moderate slipped capital femoral epiphysis in adolescence. Degenerative changes in articular cartilage were found on dGEMRIC in the absence of joint space narrowing that seemed to relate to the initial degree of pathology.

Figure 7



T1 map (**A**) and T1-weighted (**B** and **C**) delayed gadolinium-enhanced MRI of cartilage images of the medial femoral condyle in a woman who underwent autologous chondrocyte implantation 11.3 years earlier. An intralesional osteophyte is seen (**A,** arrow), as well as decreased proteoglycan surrounding the repair tissue (region of interest [ROI] 1, 420) compared with the healthier articular cartilage in ROI 2 (574). The scale on the right reflects T1 values, with lower numbers signifying lower proteoglycan concentration. The white line in panel A demarcates the border of ROI 1 and ROI 2. (Adapted with permission from Vasiliadis HS, Danielson B, Ljungberg M, McKeon B, Lindahl A, Peterson L: Autologous chondrocyte implantation in cartilage lesions of the knee: Long-term evaluation with magnetic resonance imaging and delayed gadolinium-enhanced magnetic resonance imaging technique. *Am J Sports Med* 2010;38[5]:943-949.)

Internal Knee Derangement

Biochemical imaging of cartilage may provide the added benefit of assessing the status of the articular surface after internal derangement of the knee, such as tear of the meniscus or cruciate ligament. Tiderius et al[31] assessed 24 patients with dGEMRIC at an average of 3 weeks after acute anterior cruciate ligament (ACL) tear and found significant GAG loss in the medial and lateral femoral condyles (P = 0.006 and P = 0.004, respectively) compared with healthy volunteers. They concluded that there may be a more global pathologic process involved after ACL tear than is indicated by the usual appearance of lateral femoral condyle or tibial plateau bony bruising that may be found on a typical T2-weighted magnetic resonance image. Fleming et al[32] also evaluated patients with ACL tears without previous history of knee injury and found that at a median follow-up of 82 days, the tibial and femoral medial compartments displayed a 13% decrease in dGEMRIC relaxation time compared with the contralateral knee (Figure 5). The order of scanning did not affect the radiographic outcome.

The authors of a recent case report also studied the changes in articular cartilage over time after acute posterior cruciate ligament injury.[33] A global decrease was noted in dGEMRIC relaxation time at 1- and 3-month follow-up in the medial and femoral compartments. However, with an appropriate nonsurgical knee rehabilitation plan, at 6 months the articular cartilage had returned to its normal state of GAG content and distribution. This report commented only on the acute postinjury phase, however, not on long-term changes of articular cartilage after an isolated posterior cruciate ligament injury, nor did it address the possible effects of physical therapy on articular cartilage.

Articular Cartilage Repair Procedures

Biochemical imaging also may have a role in evaluating reparative procedures of articular cartilage, particularly osteochondral defects and osteochondritis dissecans (Figure 7). Gillis et al[34] were the first to report on the use of biochemical imaging (ie, dGEMRIC) after autologous chondrocyte implantation (ACI) in the knee. They found that in the first 12 months postoperatively, GAG levels were lower in the repair region than in healthier regions. At follow-up ≥12 months, GAG levels in the repair zones were comparable to the levels in adjacent and remote cartilage. These findings differ from those of Pinker et al,[35] who found that at average 21-month follow-up, patients who underwent ACI had no zonal variation in GAG between deep and superficial layers of articular cartilage. In addition, measurements were lower in the repair tissue than in the controls at all time points, which suggests that at midterm follow-up, repair cartilage remains dissimilar from that of native tissue. However, Vasiliadis et al[36] recently evaluated 36 knees (31 pa-

tients) at an average of 12.9 years after ACI for isolated osteochondral defects of the knee and found no statistically significant difference between GAG content of the repair region of interest and control regions of interest, suggesting that it may take longer for this cartilage to differentiate into more normal cartilage. A recent study comparing ACI performed with a collagen-based scaffold to hyaluronate-based scaffolds at 2-year follow-up indicated that although there were no differences in clinical outcome, the collagen scaffold group had a higher T2 mapping value at the surface of the repair tissue.[37] This finding indicates that differences in scaffolding techniques may need to be taken into account at follow-up evaluation.

Other cartilage repair techniques have been evaluated. In a goat model, Watanabe et al[38] showed the feasibility of dGEMRIC to evaluate repair tissue after microfracture procedures. Using T2 mapping, it has been shown that osteochondral autograft repairs resemble the zonal organization of normal cartilage, whereas microfracture repair tissue is more disorganized and does not show typical zonal variation.[39] dGEMRIC also has shown that patients treated with microfracture may have less GAG regeneration at follow-up than patients who undergo ACI.[40]

Summary

Conventional MRI techniques have long been used to assess the quality of articular cartilage in patients with joint pain or pathology. Most current MRI techniques focus on cartilage morphology. Recent advances in biochemical imaging have allowed researchers to focus more on the biochemical composition of articular cartilage, based on the premise that early detection of pathology will result in early intervention and potentially shift management from joint reconstruction to joint preservation. To date, T2 mapping, T1rho, sodium MRI, and dGEMRIC have been used primarily in the research setting.

References

Evidence-based Medicine: Levels of evidence are described in the table of contents. In this article, references 28 and 29 are level II studies. References 26, 36, and 37 are level III studies.

References printed in **bold type** are those published within the past 5 years.

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