MAGNETIC RESONANCE IMAGING OF NORMAL AND OSTEOARTHRITIC CARTILAGE

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Cartilage is the first structure affected in many rheumatic diseases, particularly in osteoarthritis (OA). Because of a lack of early specific signs, OA can be recognized with certainty only relatively late in its course. A firm early diagnosis is desirable, however, because the sooner “chondroprotective” treatment is prescribed, the more effective it is likely to be. Since a firm diagnosis requires precise identification of the cartilaginous lesions, an accurate, sensitive, specific, reproducible, and noninvasive method of identifying such lesions is needed. The only imaging technique currently used to diagnose OA is standard radiography, which permits indirect evaluation of articular cartilage degeneration based on joint space narrowing that is seen on plain films. Although this technique has been refined, it still gives false-positive and false-negative findings. Bone sclerosis and osteophytes (1) are more specific signs, but they cannot be used as early diagnostic criteria because they occur later in the course of the disease.

Thus, radiography, although widely used in long-term evaluation of OA, is of limited value in clinical trials for early detection of OA and assessment of its short-term progression (2). Arthroscopy is the standard of reference for the evaluation of cartilage, accurately depicting swelling and ulcerations of the hyaline cartilage. However, this technique is invasive and does not show the deepest cartilage or subchondral bone alterations. It therefore cannot be used routinely for longitudinal evaluation of OA. Magnetic resonance imaging (MRI) has been slow to gain acceptance for cartilage evaluation because of its limited spatial resolution and because of the poor contrast between cartilage and adjacent structures. Continual improvement in gradient performance and coil design and the development of more efficient pulse sequences have overcome many of the early limitations of MRI. These improvements make possible high-resolution multplanar and 3-dimensional (3-D) images with a wide variety of contrast. In this article, we present recent refinements in MRI of cartilage and offer a key for interpreting the wide range of images that are produced.

Technical factors in MRI

The pattern of cartilage as seen on MRI depends on spatial resolution and contrast. These factors are related to the choice of sequence and can be modified in various ways by the addition of pulses and contrast agents. In some cases, artifacts can greatly affect the quality of the images of hyaline cartilage.

Spatial resolution and signal-to-noise ratio. “Spatial resolution” refers to the smallest size of detail that is visible. “Signal-to-noise ratio” is the ratio between the intensities of the signals from tissue and background. “Contrast” is the difference between the signal intensities of different tissues. The spatial resolution is determined by the thickness of the slice and the size of the smallest element of the image, the pixel. The pixel size, in turn, is determined by the height and width of the field of view divided by the number of lines and columns, respectively, of the matrix that forms the image. For example, the use of a field of view measuring 12 × 12 cm with a matrix of 256 × 192 units will give a pixel size of 470 × 625 μm². Spatial resolution improves as slice thickness or pixel size decreases. Until now, a slice thickness of less than 3 mm could only be obtained with volume acquisitions (3-D Fourier transform).

Spatial resolution and signal-to-noise ratio are
inversely proportional: improving one degrades the other. The best compromise depends on the apparatus and the acquisition sequences. The equipment helps to determine the quality of the image, since a high magnetic field strength (1.5T) improves the signal-to-noise ratio (which is about 3 times as high at 1.5T than at 0.5T). The quality of the coil receiving the signal also affects the signal-to-noise ratio, and therefore affects the spatial resolution. These technical factors explain why in clinical studies of the knee, the best results are obtained on the femoropatellar joint, which can be examined with a small field of view using a surface coil, whereas a larger field of view must be used for the other compartments of the knee.

**MR sequences.** *T1-weighted spin-echo (SE) sequences.* In this sequence, the contrast between tissues depends on the differences between their respective T1 relaxation times. The T1 relaxation time depends on the interaction between the spins of the excited nuclei and the surrounding molecular lattice. This type of sequence is characterized by a good signal-to-noise ratio and good spatial resolution, but poor contrast between cartilage and joint fluid (Figure 1A).

*Proton-density and T2-weighted spin-echo (SE) sequences.* The T2 relaxation time is related to interactions between neighboring nuclei which cause their progressive loss of coherence, and thus of magnetization of the excited region. Proton density refers to the concentration of protons in the tissue. Proton-density and T2-weighted images can be obtained either simultaneously or separately. These sequences are characterized by a good contrast between the cartilage (relatively hypointense) and joint fluid (hyperintense). A new SE technique known as fast spin-echo (FSE) provides both a good signal-to-noise ratio and good spatial resolution. Moreover, superimposition of a magnetization transfer effect (see below) intrinsic to the above sequence improves the delineation of the cartilage surface (Figure 1B). Finally, this sequence allows volume acquisition with very thin slices, though some blurring may alter the visibility of the cartilage interfaces (Figure 1C).

*Gradient-echo (GRE) sequences.* GRE sequences offer a wide choice of contrasts and allow volume (3-D) acquisition (Figures 1E and F). Volume acquisition makes it possible to acquire very thin slices, thus improving the spatial resolution and permitting images to be reformatted into multiple planes. The signal-to-noise ratio for a given slice thickness is better with GRE than with SE sequences. FISP (fast imaging with steady-state precession) or GRASS (gradient-recalled acquisition in the steady state) sequences used with small flip angles produce T2*-weighted images, in which cartilage is hyperintense and the joint fluid even more so (T2* is the T2 relaxation time with the added effect of the inhomogeneity of the field strength). Spoiled GRASS (SPGR) or fast low-angle shot (FLASH) sequences provide T1-weighted images in which the intraarticular fluid is less intense than the cartilage (3) (Figures 1D–F).

Tissue contrast, which depends upon the type of sequence, can also be modified in various ways by the addition of pulses or of contrast agents. These modifications are essential to improving both the quality and the accuracy of the above-mentioned sequences.

*Fat suppression (FS).* FS is compatible with all sequences. This improves the contrast between cartilage and fluid in T1-weighted sequences (4–7). When FS is combined with 3-D SPGR sequences (8,9), cartilage is the only bright articular structure. Other sequences, such as inversion-recovery turbo spin-echo sequences or gradient-echo out-of-phase images, can be used to suppress fat signal, but they are not applied routinely in cartilage imaging in clinical practice.

*Injecting a paramagnetic contrast agent (gadolinium) into the joint.* Injection of a paramagnetic contrast agent into the joint (10) combines the advantages of T1-weighted sequences with the excellent contrast resulting from the hyperintensity of intraarticular fluid. This technique, termed “MR arthrography” (11), has been advocated for detecting early chondral lesions (12). Though many studies have attested to the excellent results of the technique, it is not routinely used because of its (minimally) invasive nature and because the intraarticular injection of gadolinium is not currently approved.

*Intravenous injection of a paramagnetic contrast agent (gadolinium).* Intravenous injection of gadolinium can also enhance the intraarticular fluid signal. This enhancement, which can be by as much as 260%, improves the visibility of the cartilage surface (13,14). Gadolinium is also used to improve visualization of synovial inflammation (15,16).

*Magnetization transfer (MT).* The MT approach is based on a saturation-transfer approach, where saturation is transferred from the macromolecular proton pool to the water proton pool, when the two pools are coupled by means of dipolar interactions or chemical exchange. Applying MT results in a signal decrease of the free water protons magnetically or chemically coupled to the protons bound to macromolecules (17,18). The addition of MT to T2*-weighted or T2-weighted images markedly lessens the intensity of articular cartilage and synovium, but affects the intensity of the fluid.
Figure 1. Comparison of A, a T1-weighted fast spin-echo (FSE) axial image, B, a T2-weighted FSE axial image with fat suppression (FS), C, a 3-dimensional (3-D) T2-weighted FSE axial image with FS, D, a 2-D fast multiplanar spoiled grass (spoiled gradient-recalled acquisition in the steady state) (2-D FMP-SPGK) axial image with FS, E, a 3-D SPGR axial image with FS, and F, a 3-D fast SPGR axial image with FS of the femoropatellar joint from a 3-month-old calf (pixel size $310 \times 410 \mu m^2$) on a clinical imager (1.5T). A 1 mm-deep puncture was made at the cartilage surface. Note the plurilaminar aspect of the cartilage on the FSE and 3-D FSE images.
signal much less, thereby improving contrast at the cartilage–fluid interface.

**Pitfalls and artifacts in MRI.** Interpretation of cartilage lesions must take into account 5 major artifacts: the partial-volume effect, chemical shift, the “magic-angle” effect, truncation, and the susceptibility effect.

The partial-volume effect. The partial-volume effect results from the averaging of the signal intensities of different structures within the smallest unit of volume imaged, the so-called voxel. Characteristics of objects smaller than a voxel are not seen. This effect can give a false appearance of lesions, hide small cartilaginous changes, or lead to errors in estimates of cartilage thickness. This artifact is seen especially when the cartilage is not examined in slices perpendicular to its surface. Thus, the partial-volume effect explains why the axial plane is most suitable for analyzing patellar cartilage, but sagittal or coronal images depict abnormalities of the femorotibial joint cartilage more accurately. The partial-volume effect is directly related to the thickness of the slice, and can therefore be minimized with volume acquisitions or with FSE T2-weighted images which allow thin slices to be obtained.

Chemical shift. This refers to the difference in resonance of protons in fat and water as a result of their micromagnetic environment. Protons in water resonate at a slightly higher frequency than the corresponding protons in fat. This artifact may cause overestimation of the thickness of the cartilage and underestimation of the subchondral bone on one side of the joint, and the converse on the other side of the joint. The best method for avoiding this artifact is the FS technique.

The magic-angle phenomenon. The magic-angle phenomenon increases the cartilage signal when its orientation is about 55° with respect to the axis of the main magnetic field (19). This effect is related to variations in the orientation of the collagen fibers within the cartilage layers. This artifact is especially visible with proton-density-weighted SE images and GRE sequences and is less pronounced with T2-weighted SE sequences.

Truncation artifacts. Truncation artifacts appear as a series of ripples propagating away from any sharp discontinuity in signal intensity. Truncation interferences, which are due to the presence of 2 interfaces of sharp discontinuity, alter the appearance of the ripples. The phenomenon is summed to a maximum when the distance between the 2 interfaces is 4 pixels. The ripples are most likely to be evident in the direction of lowest resolution (larger pixels). The number of truncation lines increases with decreasing pixel size or with increasing cartilage thickness (20) (Figure 2).

Susceptibility artifact. The susceptibility artifact is due to differences in magnetic susceptibilities between two tissues. These different susceptibilities can produce field nonuniformity at their interface, leading to subtle image distortions and altering the shape and location of the resolved voxels.

**MRI patterns of normal cartilage**

Articular cartilage is a remarkable connective tissue that endows joints with both the friction and the lubrication that make normal motion possible. It also absorbs mechanical shocks and distributes the load over underlying bone. The hyaline articular cartilage consists of chondrocytes within an extracellular matrix that is
composed mainly of water, collagen, and proteoglycans (21). This matrix contains pericellular, territorial, and interterritorial regions, as defined by their proximity to the chondrocytes. These 3 regions differ in proteoglycan concentration and in the content, organization, and diameter of their collagen fibers. Water is the most abundant component of articular cartilage, with concentrations ranging from 80% in the superficial zone (22) to 65% in the deepest zone.

The proteoglycans, which are entrapped within the collagen network, are molecules with high concentrations of (negatively charged) anions, which interact with the mobile (positively charged) cations in the tissue water. Most of the water is thus located in the spaces between proteoglycans and provides a swelling pressure that is restrained by the stiffness and tensile forces of the collagen fibers. Because these spaces (‘pores’) are very small, the water encounters resistance in passing through them, giving cartilage a good deal of resistance to joint loading. With aging, the overall content of water and functional aggregates decreases because the fixed charge density becomes lower, thereby reducing the water-binding capacity of the proteoglycans (23). This phenomenon leads to thinning and stiffening of the articular cartilage (24). An increase in collagen crosslinks and interactions also contributes to cartilage stiffness. The chondrocytes' metabolic response to biomechanical stimuli diminishes (25).

The articular cartilage is composed of 4 histologic zones or layers. The most superficial (zone I, or the tangential zone) has thin collagen fibers whose long axes are parallel to the cartilage surface. This surface layer is fundamental to the fluid pressurization mechanism of load bearing by articular cartilage (26). The middle zone (zone II, or the transitional zone) has thicker, more randomly oriented collagen fibers. The zone below this (zone III, or the radial zone) contains the lowest water content and the highest proteoglycan concentration. Here, the collagen fibers are perpendicular to the surface of the cartilage. The deepest layer of cartilage (zone IV, or the calcified layer), constituting ~6–8% of the total thickness, is calcified and serves to anchor the extensive network of collagen fibrils (27,28). The junction between the noncalcified and calcified articular cartilage is visible as a line, or “tidemark.”

**MR pattern of normal cartilage.** MRI allows direct evaluation of the cartilage from its surface to its deepest zone. The great variety of methods (types of MR units or sequences, diagnostic criteria used, populations studied, and use of cadavers or animals) accounts for the diversity of the published results. The appearance of cartilage varies greatly according to the pulse sequences. It may appear as 1, 2, 3, or even more layers (Figure 3). In conventional T1- and T2-weighted SE images and in some GRE sequences, cartilage appears as a single, homogeneous layer. On T1-weighted images, the articular cartilage shows a moderate signal intensity, whereas synovial fluid, synovial tissue, and subchondral bone show a low-intensity signal. Due to the presence of fat in bone marrow, the trabecular bone presents a high signal intensity. On T2-weighted images, the cartilage signal is of low intensity, whereas synovial fluid and synovial tissue are of high intensity.

On these 2 sequences, the cartilage–bone interface is visible as a dark line corresponding to the subchondral bone and the calcified zone of the cartilage. However, distinguishing the cartilage–bone interface can be difficult with T2-weighted SE images. As T2-weighting increases, the signal intensity of normal cartilage decreases, improving the contrast at the fluid–cartilage interface but obscuring the cartilage–bone interface. On GRE sequences, cartilage may appear bright or dark with a high contrast to fluid, while subchondral and trabecular bone, owing to the susceptibility effect, remains in low or intermediate signal.

Many studies have demonstrated a plurilaminar
appearance of the normal hyaline cartilage. The number of layers and their corresponding signal depend on the specific pulse sequence used. Using strongly T1-weighted (inversion recovery) and T2-weighted images, Lehner et al (29) demonstrated a bilaminar appearance of the cartilage. The superficial lamina was in low signal on T1-weighted images and in high signal on T2-weighted images, and the signal of the deeper lamina in the two instances was the reverse. Histologic analysis indicated that the superficial lamina corresponded to the tangential and transitional zones of the cartilage, and the deep lamina corresponded to the radial and calcified layers of cartilage.

Modl et al (30) described 3 layers in articular cartilage using high-resolution T1- and T2-weighted SE images. The thin superficial lamina and the deepest lamina had a low signal intensity on both T1- and T2-weighted images. The intermediate lamina had a high or a moderate signal intensity on T1- and T2-weighted images, respectively. Histologic analysis indicated that the superficial lamina corresponded in location but not precisely in thickness to the tangential layer. The intermediate lamina corresponded to the transitional layer, and the deepest lamina corresponded to the deep radial and calcified zones of cartilage and adjacent subchondral bone.

Using a fat-suppressed 3-D SPGR sequence, Recht et al (8) confirmed a trilaminar appearance of the cartilage, although the signal patterns were different from those previously described: the superficial and deep laminae had a high signal intensity, whereas the intermediate lamina had a low signal intensity. The superficial lamina represents the tangential and transitional layers and the most superficial part of the radial layer. The deep lamina corresponds to the deepest part of the radial layer, and the intermediate lamina is thought to be a part of the radial layer. A fourth layer of low signal intensity therefore corresponds to a zone of calcified cartilage and subchondral bone.

In studies of normal bovine patellar specimens, Rubenstein et al (31) described a hyperintense superficial lamina, a hypointense middle lamina, and an intermediate deep lamina on T1-weighted, proton-density, and T2-weighted SE images. A distinct, hypointense fourth lamina, which subsequently proved to represent the calcified cartilage and subchondral bone, separated the 3 cartilage laminae from the hyperintense signal of the bone marrow. Finally, using high-resolution MRI, Waldschmidt et al (32) demonstrated a superficial hypointense cartilage layer and a deep layer consisting of dark striation perpendicular to the subchondral surface (Figure 3).

Why the appearance of normal cartilage varies with different sequences is unclear. The layers observed on MR images, though probably reflecting histologic variations in the cartilage, do not correspond exactly to the histologic layers. The thicknesses of the different MR layers vary with the spatial resolution and the sequence parameters. In Cole and colleagues' study, the thickness of the superficial layer for human patellar cartilage was ~250 μm (33). Therefore, the depiction of this layer requires high spatial resolution and minimal partial volume averaging, which could not be obtained in early MR evaluation of the cartilage (34). Besides, the demonstration of this layer requires a good contrast with the synovial fluid, accounting for the fact that this layer is not visible on 3-D SPGR or T1-weighted images. This limitation can be partially overcome by gadolinium injection.

Erickson et al (35) recently showed that the trilaminar appearance of hyaline cartilage on MR images obtained with an FS 3-D SPGR sequence is mainly due to a truncation artifact rather than to histologic zonal anatomy. The number of truncation lines increases with decreasing pixel size. Moreover, for a given spatial resolution, the appearance of the "lamina" varies with the thickness of the cartilage (see the Truncation Artifacts section above and Figure 2). Nevertheless, the absence of modifications of cartilage pattern with matrix size using FSE T2 sequences suggests that the plurilaminar pattern cannot be attributed to the truncation artifact alone (Erickson SJ: personal communication). Lehner thought that the modification of signal intensity is due to the variation of water content, which ranges from 80% to 65% (surface to deep zone). However, the gradual variation of water content does not correlate with the sharp discontinuity of signal intensity of the different cartilage layers. Paul et al (36) proposed that the signal intensity of cartilage was primarily determined by proteoglycan concentration. Those investigators based their hypothesis on a comparison of plots of MRI signal intensity across the thickness of the cartilage from the knees of normal subjects with published values of proteoglycan concentration measured as a function of cartilage depth. However, the depletion of proteoglycans in the rat hyaline cartilage does not modify this trilaminar pattern in proton-density SE images (37).

Rubenstein et al (31) argued that the appearance of the cartilage depends greatly on the orientation of the collagen fibrils. They observed that the trilaminar aspect is most apparent along the portions of the articular
surface aligned at 0° or 90° with respect to the axis of the main magnetic field, and tend to disappear at a 55° angle, making the cartilage look homogeneous (the “magic angle” phenomenon). Rubenstein et al, and recently Xia et al (38), stated that the disappearance of the trilaminar pattern at 55° is due to the minimal dipolar coupling between the free water molecules and the water molecules bound to the collagen fibrils.

All these data suggest that the MR pattern of the cartilage is probably due to a combination of different factors. In clinical practice, T2-weighted FSE sequences with F S, which are available on most MRI machines, represent the most efficient sequence for routinely depicting the laminar appearance of articular cartilage (Figure 1B). Although the MR layers do not precisely reflect the different histologic layers, the MR appearance is undoubtedly affected by the various structures of the cartilage. The disappearance of this pattern could also suggest histologic and structural modifications of the cartilage over time, reflecting an aging process. Therefore, it is not surprising that MRI of cartilage reveals a great variability in the intensity and regularity of some of the layers, which can even be completely missing (39).

Thickness of normal articular cartilage. Measurement of cartilage thickness presupposes clear recognition of both bone-cartilage and fluid-cartilage interfaces, a high spatial resolution, and a limitation of some artifacts (40). Moreover, a longitudinal evaluation of the cartilage thickness requires the recognition of the precise topography of each portion of the cartilage.

The appearance of the bone-cartilage and fluid-cartilage interfaces varies with the type of sequence. The superficial layer or the deep layer might be hardly distinguishable. Therefore, the measurements of the cartilage thickness reflect the visible cartilage, not the whole cartilage. In fact, the calcified zone is indistinguishable from the subchondral bone, and with optimal contrast, the cartilage-bone interface at best corresponds to the tidemark region. With conventional T2-weighted SE images, as T2-weighting increases, the contrast increases at the water-cartilage interface but decreases at the bone-cartilage interface, resulting in an apparent reduction of the cartilage thickness. Magnetization transfer imaging also improves the delineation of the water-cartilage interface but obscures the bone-cartilage interface. On the other hand, T1-weighted SE images and SPGR sequences clearly demonstrate the bone-cartilage interface, but the superficial layer is not visible. No sequence used thus far clearly depicts both interfaces. However, the cartilage can be more precisely identified by injecting an intraarticular contrast agent or by acquiring 2 different sequences, one delineating the cartilage-bone interface and the other the water-cartilage interface (41). By matching the images from the 2 sets and automatically extracting the cartilage, this method gives more accurate measurements of thickness. In routine evaluation, since the superficial layer represents <5% of the total cartilage thickness, FS 3-D SPGR sequences offer the best compromise for determining articular cartilage thickness (Figures 1E and F).

Moreover, high spatial resolution is necessary for accurate cartilage measurements. For a given spatial resolution, the error of measurement increases when the articular cartilage thickness decreases. Therefore, it is not surprising that the accuracy of articular cartilage thickness measurements is greater in the femoropatellar joint (mean thickness 4 mm) than in the shoulder (mean thickness 1.23 mm) (42) or the hip (mean thickness 1.3 mm) (43). Most of the studies performed on the knee show that the mean error of cartilage measurement is <12%. In contrast, Hodler et al (42) found a difference of 35% between the measurements made on MRI and those made on anatomic sections of humeral head. Using a dedicated coil and a very high spatial resolution for the evaluation of the interphalangeal cartilage, Robinson et al (44) found a measurement error of <10%.

Actually, in clinical studies, higher gradient performance and efficient sequences allow a significant improvement of the spatial resolution, with a pixel size of 270 × 540 μm². These improvements should lead to better precision and reproducibility in cartilage thickness measurements. Finally, a longitudinal evaluation of articular cartilage thickness requires identical experimental conditions and especially, identical sequences and spatial resolution.

Three-dimensional display and quantification of normal articular cartilage. The absence of specific landmarks could limit the reproducibility of cartilage thickness measurements. Thus, 3-D quantification may be a more robust and reproducible method for evaluating the cartilage over time. Because 3-D images and volume calculations are obtained by matching and interpolating the data of the original acquisition slices, their quality depends mainly on the slice thinness, and therefore are usually obtained from volume acquisition (3-D acquisition) with GRE sequences. Another advantage of 3-D acquisition is that it allows images to be reformatted in the plane best suited for evaluation of the individual structure.

Volume determination, like measurements of cartilage thickness, requires high contrast at interfaces (44–46). Accurate 3-D analysis and precise quantifica-
Figure 4. Early osteoarthritis of the femorotibial joint of a 49-year-old patient. A, Anteroposterior view of the knee, showing mild osteophytosis of the medial femorotibial joint and mild joint space narrowing. B, T2-weighted fast spin-echo coronal image with fat suppression, showing a type 3 chondral lesion (curved arrow). C, Arthroscopy confirmed a type 3 ulceration of the medial femoral condyle.

Anatomic alterations of articular cartilage accessible to imaging

In the early stages of cartilage degeneration, matrix is not depleted, since its turnover increases. Later, a net depletion of matrix aggrecans induces imbibition of water (49). The alterations observed in the early stages of OA include important changes in the subchondral bone, stressing the close relationship between articular cartilage and this tissue. Later, failure of

The percentage of error of the calculated volumes compared with the surgically removed articular cartilage was 6.53% (47). This technique overcomes the limitation imposed on measurements of cartilage thickness by the lack of precise landmarks, but because of variations of cartilage thickness from one region to another, cartilage volume measurements do not reflect the precise cartilage modifications. To some extent, if the cartilage is thinner in one region and thicker in another, the cartilage volume might not even be modified. However, by subdividing 3-D reconstructions of the articular cartilage into smaller regions (e.g., a grid of 10 voxels), the cartilage volume can be evaluated at specific sites, such as the weight-bearing surfaces of the femoral condyles (48). Therefore, this method allows an evaluation of cartilage modifications in specific locations over time.
mated in 40% of cases and underestimated in 60%; grade 2 lesions correctly graded in 25%, underestimated in 50%, and overestimated in 25%; grade 3 lesions correct in 6%, underestimated in 24%, and overestimated in 70%; and grade 4 lesions correct in 70% and underestimated in 30%. This study demonstrated the accuracy of MRI in depicting severe focal chondral alterations as well as the inability of MRI to precisely quantify the alterations.

Signal modifications in OA cartilage. Signal abnormalities of the cartilage are among the earliest signs of cartilage alterations, since they reflect changes in structure and water content. The signal abnormalities are mostly visible on T2-weighted images and are mostly associated with changes in the cartilage T2 relaxation time. Signal abnormalities may be visible as either a focal increase or a focal decrease in signal intensity.

A focal increase may be superficial or transmural, but may also appear as a deep, linear zone. In a spontaneous model of OA in rhesus monkeys, MR quantitative analysis of these regions demonstrated longer T1 and T2 relaxation times compared with normal cartilage. The superficial and transmural modifications were due to cartilaginous edema related to rupture of collagen fibers and loss of proteoglycans. Gahunia et al (53) showed that these alterations are also associated with the presence of hypertrophic and proliferating chondrocytes. Modification of the deepest zone of the cartilage may also be present as a sign of OA. In this case, signal alterations reflect basal delamination of the cartilage at the calcified layer. This abnormality is not specific to OA; it can be seen in young patients after trauma.

A focal decrease in signal intensity on T2-weighted images as well as on FLASH sequences is related to condensed collagen and decreased cellularity (54). In these regions, T1 and T2 relaxation times are shorter than those of the natural cartilage.

Thickness and volume quantifications. A global assessment of cartilage alterations can be obtained with cartilage thickness and volume measurement. As stated earlier, longitudinal evaluation of the cartilage requires optimal spatial resolution and a reproducible methodology. The 3-D-reconstructed images derived from thin-slice MRI could be useful as an additional MRI tool for monitoring changes in cartilage volume over time and for determining the distribution and severity of cartilage abnormalities in OA patients. An alternative 3-D approach is to determine the volume of the cartilage lesions. Using an FS 3-D SPGR sequence, Lavid et al...
Figure 5. Mild osteoarthritis of the femoropatellar joint in the same patient as in Figure 4. A and B, 3-D SPGR sequence with FS, before and after intravenous gadolinium injection. C and D, FMP-SPGR sequence with FS before and after gadolinium injection. Axial slices of the femoropatellar joint (pixel size $470 \times 625 \, \mu m^2$) show a small geode of the subchondral bone (curved arrow) and discrete thinning of the articular cartilage. No ulceration or signal modification of the cartilage is noted. Gadolinium injection revealed a thickening of the synovial tissue (B and D). E and F, T2-weighted FSE images with FS, showing a type 3 ulceration of the cartilage (black arrow), with thinning and signal modification of the patellar cartilage. Inset, Arthroscopy confirms a type 3 chondral lesion. Note that the thin, hypointense superficial layer of the cartilage can only be observed on the T2-weighted FSE sequences with FS. See Figure 1 for definitions.
MRI of normal and OA cartilage

(55) determined the length, width, and depth of grade 2 and grade 3 cartilage lesions, with an average percentage of error of only 8–12%. Cartilage volume can be evaluated at specific sites, such as the weight-bearing surfaces of the femoral condyles (48). Therefore, these methods allow a quantitative evaluation of cartilage modifications in specific locations.

Associated morphologic changes. MRI can very accurately depict sclerosis and fracture of the subchondral bone, small geodes and large cysts, bone marrow edema, osteophytes, synovial inflammation, joint effusion, and meniscal degeneration (56).

Narrowing of the joint space. Joint space narrowing reflects thinning of the cartilage. When sequences providing high bone–cartilage contrasts are used, MRI allows measurements of the joint space between opposing structures, thus avoiding the limitation of superimposed structures on standard radiography. However, these measurements are of limited value in detecting joint space narrowing in the knee, because MRI cannot be carried out with the knees in a weight-bearing position.

Sclerosis. Sclerosis appears as a wide, subchondral hypointense layer in weight-bearing areas in all sequences and can look thicker on T2*-weighted GRE images due to susceptibility effects. Some authors have argued that alterations in the subchondral bone seem to be related to the severity of OA and precede cartilage alterations (57). In studies of a model of spontaneous OA in guinea pigs, Watson et al (58) showed that the subchondral bone plates of the tibia and femur increased in thickness over time. We obtained similar findings in iodoacetate-induced OA in rat knees (37). The irregular appearance of the subchondral bone was predominant under zones of eroded cartilage and was confirmed by histologic evaluation of tissue sections. Subchondral bone sclerosis can induce biomechanical alterations of the bones and provoke the formation of subchondral geodes.

Geodes. Geodes are usually due to pulsation of synovial fluid through a bone defect or to hyperpressure. They appear very early in zones free of overlying cartilage, such as the tibial plateau near the tibial eminences (58). Such centrally located geodes, which may lead to large synovial cysts, are not depicted on plain films in their early stages. MRI, however, depicts them early, because it suppresses the superimposed bony structures. In weight-bearing areas, geodes may occur with or without fractures of the subchondral bone. These alterations of the trabecular pattern are the consequence of modification of the dynamic loading characteristics of both the overlying subchondral plate and the articular cartilage. The signal intensity of these lesions is low on T1-weighted images. On T2-weighted images, the signal intensity is high and increases with time as the lesions form the foci of extensive pseudocysts (Figure 5).

Bone marrow edema. Bone marrow edema in the subchondral bone is neither a specific nor a sensitive sign of OA, but it is a reliable sign of bone alterations. It appears as a region of low signal intensity on T1-weighted images and of high signal intensity on T2-weighted images. T1-weighted images and fat-suppressed T2-weighted FSE images show such lesions very sensitively.

Osteophytes. Due to its multiplanar capability and the absence of bone superimposition, MRI depicts osteophytes clearly. Moreover, this technique reveals osteophytes before their trabecular bone–like appearance occurs and permits evaluation of their progression over time (58). We have developed an experimental model of rat knee OA in which “chondrophytic” remodeling causing outward displacement of the patella is not visible on standard radiography but is clearly seen with MRI (37). In guinea pigs, the development of tibial chondrophytes begins with protrusion of the cartilage on the medial tibial plateau and leads to displacement of the collateral ligament (58). The chondrophytes gradually take on the appearance of a well-defined osteophyte with a trabecular bone–like appearance in the center.

Synovial inflammation. Synovial inflammation is a secondary event, occurring as a consequence of the release and phagocytosis of cartilage breakdown products in the joint. MRI offers the opportunity to define the extent, location, and thickness of synovial membrane involvement early during OA. Fernandez-Madrid et al (56) noted anatomic abnormalities compatible with synovial thickening in 73% of OA patients but in none of the normal reference group. Classically, the synovial thickening typically appeared in or near the intercondylar region of the knee, in the infrapatellar fat pad, or in the posterior joint margin. In OA, synovial proliferation is well depicted on T2-weighted images, appearing as a thin layer of high signal intensity, although less intense than the joint fluid. This synovial proliferation is more regular and thinner than that seen in rheumatoid arthritis. This tissue is also well demonstrated on T1-weighted SE images or SPGR sequences after intravenous gadolinium injection. Images obtained immediately after intravenous injection demonstrate intense enhancement of the synovial tissue (Figure 5).

Meniscal degeneration. MRI showed a high prevalence of meniscal degeneration in OA (2,59), which suggests a strong relationship between meniscal abnormalities and degenerative joint disease. Degeneration is
seen more frequently in the medial than in the lateral meniscus. Finally, subluxation of the meniscus is frequent in OA and seems to be related to the severity of the disease.

Conclusion

The normal articular cartilage is a complex 3-dimensional structure composed of cells and an extracellular matrix formed of collagen fibers, proteoglycans, and water. Standard radiography has been used for many years in the diagnostic imaging of cartilage disease, especially OA. Because of the lack of early specific signs, an accurate, noninvasive method is still needed for longitudinal studies. MRI can demonstrate a plurilaminar appearance of the hyaline cartilage. This appearance, though not perfectly understood, probably reflects the compositional variation of the cartilage throughout its depth. MRI can detect erosions and ulcerations of the cartilage before the joint space narrows, although the most subtle abnormalities of the cartilage surface cannot be detected accurately. MRI can also highlight changes in the signal from the cartilage substance, which are thought to reflect structural alterations and which are some of the earliest signs of OA. MRI allows quantitative evaluation of the cartilage (thickness, volume, and relaxation times). In addition, this technique clearly demonstrates the abnormalities associated with OA (subchondral bone sclerosis, edema, geodes, osteophytosis, meniscal lesions, joint effusion, and synovial inflammation).

This technique could be used not only to probe the early structural and compositional changes of cartilage, but also to study the interactions between an altered articular cartilage and the osseous, synovial, or meniscal tissues. To date, no work has been published using this tool as a probe to evaluate the efficiency of chondroprotective drugs in experimental or clinical studies of OA. However, the accuracy of the most recent MRI refinements (gradients, coils, sequences) will allow, in the very near future, new applications of this technique as a tool for the detection and followup of the progression of OA (60) as well as the influence of cartilage-protective agents.

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