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Abbreviations:

B_0 = constant magnetic induction field
OA = osteoarthritis

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Human Articular Cartilage: Influence of Aging and Early Symptomatic Degeneration on the Spatial Variation of T2—Preliminary Findings at 3 T¹

PURPOSE: To determine if age and early symptomatic degeneration alter the spatial dependency of cartilage T2.

MATERIALS AND METHODS: In 25 asymptomatic volunteers and six volunteers with symptoms of patellar chondromalacia, quantitative T2 maps of patellar cartilage were obtained with a multiecho, spin-echo magnetic resonance imaging sequence at 3.0 T. Spatial variation in T2 was evaluated as a function of participant age and symptoms.

RESULTS: All asymptomatic volunteers demonstrated a continuous increase in T2 from the radial zone to the articular surface. In the population aged 46–60 years compared with younger volunteers, there was a statistically significant ($P < .05$) increase in T2 of the transitional zone. In symptomatic volunteers, the increase in T2 was larger in magnitude and focal in distribution. In five of the six symptomatic volunteers, the increase in T2 was greater than the 95% prediction interval determined from data in the corresponding age-matched asymptomatic population.

CONCLUSION: Aging is associated with an asymptomatic increase in T2 of the transitional zone of articular cartilage. Preliminary results indicate this diffuse increase in T2 in senescent cartilage is different in appearance than the focally increased T2 observed in damaged articular cartilage.

The syndrome of osteoarthritis (OA) is characterized by changes in structure and function of the joint (1). A component of OA is softening, fibrillation, and subsequent loss of articular cartilage. Currently, there is no definitive test to diagnose OA. The diagnosis of OA is based on a combination of clinical and radiographic findings (2). It is desirable to develop sensitive clinical diagnostic tools to identify and monitor the early degenerative processes of OA that precede the loss of cartilage thickness identified on radiographs. Such techniques could provide new information on mechanisms of cartilage aging and degeneration. A reliable measure of early cartilage damage would have widespread application in the development of chondroprotective agents and techniques, which are likely to be more efficacious when used before there is destruction of the solid cartilage matrix (3,4).

Characterization of the macromolecular environment of cartilage water may provide unique information that can lead to a better understanding of cartilage physiology and degeneration. Because slow molecular motion of cartilage water protons and structure of the extracellular matrix influence proton spin-spin relaxation, quantitative T2 measurements may serve as a useful, noninvasive measure of cartilage integrity. Findings in several studies have indicated an increase in cartilage T2 may be an important finding in the diagnosis of cartilage degeneration (5–7). Previous publications demonstrate a spatial dependency of cartilage T2 in both isolated cartilage explants (8–11) and in vivo human patella (12). Changes in this spatial distribution of T2 are likely to occur with both normal aging and degradation. Because the prevalence of OA increases with age, it is necessary to

determine if normal senescent change will interfere with the identification of T2 change that may result from early symptomatic damage. In this study, we evaluated and compared the effects of age and early symptomatic OA on spatial variation in cartilage T2, and we compared these findings with preliminary results obtained in volunteers with early symptomatic OA.

MATERIALS AND METHODS

Patient Population

From October 1997 through February 1998 we performed quantitative T2 mapping of the patellofemoral joint in 31 volunteers (29 men and two women; age range, 27–60 years; mean age, 41 years). After the nature of the procedure was fully explained, all participants provided informed consent to participate in the study, which was approved by the institutional review board. Immediately before the magnetic resonance (MR) examination, the volunteers were questioned to determine if there was a history of knee surgery or current joint pain, swelling, or stiffness. Volunteers were considered asymptomatic if they responded negatively to these questions. The asymptomatic study population comprised 25 men aged 27–60 years (mean age, 41 years); four were aged 19–30 years (young adult); 13, 31–45 years (adult); and eight, 46–60 years (mature adult).

The symptomatic population included six volunteers: two women and four men aged 34–48 years (mean age, 41 years). All symptomatic volunteers reported symptoms of patellofemoral OA consisting of anterior knee pain exacerbated with climbing stairs, joint stiffness, and intermittent joint swelling. Two volunteers had undergone arthroscopic knee surgery for pathologic patellar cartilage, with an interval between the prior surgery and the MR imaging examination of greater than 2 years.

Image Acquisition

MR images of the patellofemoral joint were obtained with a 3.0-T MR imaging spectrometer (Medspec S300; Bruker Instruments, Karlsruhe, Germany) with a 9-cm transmit-receive surface coil operating at 125 MHz for protons. An asymmetric gradient insert capable of delivering plus or minus 3 G/cm field profile was used in all studies. Volunteers were positioned supine within the imager, with the patellofemoral joint placed at the gradient isocenter. Both gradient-echo and

spin-echo images were obtained through the patella in the transverse plane, prescribed on the basis of a sagittal locator image. The gradient-echo images were obtained with the following parameters: repetition time msec/echo time msec of 200/21, 45° flip angle, 3-mm section thickness, five sections, 8.2-cm field of view, 256 × 256 image matrix, 25-kHz bandwidth, section-selection pulse duration of 4 msec, and four signals acquired for a total acquisition time of 3.5 minutes.

The T2 maps were calculated from data obtained with a multiple spin-echo sequence with the following parameters: 1,500/9–99, echo train length of 11, 3-mm section thickness, five sections, 8.2-cm field of view, 128 × 128 image matrix, 50-kHz bandwidth, section-selection and refocusing pulse duration of 2 msec, and two signals acquired for a total acquisition time of 6.5 minutes. Frequency encoding was left to right across the patella to minimize chemical shift artifact at the patellar cartilage-bone interface.

Data Analysis

The gradient-echo images were used to assess the articular cartilage of the patellofemoral joint by consensus (T.J.M., B.J.D., M.B.S.) for focal signal intensity abnormalities or surface irregularities, with the MR imaging staging criteria previously described by Rose et al (13). Magnitude images and T2 maps were calculated from 10 spin-echo images by means of nonlinear least squares curve fitting, on a pixel-by-pixel basis with the interactive data language (IDL; Research Systems, Boulder, Colo). Because echoes 2–11 contain signal from the stimulated echo, exclusion of the initial spin echo minimizes artifact in the T2 calculation. The influence of this error in the determination of in vivo T2 measurement has been previously discussed (12,14). Fitting of the signal intensity (SI) for the i^{th} , j^{th} pixel as a function of time, t , can be expressed as follows:

$$SI_{i,j}(t) = SI_{0,i,j} \cdot \exp(-t/T2_{i,j}), \quad (1)$$

where $SI_{0,i,j}$ is the pixel intensity at $t = 0$ and $T2_{i,j}$ is the T2 time constant of pixel i, j . A magnitude image is generated from the pixel $SI_{0,i,j}$ data, and a T2 map is generated from the $T2_{i,j}$ data. The T2 map is then bilinearly interpolated to a 512 × 512 image matrix. Comparison between populations is performed with T2 profiles (T2 as a function of distance from the subchondral bone) by using the magnitude image to identify the cartilage borders. T2 profiles, acquired through the

median ridge and the middle of the medial and lateral facet, were generated directly from the calculated T2 maps with a software subroutine written in our laboratory. Only sections in which the patellar cartilage thickness was greater than 3 mm were included in the data analysis. This allowed a minimum of four pixels per profile in the original data and 18 points per profile in the interpolated 512 × 512-matrix T2 maps. A total of 132 profiles were obtained for the asymptomatic population. For comparison between volunteers, each profile was normalized for cartilage thickness as follows: normalized distance equals the distance from the subchondral bone divided by cartilage thickness.

Thus, for each profile, cartilage at the subchondral surface has a normalized distance of 0, and cartilage at the articular surface has a normalized distance of 1.

Analysis of the Effect of Age

A comparison of response functions was used to assess the influence of age on cartilage T2. The response function is a mathematic equation that best approximates T2 as a function of normalized distance for each age group. To minimize bias in selection of a response function, data points from all 132 profiles from the asymptomatic population were initially pooled and fit to 3,665 candidate equations with a standard commercially available curve-fitting software package (TABLECURVE; Jandel Scientific Software, San Rafael, Calif). The response function was determined by sorting the fit of the candidate equations by a degrees of freedom-adjusted r^2 . Because the data consistently demonstrate a best fit to polynomial equations, singular value decomposition was used in the fitting process to minimize error when fitting to higher order polynomials.

The response function used to approximate the spatial variation in T2 of the normalized profiles of the entire data set was the 3×2 Fourier series polynomial:

$$T2_{\text{msec}} = a + b \cos(\pi x) + c \sin(\pi x) + d \cos(2\pi x) + e \sin(2\pi x) + f \cos(3\pi x) + g \sin(3\pi x), \quad (2)$$

where the calculated coefficients for the data from all age groups are the following: $a = 79.4$, $b = -22.7$, $c = -58.2$, $d = -27.9$, $e = 13.4$, $f = 4.4$, and $g = 6.9$.

After identification of the response function, the 132 T2 profiles were stratified into three age populations: (a) young adult (18 profiles), (b) adult (76 profiles),

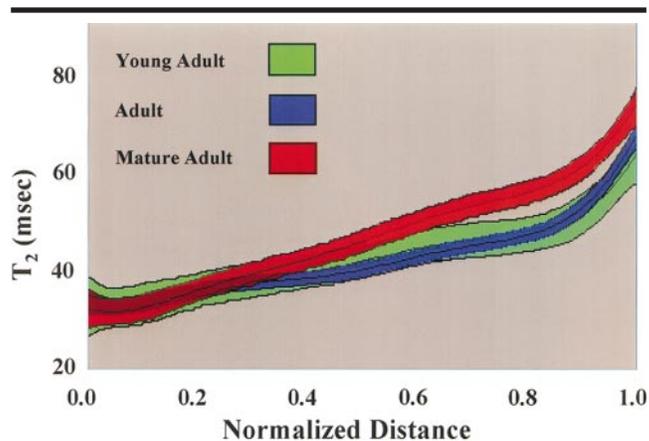


Figure 1. Spatial variation in cartilage T₂ as a function of age for the following groups: young adult (18–30 years), adult (31–45 years), and mature adult (46–60 years). Normalized distance is from the subchondral bone (0.0) to the articular surface (1.0). The shaded regions represent the 99.99% CI of the response function for each of the three populations. Although there is no difference between the young adult and adult populations, the mature adult population demonstrates significantly higher T₂ values in the outer third of the cartilage (normalized distance, 0.64–1.00).

and (c) mature adult (38 profiles). The profiles from each population were then pooled and fit to Equation (2) to determine a response function for each age group. The 99.99% CI for the response function of each population was calculated to determine the difference in T₂ between groups as a function of normalized distance. Regions of the response function where there is no overlap of the 99.99% CI are significantly different, with a Bonferroni-corrected *P* value less than .05 (15).

Analysis of Symptomatic Degeneration

All T₂ maps were reviewed by consensus (T.J.M., B.J.D., M.B.S.) for the presence of focal sites of increased or decreased T₂. A quantitative assessment was then performed by comparing normalized T₂ profiles through these areas, with the 95% prediction interval calculated from the corresponding age-matched asymptomatic population. The 95% prediction interval differs from a CI and is the T₂ range for a given normalized distance where there is a 95% probability that the next measured T₂ will occur, on the basis of values observed in the asymptomatic population (TABLECURVE 2D automated curve fitting and equation discovery: user's manual. San Rafael, Calif: Jandel Scientific Software, 1996; 9).

Lesions were considered abnormal if three adjacent T₂ values were outside the 95% prediction interval for the age-matched asymptomatic population.

RESULTS

Asymptomatic Population

All subjects demonstrated a spatial dependency in T₂ of the patellar cartilage, increasing from approximately 30 msec near the subchondral bone to approximately 65 msec near the articular surface. Review of the T₂ maps demonstrated a nonfocal increase in T₂ of the outer cartilage, which occurred equivalently within both patellar facets and the median ridge. Data from all three locations were combined to determine the response functions presented in Figure 1. In the deep radial zone, all age groups had similar T₂ values. In the outer 36% of patellar cartilage, however, the mature adult population had T₂ values longer than that observed in the young adult and adult populations.

Symptomatic Volunteers

Unlike the continuous increase in T₂ observed in the asymptomatic population, the increased T₂ in symptomatic volunteers was focal. Three patterns of increased T₂ were identified. As represented by the example in Figure 2, two of six symptomatic volunteers demonstrated small focal areas of increased T₂ limited to the deep radial zone. For both volunteers, the T₂ was greater than the 95% prediction interval calculated from the adult age-matched control population. These areas of increased T₂ were slightly hyperintense on the T₂*-weighted gradient-echo images, with no evidence of

focal surface irregularity. Three symptomatic volunteers demonstrated a second pattern of heterogeneously increased T₂, one each within the medial facet, median ridge, and lateral facet, that was greater than the 95% prediction interval calculated from the age-matched asymptomatic population (Fig 3). All volunteers in this group had corresponding heterogeneously increased signal intensity on the gradient-echo images with irregularity of the surface. One volunteer had a central osteophyte in the medial facet, and a second volunteer, who had undergone arthroscopic surgery, had lateral patellar subluxation. A third pattern was observed in one symptomatic volunteer with prior arthroscopic surgery for patellar chondromalacia. This subject had lateral patellar subluxation and evidence of a flap tear of the median ridge on the gradient-echo images. The T₂ map and profile, presented in Figure 4, demonstrated increased T₂ superficial to the flap tear that did not exceed the 95% prediction interval.

DISCUSSION

Spatial Variation in T₂ of Articular Cartilage in Asymptomatic Volunteers

All age groups demonstrate a smooth increase in T₂ from the deep radial zone to the outer transitional zone, which confirms initial observations made in young male volunteers (12). In this study, the mean T₂ of the adult population (mean age, 38 years) was 34 msec ± 4 (SEM) in the deep radial zone, 41 msec ± 7 in the outer radial zone, and 60 msec ± 9 in the outer transitional zone. This compares well with published measurements of 32 msec ± 1, 48 msec ± 1, and 67 msec ± 2, respectively, in a population with a mean age of 34 years (12). The small discrepancy in T₂ measurements is likely due to two differences in study protocol. First, unlike the single-section T₂ map used in the prior study (12), a multisection sequence was used in this study that can result in magnetization transfer owing to off-resonance radio-frequency irradiation (16). Second, a different technique for postprocessing of the T₂ profiles was used in this study. Previously, profiles were modeled with a cubic polynomial equation. In this study, a degree of freedom-limited *r*² fit of the T₂ profiles was performed to determine an appropriate mathematic model. This allows accurate mathematic modeling of the T₂ profiles without making a priori assumptions regarding the shape of the profile.

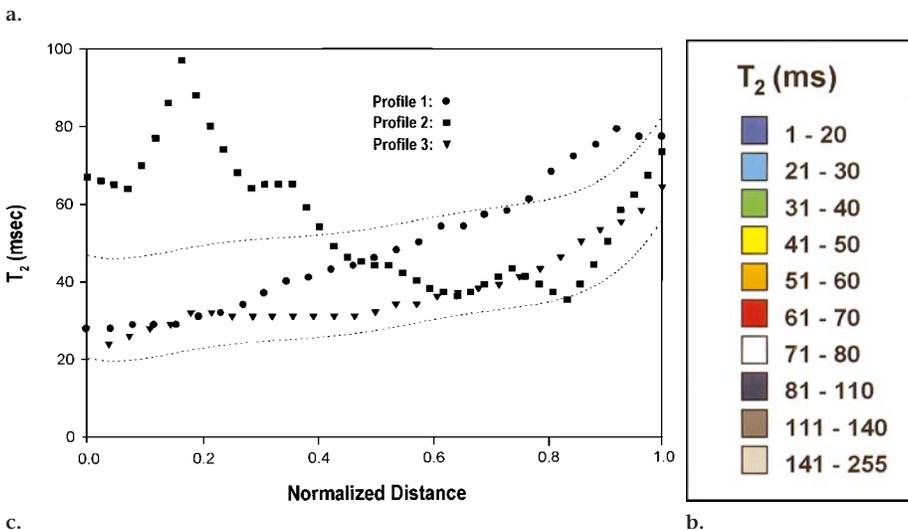
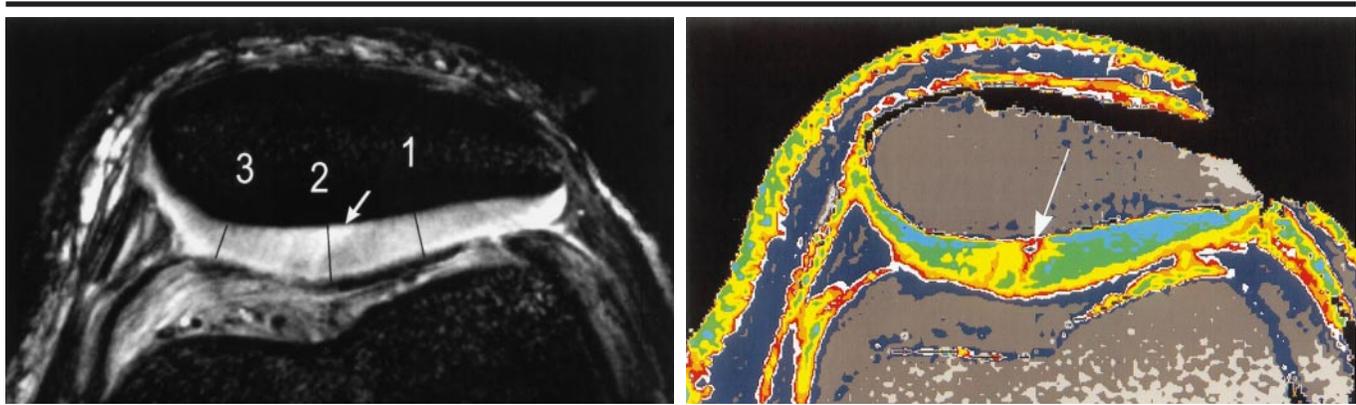


Figure 2. Pattern 1. Focally increased T2 limited to the radial zone in a 42-year-old man with intermittent anterior knee pain. (a) Transverse T2*-weighted gradient-echo image (200/21, 45° flip angle) demonstrates focal hyperintensity in the radial zone of the lateral patellar facet (arrow) with no evidence of surface irregularity. 1 = T2 profile 1, 2 = T2 profile 2, 3 = T2 profile 3. (b) Corresponding transverse T2 map (top) and color scale (bottom) demonstrate focally increased T2 in the deep radial zone (arrow), with a normal spatial dependency of T2 in the remainder of the articular cartilage. (c) T2 profile (T2 as a function of normalized distance) through the area of increased T2 (profile 2) is more than twice the 95% prediction interval (dotted lines) calculated from the asymptomatic adult volunteers. The superficial 20% of profile 1, obtained through the lateral facet, is slightly increased compared with that for age-matched control subjects. Profile 3, obtained through the medial facet, demonstrates a normal T2 spatial distribution.

As identified in Figure 1, cartilage T2 varies almost linearly with distance in the deepest 70% and then increases abruptly in the outer 30%, which suggests two regions with differing spatial variation in T2. These regions are compatible with known histologic zones in articular cartilage, characterized by regional differences in water content, as well as structure and composition of the collagen framework and proteoglycan matrix (17).

The deeper radial zone, located near the subchondral bone, has a highly ordered extracellular matrix. In addition to parallel collagen fibers, oriented perpendicular to the subchondral surface, Dunham and co-workers (18) have demonstrated orientation of the glycosaminoglycans in the radial zone. In the radial zone, compared with the more superficial transitional zone, there is less

spatial variation in water (19–21) and proteoglycan content (20,22,23), which increase linearly with distance from the subchondral bone.

With use of high-spatial-resolution spin-echo imaging at 1.5 T, Waldschmidt and co-workers (24) correlated the radial zone with a hypointense band demonstrating striations oriented perpendicular to the subchondral bone. These hypointense bands, previously observed with a high constant magnetic induction field (B_0) (25), are thought to be secondary to collagen fibers (24). The radial zone demonstrates T2 anisotropy, where measurements of T2 are dependent on orientation of B_0 (9,26). The highly ordered collagen and proteoglycan matrix results in anisotropic motion of the water, which prevents averaging of dipolar coupling between water protons. This provides an

efficient mechanism for spin-spin relaxation and lowers the T2 of the radial zone in normal cartilage (27).

T2 variation is greater in the outer 30% of articular cartilage, which corresponds to the histologic transitional zone. This layer is characterized by a more random orientation of the collagen fibers and increased water and proteoglycan content compared with those in the radial zone (17). Unlike in the radial zone, there is no evidence of orientation of the glycosaminoglycans in this zone (18). This layer does not demonstrate T2 anisotropy (9,11) and is hyperintense to the radial zone at intermediate-weighted imaging (24). Our results demonstrate increasing T2 in the transitional zone with higher values observed near the subarticular surface. The pattern of T2 variation observed in the deeper transitional zone resembles

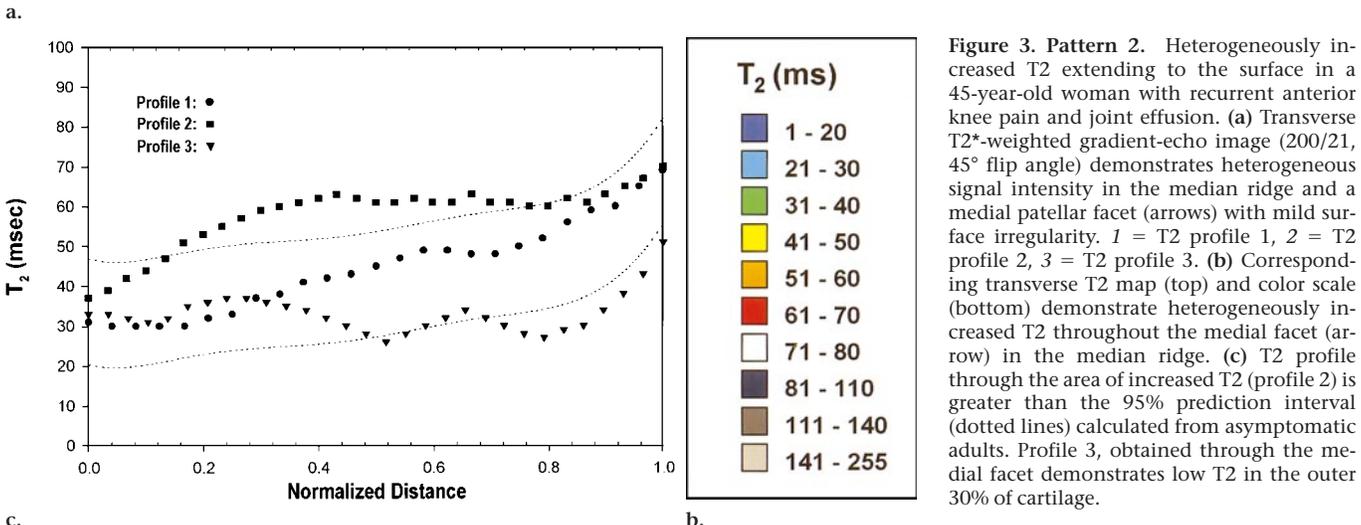
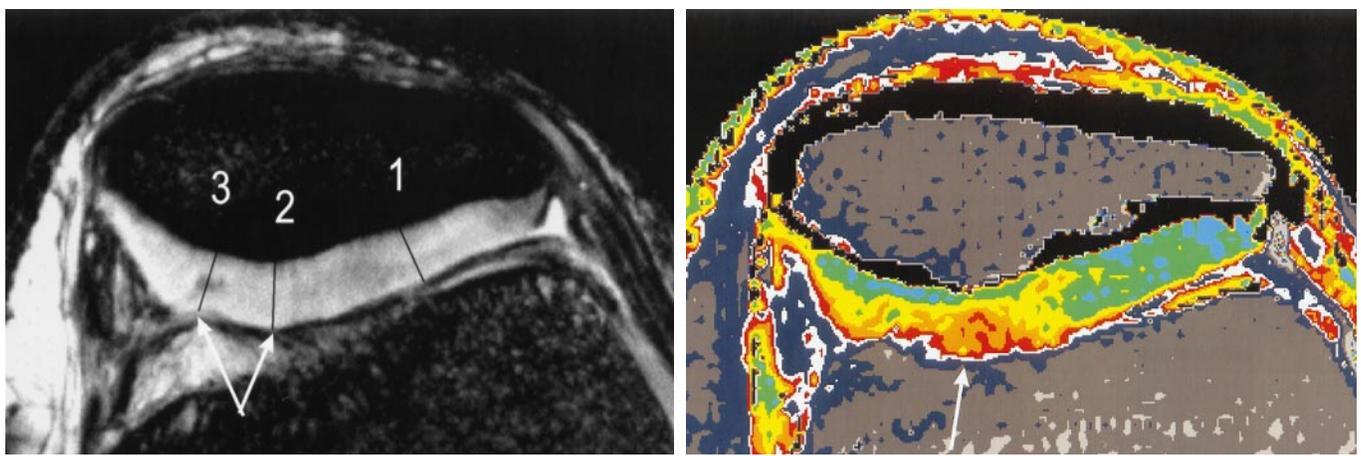


Figure 3. Pattern 2. Heterogeneously increased T₂ extending to the surface in a 45-year-old woman with recurrent anterior knee pain and joint effusion. (a) Transverse T₂*-weighted gradient-echo image (200/21, 45° flip angle) demonstrates heterogeneous signal intensity in the median ridge and a medial patellar facet (arrows) with mild surface irregularity. 1 = T₂ profile 1, 2 = T₂ profile 2, 3 = T₂ profile 3. (b) Corresponding transverse T₂ map (top) and color scale (bottom) demonstrate heterogeneously increased T₂ throughout the medial facet (arrow) in the median ridge. (c) T₂ profile through the area of increased T₂ (profile 2) is greater than the 95% prediction interval (dotted lines) calculated from asymptomatic adults. Profile 3, obtained through the medial facet demonstrates low T₂ in the outer 30% of cartilage.

the spatial distribution of water content (19–21); however, variation in water content does not explain the large increase in cartilage T₂ observed in the immediate subarticular cartilage. The immediate subarticular region of cartilage, which demonstrates a focal increase in T₂ (Fig 1), is characterized by a lower concentration of proteoglycan (21–23).

The most superficial layer of cartilage is approximately 200 μm thick and consists of collagen fibers oriented parallel to the subchondral bone. This has been described as a hypointense band at intermediate-weighted imaging (24) and demonstrates T₂ anisotropy (9). This layer is not resolved with our T₂ measurements.

Age-dependent Variation in Cartilage T₂

In the mature adult population (aged 46–60 years), the increase in T₂ corresponds in location to the transitional zone of articular cartilage. The elevated

T₂ values suggest an age-dependent increase in water mobility. To our knowledge, this has not been previously reported. We postulate the senescent increase in T₂ is secondary to age-dependent changes in structure of the proteoglycan aggregates that alter the mobility of cartilage water. As shown in Figure 5, the difference in T₂ between the mature adult and adult populations closely parallels the spatial variation in proteoglycan concentration reported in three previous studies (20,22,23). The maximal senescent increase in T₂ occurs in the transitional zone, the region of cartilage with the highest proteoglycan content. An age-dependent increase in T₂ is not observed in the radial zone, where tissue anisotropy strongly influences cartilage T₂.

Unlike collagen and water content, which remain relatively constant after skeletal maturity (17), there are known senescent changes in proteoglycan composition (28). With age, there is continued degradation of proteoglycan aggregates

that exceeds the rate of synthesis (29). This results in smaller, fragmented proteoglycan aggregates, with a corresponding increase in the breakdown products, aggrecan monomers and hyaluronate (28,29). Under normal conditions, highly charged proteoglycan aggregates hold water in a gel phase (30), restricting water movement and providing compressive stiffness to cartilage (31). A reduction in aggregate size and altered composition reduces the ability of the proteoglycan matrix to restrict water mobility (28). Because the transitional zone contains the highest concentration of proteoglycan (20), it is hypothesized that age-related aggregate degradation should produce the greatest increase in T₂ in this region.

Changes in Cartilage T₂ in Symptomatic Volunteers

Although limited to a small population, our results suggest three patterns of

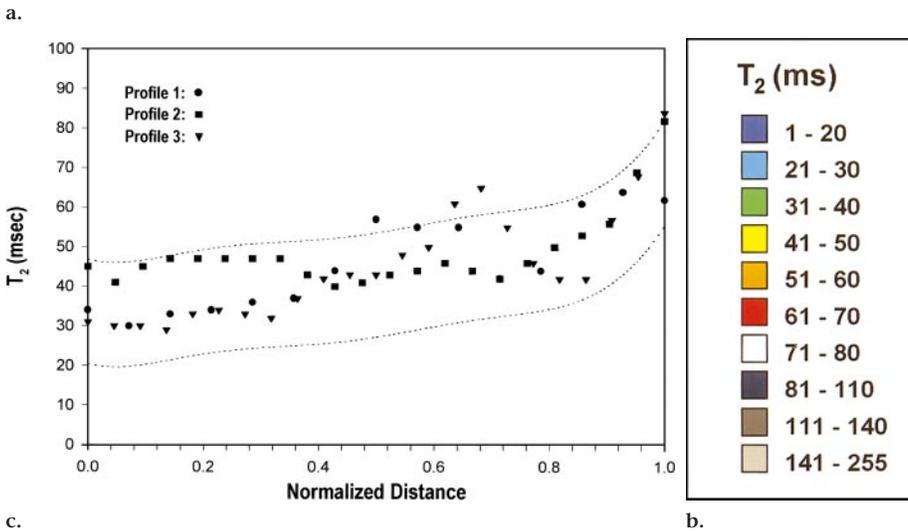
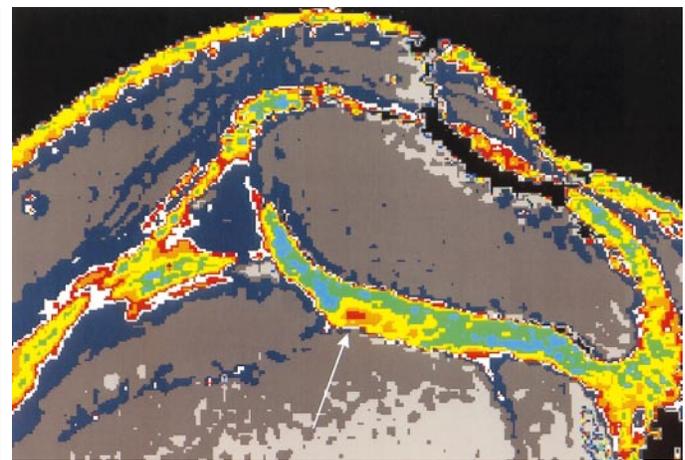
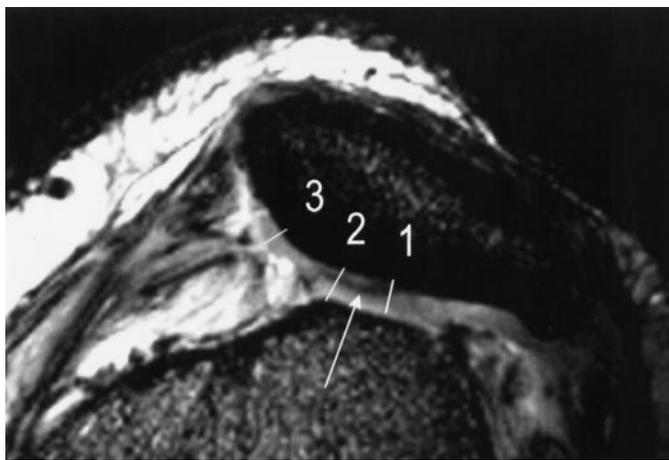


Figure 4. Pattern 3. Focal increased T2 associated with a flap tear extending to the radial zone in a 34-year-old woman with intermittent anterior knee pain. (a) Transverse T2*-weighted gradient-echo image (200/21, 45° flip angle) demonstrates linear hypointensity (arrow) extending to the surface of the median ridge, compatible with a flap tear previously identified at arthroscopy. Lateral patellar subluxation is seen. 1 = T2 profile 1, 2 = T2 profile 2, 3 = T2 profile 3. (b) Corresponding transverse T2 map (top) and color scale (bottom) demonstrate focally increased T2 superficial to the tear (arrow), with a normal pattern of T2 in the deeper cartilage. (c) T2 profile through the flap tear did not exceed the 95% prediction interval (profiles 1 and 2).

increased cartilage T2 in symptomatic volunteers: (a) focal increased T2 confined to the radial zone, (b) heterogeneously elevated T2 extending to the articular surface, and (c) a focal tear of the cartilage with associated change in the spatial distribution of T2. The spatial variation of cartilage T2 in the symptomatic population differs from that in the asymptomatic population in both magnitude and location. For five of the six volunteers, the focal increase in T2 was greater than the 95% prediction interval calculated from the corresponding age-matched asymptomatic population. Unlike the age-dependent increase in T2 observed in the asymptomatic mature adult population, the spatial dependency of T2 in the symptomatic population was more heterogeneous. In addition to the zonal dependency of T2, which is similar to that observed in the asymptomatic volunteers, focal areas of increased T2 were observed that typically involved the radial zone. In two of the six symptomatic

volunteers, focally increased T2 was limited to the radial zone, a pattern not observed in the asymptomatic group.

Increases in cartilage T2 have been previously associated with cartilage damage in both animal and clinical studies. Elevated cartilage T2 has been reported in a spontaneous model of OA in the guinea pig (32) and Rhesus monkey (33) and after proteolytic degradation of cartilage (34). Several clinical MR imaging studies have associated foci of increased T2-weighted signal intensity with cartilage damage. McCauley and co-workers (5) correlated foci of abnormal T2 signal or contour defect with the arthroscopic diagnosis of chondromalacia. Brown and Quinn (6) found the most reliable indicators of chondromalacia are focal contour irregularities of the hyaline cartilage and/or thinning of the hyaline cartilage associated with high-signal-intensity changes on T2-weighted images. In a retrospective study of 75 patients, De Smet and co-workers (7) found hyperintense signal

intensity abnormalities or fissures on sagittal T2-weighted images had a high specificity but low sensitivity in the diagnosis of patellar chondromalacia. Our preliminary results with quantitative T2 maps indicate focal sites of increased T2 are associated with symptoms of joint pain and stiffness. These results disagree with those in an early study performed at 0.02 T that correlated cartilage damage with increased T1 but found no correlation with T2 (35).

Limitations of This Study

In this cross-sectional study design, asymptomatic volunteers were stratified by age. There was no attempt to adjust for possible cofactors such as patient weight or level of physical activity. The evaluation of the effect of age on cartilage T2 was limited to male volunteers, and additional studies are needed to identify potential gender differences in the results of this study. Also, this study did not include evaluation of the elderly population (older than 60 years) to determine if these findings persist in later stages of life.

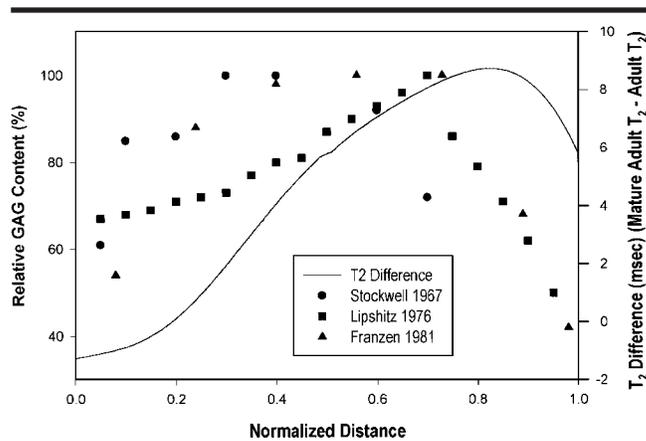


Figure 5. Graph depicts difference in cartilage T2 between the mature adult and adult populations, and values of glycosaminoglycan (GAG) content in the literature are plotted as a function of normalized distance from the subchondral bone. The pattern of increased T2 in the mature adult population, reflected by the difference in T2 between the mature adult and adult populations (*T2 Difference*), is similar to the distribution of proteoglycan content reported in three prior publications (20 [Lipshitz 1976], 22 [Stockwell 1967], 23 [Franzen 1981]). This indirect evidence supports the hypothesis that senescent change in proteoglycan content is responsible for the age-related increase in cartilage T2 observed in the transitional zone of the mature adult population.

Patient-reported symptoms were used to define the symptomatic population. For longitudinal studies evaluating disease progression, a measure of patient-reported symptoms is the most appropriate clinical outcome (36,37), as destructive assessment of cartilage degradation with histochemical or biochemical techniques is not possible. Given the relatively small population studied, we did not attempt to correlate the MR imaging findings with severity of symptoms. Two patients in the symptomatic cohort had undergone surgery for pathologic cartilage, which may contribute to the abnormalities observed with quantitative T2 mapping. Longitudinal studies are planned to determine if the observed focal areas of increased cartilage T2 will progress to more advanced damage or if these patients will develop increased severity of symptoms. Although the results of this study suggest structural changes in articular cartilage produce a measurable difference in T2, separate correlation studies are needed to elucidate the mechanism(s) of T2 variation observed in cartilage.

Although this study was performed with a 3.0-T magnet, there is little dependence of cartilage T2 on magnetic field strength, which is 51–77 msec at 0.5 T (38), 39 msec at 1.5 T (39), 55 msec at 2.0 T (33), 25 msec at 4.0 T (39), and 48 msec at 7.0 T (9). The similarity of T2 values over this wide range of B_0 strengths sug-

gests our reported T2 values should be similar to measurements obtained with current clinical imagers.

In conclusion, our results in a larger population confirm the initial observation of a spatial variation in T2 reported by Dardzinski et al (12). These results indicate aging is associated with an asymptomatic increase in T2 in the transitional zone of articular cartilage, compatible with an age-dependent increase in water mobility. Although preliminary, the results with *in vivo* quantitative T2 mapping of symptomatic volunteers are consistent with previous observations that cartilage degeneration is associated with focal areas of elevated cartilage T2.

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