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Longitudinal assessment of bone marrow edema-like lesions and cartilage degeneration in osteoarthritis using 3 T MR T1rho quantification

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Abstract

Objective—To quantitatively assess the relationship between bone marrow edema-like lesions (BMELs) and the associated cartilage in knee osteoarthritis (OA) using T_{1ρ} quantification at 3 T MRI.

Materials and Methods—Twenty-four patients with knee OA and 14 control subjects underwent 3 T MRI. Nineteen patients and all control subjects had 1-year follow-up studies. The volume and signal intensity difference of BMELs were calculated. Cartilage degeneration was graded using the cartilage subscore of Whole-Organ MRI Score (WORMS) analysis. Cartilage T_{1ρ} values were calculated in each compartment as well as in cartilage overlying BMELs (OC) and surrounding cartilage (SC).

Results—At baseline, 25 BMELs were found in 16 out of 24 patients. The overall T_{1ρ} values were significantly higher in patients with BMELs than in those without BMELs. At baseline and follow-up, both T_{1ρ} values and WORMS cartilage subscore grading were significantly higher in OC than SC. Cartilage T_{1ρ} increase from baseline to follow-up in OC was significantly higher than that in

SC. An increase in $T_{1\rho}$ values in OC was correlated with signal intensity of BMEL at both baseline and follow-up, but was not correlated with BMEL volume.

Conclusions—The results of this study suggest a local spatial correlation between BMELs and more advanced and accelerated cartilage degeneration. MRI $T_{1\rho}$ quantification in cartilage provides a sensitive tool for evaluating such correlations.

Keywords

MR imaging; Osteoarthritis; Cartilage; Bone marrow edema-like lesion; $T_{1\rho}$

Introduction

Osteoarthritis (OA) is one of the leading disabling diseases and a major medical, social, and economic problem in both developed and developing countries [1–3]. The disease affects not only cartilage, but also other tissues in the joint, including menisci, ligaments, and subchondral bone. Bone marrow edema-like lesions (BMELs), defined as regions with increased signal intensity in areas of subchondral bone marrow in fluid-sensitive sequences (such as fat-saturated T2-weighted fast spin-echo sequences or short tau inversion recovery [STIR] sequences) in magnetic resonance imaging (MRI), are prevalent in patients with knee OA. Previous studies revealed that BMELs represent a number of noncharacteristic histological abnormalities, including bone marrow necrosis, bone marrow fibrosis, trabecular abnormalities, and a small amount of edema in osteoarthritic knees [4,5].

Previous studies have associated BMELs with increased severity of OA as defined by Kellgren–Lawrence (KL) scores based on radiographs [6], and with disease progression [7] and cartilage loss [8,9]. Correlation between BMELs and pain in OA remains controversial in the literature [6,10–12]. These cohort studies suggested that BMELs may play an important role for OA pathophysiology. However, our understanding of the underlying mechanism is very limited. Investigations into the potential local spatial relationship between BMELs and cartilage degeneration may advance our understanding of this pathological interrelationship.

Despite the common observation of the coincidence of BMELs and cartilage focal lesions, few studies have documented and quantified such a relationship [13–15]. Furthermore, previous studies were normally limited to using qualitative or semi-quantitative methods for evaluating cartilage degeneration. Quantitative assessment of early cartilage degeneration would require the ability to non-invasively detect biochemical changes in proteoglycan (PG) concentration and collagen integrity starting at the early stage of OA. Standard radiography and conventional clinical MRI techniques are limited to detecting morphological changes in cartilage that occur at a relatively late stage of degeneration. Advanced MRI techniques for probing biochemical changes in cartilage matrix include $T_{1\rho}$ [16–18] and T2 relaxation time quantification [19, 20], delayed gadolinium-enhanced MRI for cartilage (dGEM-RIC) [21], and sodium imaging [22]. The ability of $T_{1\rho}$ to reflect the degree of PG loss may allow us to critically assess the relationship between BMELs and cartilage degeneration.

The goals of this study were therefore to first to quantitatively assess the relationship between BMELs (volume and signal intensity) and the cartilage overlying these lesions (using WOMS cartilage subscore grading and $T_{1\rho}$) in patients with knee OA using 3 T MRI; and second to evaluate the longitudinal changes in BMELs and the associated cartilage in patients with knee OA on 1-year follow-up MR examinations.

Materials and methods

Subjects

The study was approved by the Committee for Human Research at our institution and informed consent was obtained from all of the subjects after the nature of the examinations had been fully explained. Twenty-four patients (11 male, 13 female, mean age 51.9 ± 11.3 years) with clinically diagnosed knee OA were recruited to the study. The patient recruitment was a combination of referral from orthopedic surgeons at UCSF orthopedic clinic and recruitment from the general public. Inclusion criteria for OA patients were frequent clinical symptoms of OA (including pain, stiffness, and dysfunction) and demonstration of typical signs of OA on radiographs, i.e., osteophytes, subchondral sclerosis, and joint space narrowing. Subjects with inflammatory arthritis, knee OA that was secondary to other conditions (acute or chronic infection and metabolic abnormalities, for example), and any previous knee surgeries were excluded. Fourteen healthy volunteers (10 male, 4 female, mean age 37.1 ± 9.1 years) who had no history of diagnosed OA, no clinical OA symptoms, no knee surgery, and no previous knee injuries were recruited as control subjects. Subjects with standard MRI contra-indications were excluded. In all subjects, radiographs were obtained prior to 3 T MR examinations. The radiographs were scored based on the Kellgren–Lawrence (KL) scale [23].

At 1-year follow-up, 19 of the OA patients were scanned. Three patients with severe OA underwent total knee replacement after baseline MR scans, and therefore had no follow-up scans. Two patients with mild OA were lost to follow-up. All control subjects were scanned at 1-year follow-up.

Clinical symptoms were quantified using Western Ontario and McMaster University (WOMAC) scores in all subjects. The WOMAC index is a multidimensional, self-administered health status evaluation instrument for patients with knee OA [24]. It is composed of 24 items that are grouped into three dimensions, including pain (5 items), stiffness (2 items), and function (17 items).

Imaging protocol

The standard knee radiographic protocol included bilateral standing flexion weight-bearing view, 30° flexion lateral, and bilateral patellofemoral, sunrise views. All MR examinations were acquired using a 3 T GE MR scanner (Signa Excite HDx; GE Healthcare, Milwaukee, WI, USA) with an 8-channel phased array transmit/receive knee coil. The protocol included three sequences:

1. Sagittal T2-weighted fat-saturated fast spin-echo (FSE) images (TR/TE=4,300/51 ms, FOV=14 cm, matrix=512×256, slice thickness (ST)=2.5 mm, gap=0.5 mm)
2. Sagittal high-resolution water excitation 3D spoiled gradient echo (SPGR) images (TR/TE=9.3/3.5 ms, FOV=14 cm, matrix=512×512, ST=1 mm)
3. Sagittal 3D T_{1ρ}-weighted images were obtained using the sequence previously described (MAPSS, [25]).

The sequence was composed of two parts: magnetization preparation based on spin-lock techniques for the imparting of T_{1ρ} contrast, and an elliptical-centered segmented 3D SPGR acquisition immediately after T_{1ρ} preparation during transient signal evolution. The duration of the spin-lock pulse was defined as the time of spin-lock (TSL), and the strength of the spin-lock pulse was defined as spin-lock frequency (F_{SL}). The number of α pulses after each T_{1ρ} magnetization preparation was defined as views per segment (VPS). There was a relatively long delay (time of recovery, T_{rec}) between each magnetization preparation to allow enough and equal recovery of the magnetization before each T_{1ρ} preparation. The imaging parameters

are: TR/TE=9.3/3.7 ms, FOV=14 cm, matrix=256×192, ST=3 mm, BW=31.25 kHz, VPS=48, $T_{rec}=1.5$ s, TSL=0, 10, 40, 80 ms, $F_{SL}=500$ Hz.

Radiograph analysis

All radiographs were reviewed by two radiologists (JZ, TML) in consensus without knowledge of patient age, sex, and clinical symptoms. The radiographic findings were scored according to the KL scale, which is a standard grading system for OA [23]. Osteophytes at the joint margins, narrowing of the joint spaces, and subchondral sclerosis have been considered radiological features of OA. Based on these features, the following KL scores were defined [6]: 0, no features of OA; 1, doubtful OA, with minute osteophytes of doubtful importance; 2, minimal OA, with definite osteophytes, but unimpaired joint space; 3, moderate OA, with osteophytes and moderate diminution of joint space; and 4, severe OA, with greatly impaired joint space and sclerosis of subchondral bone.

Magnetic resonance images post-processing

Magnetic resonance images were transferred to a Sun workstation (Sun Microsystems, Palo Alto, CA, USA) for off-line quantification of BMEL volume and signal intensity, as well as cartilage volume, thickness, and $T_{1\rho}$ relaxation times.

Quantification of bone marrow edema-like lesions

In all subjects BMELs were defined as focal subchondral high signal intensity lesions on the T2-weighted fat-saturated FSE images. BMELs were segmented semi-automatically using a threshold method developed previously by our lab [26]. Briefly, normal bone marrow (NBM) was manually defined by a radiologist (JZ) on FSE images in the same compartment where BMELs were present (Fig. 1). The threshold to segment BMELs was determined by the mean and standard deviation (SD) of signal intensity of NBM using an auto-regression model [26]. Then, a 3D contour was generated based on this threshold, and the volume of BMELs was calculated with custom software based on IDL (Boulder, CO, USA). The signal intensity (SI) increase of BMEL vs NBM was calculated as: $(SI_{BMEL} - SI_{NBM})/SI_{NBM} \times 100\%$. Subchondral cysts were defined as well-defined hyperintense areas with a circular or elliptical configuration, and were excluded from this study. The final regions of interest for BMELs were verified by a musculoskeletal radiologist (JZ).

Cartilage quantification

The cartilage was segmented semi-automatically on SPGR images using an program developed in-house with MAT-LAB based on edge detection and Bezier splines [27]. Five compartments were defined: patella, lateral femoral condyle (LFC), medial femoral condyle (MFC), lateral tibia (LT), and medial tibia (MT). The segmentation was corrected manually by a radiologist (JZ) to avoid synovial fluid or other surrounding tissue, and 3D cartilage contours were generated.

The $T_{1\rho}$ map of the hyaline cartilage was reconstructed by fitting the $T_{1\rho}$ -weighted image intensity pixel-by-pixel to the equation below using a Levenberg–Marquardt monoexponential fitting algorithm developed in-house with C language:

$$S(TSL) \propto \exp(-TSL/T_{1\rho})$$

$T_{1\rho}$ -weighted images with the shortest TSL (therefore with the highest SNR) were rigidly registered to high-resolution T1-weighted SPGR images acquired in the same examination using the VTK CISC Registration Toolkit [28]. The transformation matrix was applied to the

reconstructed $T_{1\rho}$ map. The 3D cartilage contours were overlaid to the aligned $T_{1\rho}$ maps. The mean and SD of $T_{1\rho}$ values in each compartment were calculated.

In order to determine the cartilage overlying BMELs (OC) and the surrounding cartilage (SC), the T2-weighted fat-saturated FSE images were also aligned to the high-resolution SPGR images. The 3D cartilage contours generated from SPGR images were overlaid to the aligned FSE images from which BMELs were identified. 3D cartilage contours of OC were then manually defined accordingly as the cartilage overlying BMELs (Fig. 1). SC was defined as the rest of the cartilage within the same compartment. $T_{1\rho}$ values were calculated from the OC and SC respectively. $T_{1\rho}$ value changes from baseline to follow-ups were calculated in the OC and SC based on the equation: (follow-up – baseline)/baseline.

Cartilage grading

In the compartment with BMELs present, cartilage abnormalities were graded using a modified cartilage subscore of the Whole-Organ MRI Score (WORMS) on FSE images [29]. Cartilage signal and morphology were scored using a eight-point scale: 0 for normal thickness and signal; 1 for normal thickness, but increased signal on T2- or intermediate-weighted FSE images; 2 for solitary, focal, partial-thickness defects ≤ 1 cm in width; 2.5 for solitary, focal, full-thickness defects ≤ 1 cm; 3 for multiple areas of partial-thickness loss or a grade 2 lesion > 1 cm, with areas of preserved thickness; 4 for diffuse, $>75\%$, partial-thickness loss; 5 for multiple areas of full-thickness loss, or a full-thickness lesion > 1 cm, with areas of partial-thickness loss; and 6 for diffuse, $>75\%$, full-thickness loss. The OC and SC were graded separately. WORMS cartilage subscores for OC and SC were recorded according to the most degenerated part of OC and SC, respectively.

The WORMS cartilage subscore changes from baseline to follow-up were calculated in OC and SC based on the equation: (follow-up – baseline)/baseline.

Statistical analysis

A Student's t test was used to compare the KL and WOMAC scores, and $T_{1\rho}$ values between controls, OA patients with and without BMELs. A paired Student's t test was used to compare the $T_{1\rho}$ and WORMS cartilage subscore grading between OC and SC at baseline and follow-up respectively. A Student's t test was used to compare BMEL volume and SI between baseline and follow-up. The signed rank test was used to compare the $T_{1\rho}$ and WORMS cartilage subscore from baseline to follow-up of OC and SC respectively. Pearson's correlation coefficients were calculated between $T_{1\rho}$ values in OC and BMEL volume, and between $T_{1\rho}$ values in OC and BMEL SI increase respectively. All of the statistical computations were processed using JMP 7 (SAS Institute, Cary, NC, USA). The significance level was 0.05.

Results

Clinical evaluation and radiographic findings

The KL and WOMAC scores were significantly higher in OA patients than in control subjects (Table 1). All control subjects had a KL score of 0. All OA patients had a KL score of 1 or higher (number of patients=11, 10, 2, 1 with KL=1, 2, 3, 4 respectively). No significant difference was found in KL and WOMAC scores between OA patients with and without BMELs (Table 2).

Quantification of bone marrow edema-like lesions

At baseline, 25 BMELs were found in 16 of the 24 OA patients. Eleven BMELs were located in the patella, 8 at the LFC, 3 at the MFC, 2 at the MT, and 1 at the LT. The mean volume of BMELs was $2.88 \pm 3.21 \text{ cm}^3$, and the mean SI increase was $265\% \pm 110\%$ compared with

surrounding normal bone marrow. In the 19 OA patients who had follow-up scans, all BMELs that were found at baseline presented at 1-year follow-up, and no new BMELs were found at 1-year follow-up. There was a total of 14 BMELs from 12 patients at 1-year follow-up: 6 BMELs were located at the patella, 6 at the LFC, and 2 at the LT. The mean volume of BMELs was $3.83 \pm 4.61 \text{ cm}^3$, and the mean SI increase was $281\% \pm 123\%$.

No significant differences were found in volume and SI of BMELs between baseline and 1-year follow-up. The volume of 6 BMELs had increased (changed more than 5%) by the follow-up examination, that of 5 had decreased, and 3 remained stable. Concerning SI, 9 BMELs showed an increase (changed more than 5%) at follow-up, 4 a decrease, and 1 remained stable.

T_{1ρ} quantification of cartilage

At baseline, T_{1ρ} values were higher in OA patients than in control subjects at ($41.0 \pm 2.5 \text{ ms}$ vs $37.0 \pm 2.1 \text{ ms}$, $P < 0.001$). Among OA patients, significantly elevated T_{1ρ} values were found in OA patients with BMELs compared with OA patients without BMELs ($42.0 \pm 2.7 \text{ ms}$ vs $38.9 \pm 2.2 \text{ ms}$, $P = 0.05$). In each compartment, T_{1ρ} values were higher in OA patients with BMELs than those without BMELs. This difference was significant in the LFC and MT ($P < 0.05$, Fig. 2).

At 1-year follow up, T_{1ρ} values stayed stable for controls ($37.2 \pm 2.4 \text{ ms}$) compared with baseline ($37.0 \pm 2.1 \text{ ms}$). For OA subjects who had both baseline and follow-up scans, no significant differences were found in overall T_{1ρ} values from baseline to 1-year follow-up. Significantly increased T_{1ρ} values were observed in the patella cartilage at 1-year follow-up compared with baseline in all OA patients ($42.9 \pm 4.3 \text{ ms}$ vs $41.3 \pm 4.4 \text{ ms}$, $P = 0.042$) and in patients with BMELs ($45.1 \pm 4.1 \text{ ms}$ vs $42.5 \pm 3.7 \text{ ms}$, $P = 0.019$). Similar to baseline data, at 1-year follow-up, T_{1ρ} values were significantly higher in OA patients than in control subjects ($P = 0.018$), and T_{1ρ} values were significantly higher in OA patients with BMELs than OA patients without BMELs in overall cartilage and in the patella and LFC cartilage ($P < 0.05$, Fig. 2).

In patients with BMELs, baseline T_{1ρ} values were significantly elevated in OC compared with SC. Similarly, at 1-year follow-up, T_{1ρ} values were significantly higher in OC than in SC (Fig. 3, Table 3). T_{1ρ} value increase from baseline to follow-up in OC was $8.6\% \pm 7.4\%$, which was significantly higher than the increase from baseline to follow-up in SC ($3.1\% \pm 3.4\%$, $P < 0.05$).

Clinical grading of cartilage

In OA patients with BMELs, WORMS cartilage subscores were significantly higher in OC than in SC both at baseline and at 1-year follow-up (Fig. 3, Table 3). No significant differences were found in WORMS between baseline and 1-year follow-up. No significant differences in WORMS cartilage subscore change from baseline to follow-up were found between the OC and SC regions.

Correlation between BMEL and cartilage T_{1ρ}

Increased T_{1ρ} values in OC were correlated with increased SI of BMELs at both baseline and follow-up ($R^2 = 0.51$, $P < 0.05$ for baseline, $R^2 = 0.42$, $P < 0.05$ for follow-up), but were not correlated with BMEL volume ($R^2 = 0.11$, $P = 0.59$ for baseline, $R^2 = 0.19$, $P = 0.60$ for follow-up; Table 4). No significant correlation was found between the WORMS cartilage subscores of OC and BMEL severity (volume or SI).

Discussion

This study quantitatively examined the relationship between BMELs and cartilage degeneration of knee OA. Despite documentation of the potential relationship between BMELs

and cartilage degeneration, previous reports are limited to qualitative or semi-quantitative evaluation of morphological cartilage changes using clinical scoring systems. To the best of our knowledge, this is the first study to quantify biochemical changes within the cartilage matrix in areas overlying BMELs, cross-sectionally and longitudinally, in OA knees. This study also investigated the signal intensity changes within BMELs, which may provide additional valuable information related to disease severity. Quantification of BMELs and associated cartilage degeneration using advanced quantitative MRI may help to better stratify patients who are at high risk of disease progression.

In the present study, 25 BMELs were found in 16 of the 24 OA patients at baseline. This high prevalence of BMELs in OA knees is consistent with previous reports [6–9]. At 1-year follow-up, no complete resolution of BMEL was observed, and no new BMEL was observed. Furthermore, no significant differences were found in volume and signal intensity difference in BMELs between baseline and follow-up. However, there was a large variation from patient to patient. Six BMELs had increased in volume (changed more than 5%) by the 1-year follow-up, 5 had decreased, and 3 remained stable. Nine BMELs experienced an increase in SI (changed more than 5%) during follow-up, while 4 had a decrease and 1 remained stable. These results suggest that BMELs in OA patients may be relatively stable over a period of 1 year, but large individual variations are present.

Bone marrow edema-like lesions had been proposed to contribute to the central disabling feature of OA: pain. The periosteum and bone marrow are richly innervated with nociceptive fibers representing a potential source of pain in patients with knee OA [30]. However, efforts to correlate BMELs with pain in OA have demonstrated inconsistent results in the literature—some investigators suggested an association between BMELs and knee pain [10,12], while others demonstrated no significant correlation between these two entities [6,11,31,32]. Our study compared WOMAC grading in OA patients with and without BMELs. Pain and Function subscores of WOMAC were higher in OA patients with BMELs, but the difference was not significant. These results are consistent with a previous MRI study by Phan et al. [31], who found that changes in cartilage and BMELs morphologies were not strongly associated with changes in pain, stiffness, and function, as assessed with the WOMAC scores. The authors speculated that, in addition to cohort differences, the lack of significant correlation between MRI findings and clinical findings may in part be due to the fact that patients get more accustomed to their pain as the knee progressively degenerates. Clearly, further investigation into correlating BMELs and other imaging findings with pain and other clinical symptoms are warranted.

Despite questionable correlation with pain, BMELs have been associated with the severity and progression of articular cartilage degeneration in OA. Link et al. reported a significant increase in the presence of BMELs with increased KL score based on radiographs [6]. Felson et al. found a correlation between BMELs and structure deterioration in knee OA, and between BMELs and frontal plane malalignment [7]. The authors concluded that OA disease progression in patients with BMELs may be the consequence of the lesions themselves, or that malalignment may produce both the traumatic BMELs and the loss of local cartilage. In a natural history study with 217 OA patients being scanned at baseline, at 15 months, and at 30 months, Hunter et al. found that, compared with BMELs that stay the same, enlarging BMELs are strongly associated with more cartilage loss [8]. Furthermore, any change in BMELs was mediated by limb alignment [8].

The results from these large cohort studies have suggested that BMELs may play an important role in the pathophysiology of OA, and have motivated investigators to further study the potential local relationship between BMELs and cartilage degeneration. Rubin et al. reported a strong correlation between arthroscopically-proven traumatic cartilage defect and the

presence of subchondral BMELs in 18 knees [15]. In a retrospective study with a cohort of 32 patients, a significant association was found between BMELs and adjacent cartilage defect [13]. Using arthroscopic validation, Kijowski et al. found that higher grades of articular cartilage defects were correlated with higher prevalence and greater depth and cross-sectional area of subchondral BMELs [14]. These results supported a local spatial correlation between BMELs and more advanced cartilage degeneration during OA. These studies, however, were limited to qualitative or semi-quantitative (grading) evaluation of cartilage degeneration. In the present study, we have applied advanced $T_{1\rho}$ quantification techniques to evaluate changes in cartilage matrix composition that are associated with BMELs.

The $T_{1\rho}$ values were significantly higher in OA patients with BMELs than those without BMELs, although no differences were found in KL scores between these two groups of patients. In each defined compartment, the mean $T_{1\rho}$ values were also higher in OA patients with BMELs than those without BMELs. In particular, this difference was significant in the LFC and MT at baseline (the difference in patella at baseline was also approaching significance with $P=0.09$), and in the LFC and patella at follow-up. As this cohort showed a high prevalence of BMELs in the patella and LFC compartments, these results suggest that BMELs were associated with advanced cartilage degeneration.

No significant difference in $T_{1\rho}$ values of OA subjects from baseline to 1-year follow-up was observed in this study. Interestingly, the increase in $T_{1\rho}$ values from baseline to follow-up reached significance at the patella ($P=0.042$). When we investigated the $T_{1\rho}$ value increase in the patella separately in patients with BMELs and without BMELs, this difference was primarily driven by the patients with BMELs (45.1 ± 4.1 ms vs 42.5 ± 3.7 ms, $P=0.019$). This result implies that BMELs may be related to more progressive or accelerated progression of cartilage degeneration.

In order to study the detailed local relationship between BMELs and cartilage degeneration, we compared cartilage overlying BMELs (OC) with cartilage distant from BMELs, the surrounding cartilage (SC). We found that both WORMS cartilage subscore and $T_{1\rho}$ values were significantly higher in OC than SC at both baseline and 1-year follow-up. This result is indicative of a local relationship between BMELs and more advanced cartilage degeneration.

We have also observed higher WORMS cartilage subscore and $T_{1\rho}$ values in the OC and SC at 1-year follow-up than at baseline. The difference, however, was not significant for either WORMS cartilage subscore or $T_{1\rho}$ values. This current study is limited by a short follow-up period of 1 year. A longer follow-up may be needed in order to observe significant changes of these measurements.

Interestingly, when we compared the WORMS cartilage subscore and $T_{1\rho}$ increase in the OC and SC separately, the increase in $T_{1\rho}$ values from baseline to 1-year follow-up was significantly higher in the OC than in the SC. The increase in the WORMS cartilage subscore from baseline to 1-year follow-up, however, was not significantly higher in the OC than in the SC. These results imply that first, a local relationship exists between BMELs and more accelerated cartilage degeneration, and second, quantitative MRI (such as $T_{1\rho}$) is more sensitive than conventional MRI (WORMS) in detecting such correlations.

Finally, we investigated quantitatively the correlation between cartilage degeneration (measured with WORMS and $T_{1\rho}$) and BMEL severity (measured with size and SI difference compared with normal bone marrow). The SI of BMELs significantly correlated with the degree of $T_{1\rho}$ elevation in OC. However, no correlation was found between the volume of BMELs and cartilage degeneration. The lack of correlation between quantification of cartilage degeneration and BMEL volume may be due to the small sample size of the present study and larger cohorts may be required to increase the statistical power. Meanwhile, this result suggests

that the signal intensity difference in BMELs may be more indicative of BMEL severity, which consequently correlates with local cartilage composition measured with $T_{1\rho}$. By quantifying both volume and signal intensity of BMELs, we can evaluate the overall lesion burden more comprehensively.

Despite promising results, there are a number of limitations of the current study. We had a relatively small cohort of controls and OA subjects and a short follow-up of 1 year, and the controls were younger and had a lower BMI compared with the OA subjects. There is no surgical correlation or gold standard for the presence or absence of cartilage lesions. No alignment data were collected from the subjects studied. Finally, there is potential partial volume averaging of fluid-filled cartilage fissures and defects that are smaller than the slice thickness, which may affect $T_{1\rho}$ quantification, even after careful image analysis to remove regions that showed obvious partial volume averaging from surrounding fluid.

In summary, this study demonstrated a local spatial relationship between BMELs and cartilage degeneration in OA knees. It contributed to advancing our knowledge at four levels:

1. The overall $T_{1\rho}$ values in cartilage were higher in patients with BMELs than in patients without BMELs.
2. $T_{1\rho}$ values were higher in cartilage overlying BMELs than in the surrounding cartilage in the same compartment, indicating quantitatively a local spatial correlation between BMELs and advanced cartilage degeneration.
3. Increase in $T_{1\rho}$ values over time was significantly higher in OC than in SC, while the WORMS cartilage subscore showed no significant differences, suggesting that $T_{1\rho}$ might be more sensitive than conventional MRI in detecting progression of subtle cartilage degeneration.
4. The degree of $T_{1\rho}$ elevation in OC was correlated with the increase in BMEL signal intensity, but not with BMEL volume, suggesting that BMEL signal intensity might provide valuable information related to lesion severity.

Based on the results of this study we believe that quantitative MRI has great potential to be a valuable diagnostic tool for evaluating cartilage and bone degeneration in OA, giving information beyond that of morphological MR evaluation.

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Fig. 1.

Bone marrow edema-like lesions (BMELs; *yellow dotted line*) were semi-automatically segmented on sagittal fat-suppressed T2-weighted fast spin-echo (FSE) images using a thresholding method. The threshold was calculated based on the mean and standard deviation (SD) of signal within normal bone marrow in the same compartment. Cartilage was segmented semi-automatically on spoiled gradient echo (SPGR) images. The FSE images were registered to SPGR images. Cartilage overlying BMEL (*red line*) and surrounding cartilage (*green line*) were then defined manually according to the size and location of BMELs

(a)

(b)

Fig. 2.

Significantly elevated $T_{1\rho}$ values were found in osteoarthritis (OA) patients with BMELs (blue) compared with OA patients without BMELs (red) at both **a** baseline and **b** 1-year follow-up. In each compartment, $T_{1\rho}$ values were higher in OA patients with BMELs than those without BMELs. This difference was significant in the lateral femoral condyle (LFC) and medial tibia (MT) at baseline and in the patella and LFC at 1-year follow-up (* $P < 0.05$). *P* patella, *MFC* medial femoral condyle, *LT* left tibia

Fig. 3.

T_{1ρ} color-coded maps obtained in a 57-year-old man with mild OA at **a** baseline and **b** 1-year follow-up. Sagittal fat-suppressed T2-weighted FSE image obtained in the same patient at **c** baseline and **d** 1-year follow-up. T_{1ρ} values of the LFC were significantly higher in cartilage overlying (OC) the BMEL than surrounding cartilage (SC) at both baseline and 1-year follow-up (49.5 ± 4.3 ms vs 43.3 ± 4.0 ms, $P=0.0006$ for baseline; 49.8 ± 3.9 ms vs 43.2 ± 2.2 ms, $P=0.0005$ for follow-up). From baseline to 1-year follow-up, the T_{1ρ} values increased in OC BMEL, accompanied by increased signal intensity and size of the BMEL at the LFC. Sagittal FSE sequences demonstrate cartilage defects within cartilage overlying BMEL at the LFC (arrows). The WORMS was higher in OC than in SC both at baseline and at 1-year follow-up (4.7 ± 1.7 vs 1.2 ± 1.6 , $P=0.00005$ for baseline; 5.1 ± 1.4 vs 1.5 ± 1.5 , $P=0.00003$ for follow-up)

Summary of subject characteristics: age, gender, body mass index (BMI), Kellgren–Lawrence (KL) score, and Western Ontario and McMaster University (WOMAC) score for patients and controls. *OA* osteoarthritis

Table 1

	Gender (male/female)	KL score	BMI	WOMAC		
				Pain	Stiffness	Function
OA patients (<i>n</i> =24)	11/13	1.7±0.8	27.4±5.7	4.8±4.4	2.6±1.9	16.1±16.8
Controls (<i>n</i> =14)	10/4	0	23.7±3.5	1.7±2.1	0.8±1.2	2.2±5.1
<i>P</i> value	–	<0.0001	0.02	0.006	0.001	0.001

Table 2

Kellgren–Lawrence (*KL*) and Western Ontario and McMaster University (*WOMAC*) gradings for patients with and without bone marrow edema-like lesions (*BMELs*). *OA* osteoarthritis

	KL score	WOMAC score		
		Pain	Stiffness	Function
OA with BMEL (<i>n</i> =16)	1.9±0.8	5.1±4.5	2.6±2.0	18.1±18.2
OA without BMEL (<i>n</i> =8)	1.4±0.7	4.1±4.2	2.5±1.8	12.5±14.0
<i>P</i> value	0.15	0.60	0.90	0.43

T_{1ρ} values and Whole-Organ MRI Score (WORMS) of cartilage overlying BMEL (OC) and surrounding cartilage (SC) at baseline and 1-year follow-up in OA patients

Table 3

	T _{1ρ} values (ms)		WORMS		
	OC	SC	P value	OC	SC
Baseline	45.9±2.8	42.3±2.3	0.0006	4.7±1.7	1.2±1.6
Follow-up	49.8±3.9	43.2±2.2	0.0005	5.1±1.4	1.5±1.5
					P value
					0.00005
					0.00003

Table 4

R^2 and P values of correlations between $T_{1\rho}$ of cartilage overlying BMEL with BMEL volume and signal intensity (SI) increase at baseline and follow-up

$T_{1\rho}$	Volume		SI increase	
	R^2	P	R^2	P
Baseline	0.11	0.59	0.51	<0.05
Follow-up	0.19	0.60	0.42	<0.05