



Original contribution

The comparison of the performance of 3 T and 7 T T₂ mapping for untreated low-grade cartilage lesions

Vladimir Juras^{a,b,*}, Markus Schreiner^{a,c}, Didier Laurent^d, Štefan Zbýň^{a,e}, Vladimír Mlynarik^{a,k}, Pavol Szomolanyi^{a,b}, Benedikt Hager^a, Celeste Scotti^d, Jörg Goldhahnⁱ, Rahel Heule^j, Oliver Bieri^f, Siegfried Trattnig^{a,g,h}

^a High-Field MR Centre, Department of Biomedical Imaging and Image-Guided Therapy, Medical University of Vienna, Vienna, Austria

^b Institute of Measurement Science, Slovak Academy of Sciences, Bratislava, Slovakia

^c Department of Orthopaedics, Medical University of Vienna, Waehringer Guertel 18-20, A-1090 Vienna, Austria

^d Novartis Institutes for Biomedical Research, Department of Translational Medicine, CH-4056 Basel, Switzerland

^e Center for Magnetic Resonance Research, Department of Radiology, University of Minnesota, Minneapolis, Minnesota, USA

^f Division of Radiological Physics, Department of Radiology, University of Basel Hospital, Basel, Switzerland

^g Christian Doppler Laboratory for Clinical Molecular MR Imaging, Vienna, Austria

^h Austrian Cluster for Tissue Regeneration, Austria

ⁱ ETH Zurich, Institute of Translational Medicine, Leopold-Ruzicka-Weg 4, CH-8093 Zurich, Switzerland

^j High Field Magnetic Resonance, Max Planck Institute for Biological Cybernetics, Tübingen, Germany

^k Karl-Landsteiner Gessellschaft, St. Pölten, Austria

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ABSTRACT

Objective: To investigate T₂ mapping as a possible marker for low-grade human articular cartilage lesions during a one-year follow-up, possible changes during the follow-up and compare the reliability and sensitivity of these measurements on high-field (3 T) and ultra-high-field (7 T) MRI scanners.

Design: Twenty-one patients with femoral, tibial and patellar cartilage defect in the knee joint participated in the study. The MRI protocol consisted of morphological, as well as three-dimensional triple-echo steady-state (3D-TESS) T₂ mapping sequences with similar parameters at 3T and 7T. Patients were scanned at five time-points up to 12 months. T₂ values were evaluated in the lesion and healthy-appearing regions for superficial and deep cartilage zone. The repeated ANOVA was used to determine differences in T₂ values at various time points.

Results: A significant decrease in T₂ values was observed between baseline and six months in the superficial layer of the lesion in patients at 3 T (decrease from 41.89 ± 9.3 ms to 31.21 ± 7.2 ms, which is a difference of -5.67 ± 2.2 ms (p = 0.031)), and at 12 months in the superficial layer of the lesion in patients at 3 T (decrease from 41.89 ± 9.3 ms to 35.28 ± 4.9 ms, which is a difference of -6.60 ± 4.4 ms (p = 0.044)). No significant differences were recorded at 7 T.

Conclusion: The change in T₂ values acquired with 3 T 3D-TESS appears to be reflecting subtle changes of cartilage composition in the course of low-grade lesion development. 7 T T₂ mapping does not reflect these changes probably due to completely decayed short T₂ component.

1. Introduction

Cartilage degeneration is a major source of pain and disability in Western societies. Biochemical changes of the extracellular matrix often precede the morphological changes [1]. Thus, early diagnosis of

articular cartilage degradation is crucial for successful treatment. However, the detection of low-grade cartilage lesions can be rather challenging. MRI is the modality of choice because of its non-invasive nature, good reliability, and diagnostic power [2–4].

Mature cartilage tissue is characterized by small amount of cells

* Corresponding author at: High-Field MR Centre, Department of Biomedical Imaging and Image-Guided Therapy, Medical University of Vienna, Waehringer Guertel 18-20, A-1090, Vienna, Austria.

E-mail addresses: vladimir.juras@meduniwien.ac.at (V. Juras), markus.schreiner@meduniwien.ac.at (M. Schreiner), didier.laurent@novartis.com (D. Laurent), szbyn@umn.edu (Š. Zbýň), vladimir.mlynarik@meduniwien.ac.at (V. Mlynarik), pavol.szomolanyi@meduniwien.ac.at (P. Szomolanyi), benedikt.hager@meduniwien.ac.at (B. Hager), celeste.scotti@novartis.com (C. Scotti), jgoldhahn@ethz.ch (J. Goldhahn), Rahel.Heule@tuebingen.mpg.de (R. Heule), oliver.bieri@unibas.ch (O. Bieri), siegfried.trattnig@meduniwien.ac.at (S. Trattnig).

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which account only for small volume of hydrated cartilage. Cartilage hydration and the amount various extracellular elements are dependent on age and species. The basic matrix consists of collagen fibers typically oriented in three cartilage layers and glycosaminoglycan molecules responsible for dynamic mechanical properties [5].

There is a strong demand for a noninvasive tool that would enable early diagnosis but also treatment monitoring and benchmark of success for new therapeutic interventions. Such a tool would allow physicians to monitor the patients treated with any treatment options and therapeutic advice to slow down the onset or progression of osteoarthritis (OA) disease. MRI has been previously successfully used for quantification of the cartilage thickness and for volumetry [6], water content [7], as well as proteoglycan and collagen content assessment [8–10]. MRI can also detect focal cartilage disorder that precedes subsequent structural changes of the tissue. The changes in articular cartilage during OA or in acute lesions result in an increased hydrodynamic fluid pressure and increased stress throughout the matrix. This leads to the proteoglycan-collagen matrix degeneration and cartilage tissue loss [11].

Quantitative MRI has shown a great potential to non-invasively detect cartilage tissue alterations, especially with T_2 mapping, which is sensitive to collagen matrix anisotropy/organization and water content [9]. There are several methods currently used for T_2 mapping in articular cartilage. As a gold standard for T_2 mapping, a multi-echo spin echo sequence is usually employed [12,13]. It provides robust, reproducible, and fast T_2 mapping; however, its use at ultra-high-fields is compromised by specific-absorption rate (SAR) limitations due to multiple 180° pulses needed for repeated refocusing. The recently introduced technique of 3D Triple-Echo Steady-State (TESS) T_2 mapping has been shown a faster and more reproducible alternative to multi-echo spin-echo T_2 mapping [14,15]. The reproducibility of T_2 mapping with 3D-TESS observed in this study was comparable to the previously published works [16,17]. At ultra-high-field MRI, the advantage of 3D-TESS over multi-echo spin echo is even more prominent since TESS imaging is not prone to specific absorption rate (SAR) issues due to the low optimal excitation flip angles and the derived T_2 maps are intrinsically insensitive to transmit field (B_1) inhomogeneities. It was shown previously, cartilage tissue has multiple water compartments resulting in multi-component T_2 values [18]. Reiter et al. demonstrated in bovine cartilage three components of T_2 , specifically $T_{2,1} = 2.3$ ms, $T_{2,2} = 25.2$ ms, and $T_{2,3} = 96.3$ ms, with fractions $w_1 = 6.2\%$, $w_2 = 14.5\%$, and $w_3 = 79.3\%$, respectively, using multi-echo spin-echo sequence at 9.4 T [19]. With conventional multi-echo spin-echo the minimal echo time is rarely below 10 ms, however by using TESS T_2 mapping with the echo time as short as 5 ms, there are still some residuals from the shortest component which might contribute to the global T_2 . As this short component is said to be related to bound water molecules, it may bring an interesting information about the cartilage tissue composition. T_2^* might also provide an interesting information on cartilage composition [20,21], especially because it allows for ultra-short echo times [22,23], however, the previous studies showed this information is not substantially different for T_2 [24].

Low-grade cartilage lesions are challenging to diagnose since morphological alterations are often subclinical, but are accompanied by changes in water content and disruption of collagen fibers [25]. As a result, T_2 mapping could be a very helpful tool for the initial diagnosis of cartilage lesions as well as for monitoring their subsequent development over time. Several longitudinal studies have used quantitative MRI to describe the cartilage repair process. Krusche-Mandl et al. used quantitative MRI parameters to follow-up patients with autologous chondrocyte transplantation where T_2 was the only quantitative parameter that correlated with the modified Lysholm score [26]. A strong correlation between qualitative MRI and clinical score was also found by Salzmann et al.; the correlation with quantitative MR (T_2 mapping), on the other hand, was only moderate [27]. However, to establish sensitivity of T_2 mapping to cartilage tissue alteration, the natural

course of cartilage degradation should be established. To date, no study compared the clinical value of quantitative MRI at different field-strengths in patients with untreated, low-grade cartilage lesions.

Therefore, in this study we investigated 3D-TESS T_2 mapping as a possible marker of changes in cartilage status over one year after baseline examination in patients with low-grade cartilage lesions and with risk factors for further cartilage degeneration, such as a meniscal or anterior cruciate ligament tear. The sensitivity and reproducibility of T_2 mapping were evaluated at two field-strengths, 3 and 7 Tesla.

2. Methods

2.1. Subjects

The ethics committee of the Medical University of Vienna approved the study protocol (No. 1978/2014) and all patients gave written, informed consent. Twenty-one patients (mean age \pm standard deviation, 46.3 ± 11.1 years; 12 males/9 females) were enrolled. All of them had femoral ($N = 18$), patellar ($N = 2$), and tibial ($N = 1$) cartilage defect (s) in the knee joint (ICRS Grade I or II [28,29]). The grading of the lesion was performed according to the ICRS classification system by one radiologist with 26 years of experience in musculoskeletal MR (S.T.), using high-resolution morphological MR scans.

Inclusion criteria, in addition to low-grade cartilage lesions Grade I and II, were risk factors for cartilage disease progression, such as the presence of an ACL tear or meniscal tear. Patients with contraindications to MRI, such as pacemakers, implants, or pregnant patients, were excluded from the study.

2.2. MRI examination

All subjects underwent an MR examination on two MR scanners on the same day: a 3 T Trio (Siemens, Erlangen, Germany) with 8-channel knee coil (Quality Electrodynamics, Mayfield Village, Ohio, USA) and a 7 T whole-body investigational MR scanner (Siemens Healthcare, Germany) with 28-channel knee coil (Quality Electrodynamics, Mayfield Village, Ohio, USA). The examination consisted of two parts: morphological and quantitative. Morphological sequences included sagittal intermediate-weighted turbo-spin echo (sag PD TSE), coronal intermediate-weighted turbo-spin echo (cor PD TSE), and transversal intermediate-weighted turbo-spin echo (tra PD TSE) scans at 3 Tesla and an additional three-dimensional double-echo steady-state sequence (3D-DESS) at 7 Tesla. T_2 mapping was performed using 3D-TESS with similar parameters at both field-strengths [15]. The maps were reconstructed online on the scanner using an IceLuva script [30]. All sequence parameters are listed in Table 1. The measurements were repeated at four time points: at baseline (B); 8 days (8D); three months (3M); and six months (6M) after the baseline examination. Ten patients were also rescanned at 12 months (12M) after baseline examination.

2.3. Image analysis

Regions-of-interest (ROI) were defined by the radiologist using morphological images from both 3 and 7 Tesla with JiveX (Visus, Bochum, Germany) based on pathophysiological appearance of cartilage and subchondral bone [31]. The ROIs were then transferred onto T_2 maps using the co-registration feature of RadiAnt (Medixant, Poznan, Poland) to define the corresponding slices. The number of evaluated slices depended on the lesion size, and the aim was to cover a majority of the lesion. In each subject, three locations were selected: 1) cartilage lesion; 2) healthy reference cartilage in a weight-bearing area; and 3) healthy reference cartilage in a non-weight bearing area. In each of the locations, the deep and superficial layers were selected by dividing the cartilage thickness into two equal sections. The selection of ROIs is depicted in Fig. 1.

Table 1
Sequence parameters used for morphological and quantitative 3D-TESS T_2 mapping.

Field strength→	3 T			7 T	
↓Sequence parameters	sag PD TSE	cor PD TSE	3D-TESS (T_2 mapping)	3D-DESS	3D-TESS (T_2 mapping)
Image plane	Sagittal	Coronal	Sagittal	Sagittal	Sagittal
Slice thickness	2.0 mm	3 mm	3 mm	0.5 mm	3 mm
Slice spacing	2.4 mm	3.6 mm	3 mm	0.5 mm	3 mm
Repetition time	2200 ms	3030 ms	11.14 ms	8.86 ms	9.76 ms
Echo time	38 ms	29 ms	5.53 ms	2.55 ms	5.1 ms
Averages	1	1	1	1	1
Acquisition matrix	448 × 403	448 × 448	320 × 288	320 × 320	384 × 346
Field-of-view	120 × 120	150 × 150	160 × 160	160 × 160	143 × 143
Flip angle	180°	180°	15°	18°	15°
Total acquisition time	6:38 min	3:01 min	3:45 min	3:57 min	3:48 min
Pixel bandwidth	170 Hz/px	140 Hz/px	445 Hz/px	347 Hz/px	501 Hz/px

2.4. Reproducibility and inter-observer variability analysis

To assess the reproducibility of T_2 mapping with 3D-TESS, all subjects were scanned eight days after the baseline measurement. The difference between T_2 values at these two time-points was expressed as a coefficient of variation (CV) in percent for each location and layer separately. Ten subjects were evaluated by three readers to assess the inter-observer variability, calculated as an intra-class coefficient (ICC), at the baseline examination.

2.5. Statistical analysis

A repeated ANOVA test was used to determine the differences in T_2 at various time points for 3 and 7 Tesla. The T_2 values were compared at baseline with T_2 values at 3 M, 6 M, and 12 M, respectively. A P -value < 0.05 was considered statistically significant. All statistical analyses were done using IBM SPSS Statistical Package version 21.0 (IBM, Armonk, North Castle, New York, United States).

3. Results

3.1. Morphological appearance

Morphologically, no change in lesion grade in the time course was found for any patients. The size of the lesions ranged from 23.4 mm³ to 368.1 mm³ (on average, 162.5 ± 107 mm³) and did not change significantly during the observation period.

3.2. Reproducibility and inter-observer variability

The mean coefficient of variation of T_2 mapping between the baseline and the eight-day follow-up measurement ranged, in various cartilage regions, from 4.5% to 10.1% at 3 T (on average, 7.8 ± 2.0%) and from 8.9% to 12.8% at 7 T (on average, 11.0 ± 1.5%). The intra-class correlation coefficient between readers ranged from 0.81 to 0.92 at 3 T (on average, 0.85 ± 0.1) and from 0.79 to 0.91 at 7 T (on average, 0.82 ± 0.15).

3.3. T_2 mapping

An example of T_2 maps is depicted in Fig. 2. In patients with low-grade lesions, the mean T_2 values found at 3 T were (mean ± standard deviation) 31.83 ± 10.6, 41.89 ± 9.3, 29.20 ± 7.1, 34.90 ± 7.8, 25.03 ± 5.3 and 36.93 ± 5.5 ms in deep zone, superficial zone, weight-bearing deep reference, weight-bearing superficial reference, non-weight-bearing deep reference, and non-weight-bearing superficial reference, respectively. At 7 T, the values were 25.09 ± 6.9, 31.40 ± 8.6, 21.47 ± 7.0, 23.46 ± 6.0, 23.76 ± 4.7 and 32.32 ± 9.0 ms. All T_2 values for the patients with low-grade cartilage lesions are listed in Table 2.

The significant continuous decrease in T_2 values patients with lesions was observed between baseline and six months in the superficial layer of the lesions at 3 T, where the T_2 value decreased from 41.89 ± 9.3 ms to 36.21 ± 7.2 ms, which was a difference of 5.67 ± 2.2 ms ($p = 0.031$). A significant decrease in T_2 values was also observed between baseline and twelve months in the superficial layer of the lesions at 3 T, where the T_2 value decreased from 41.89 ± 9.3 ms

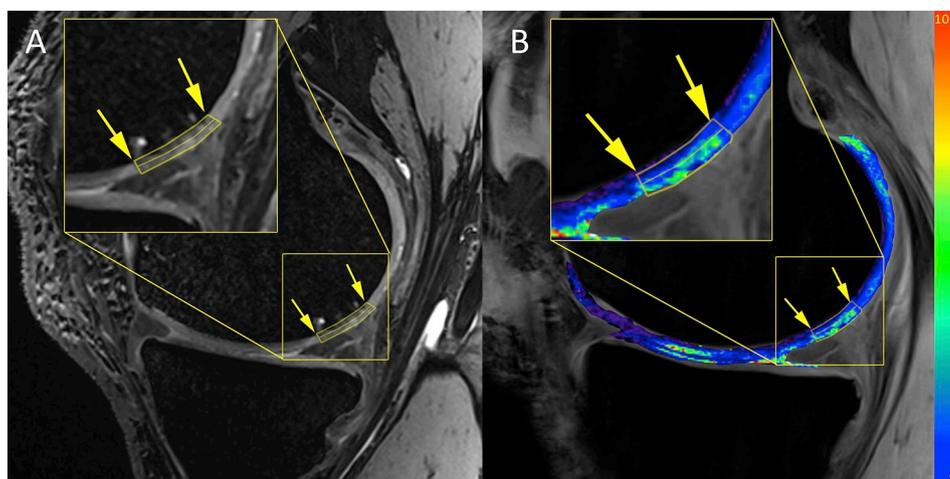


Fig. 1. An example of T_2 maps and a cartilage bilayer segmentation of a patient with a low-grade cartilage lesion acquired at 7 T, A) 3D-DESS image with the lesion delineated by the yellow arrows, B) T_2 map overlaid on F_0 contrast of a 3D-TESS image. The values of the color bars are T_2 in milliseconds. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

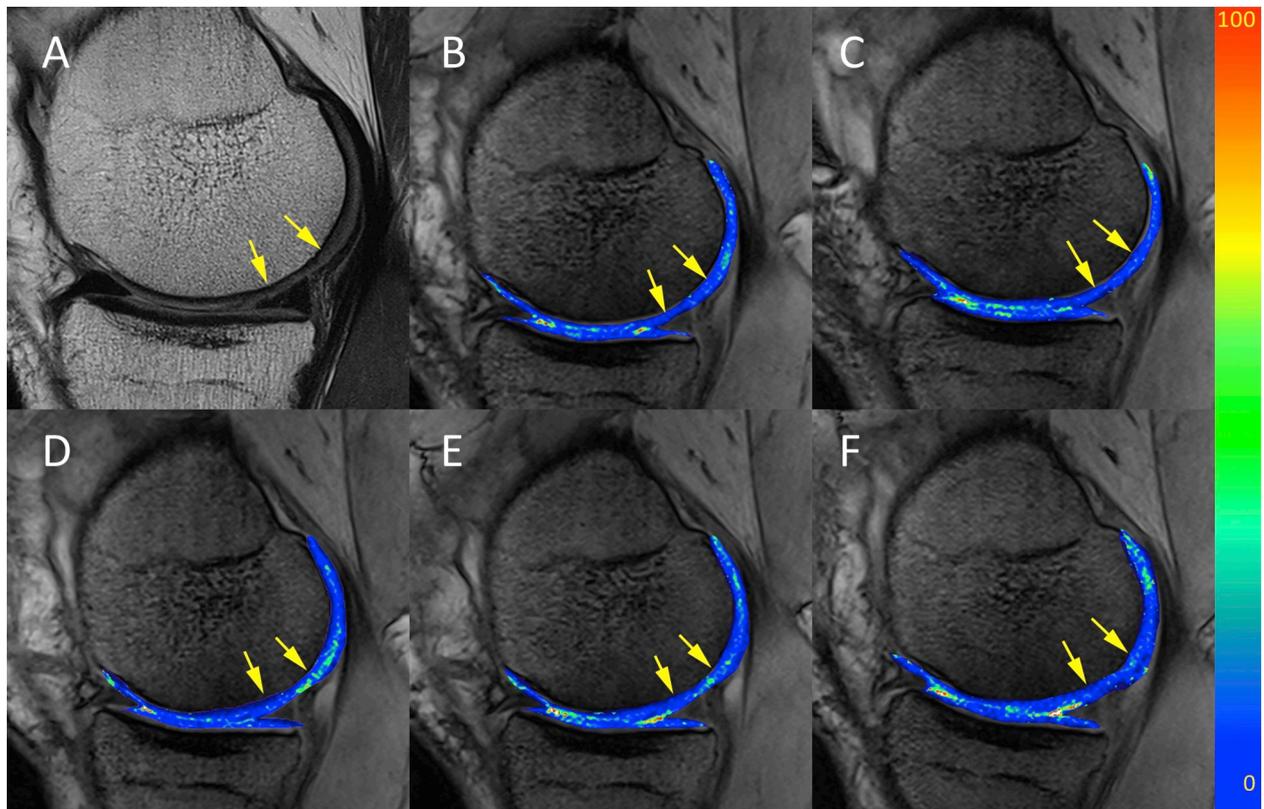


Fig. 2. A representative T₂ maps in a patient with low-grade cartilage lesion scanned at five time-points: A) morphological image; T₂ map acquired at B) baseline; C) eight days; D) three months; E) six months; and F) twelve months. T₂ maps of the segmented cartilage are overlaid on F₀ contrast of the 3D-TESS sequence. The values of the color bars are T₂ in milliseconds.

Table 2

T₂ values at different time-points and different field-strengths in patients low grade cartilage lesions.

Time-point	Location	3 T			7 T		
		T ₂ [ms] ± (st.dev.)	Change from baseline	p-values	T ₂ [ms] ± (st.dev.)	Change from baseline	p-values
Baseline	Lesion deep	31.83 ± 10.6			25.09 ± 6.9		
	Lesion superficial	41.89 ± 9.3			31.40 ± 8.6		
	Healthy weight-bearing deep	29.20 ± 7.1			21.47 ± 7.0		
	Healthy weight-bearing superficial	34.90 ± 7.8			23.46 ± 6.0		
	Healthy non-weight-bearing deep	25.03 ± 5.3			23.76 ± 4.7		
	Healthy non-weight-bearing superficial	36.93 ± 5.5			32.32 ± 9.0		
Month 3	Lesion deep	32.66 ± 9.8	0.83 ± -0.8	0.487	26.84 ± 7.9	1.75 ± 1.0	0.309
	Lesion superficial	41.81 ± 10.4	-0.08 ± 1.1	0.406	34.36 ± 10.0	2.96 ± 1.4	0.237
	Healthy weight-bearing deep	28.74 ± 7.0	-0.47 ± -0.1	0.368	19.57 ± 3.5	-1.90 ± -3.5	0.343
	Healthy weight-bearing superficial	34.82 ± 7.2	-0.08 ± -0.5	0.377	24.02 ± 2.8	0.55 ± -3.2	0.211
	Healthy non-weight-bearing deep	28.44 ± 6.2	3.41 ± 0.9	0.469	21.75 ± 3.7	-2.01 ± -1.0	0.186
	Healthy non-weight-bearing superficial	37.72 ± 7.3	0.79 ± 1.7	0.104	30.07 ± 6.1	-2.25 ± -2.9	0.066
Month 6	Lesion deep	29.83 ± 7.1	-2.00 ± -3.5	0.200	27.21 ± 8.1	2.12 ± 1.4	0.082
	Lesion superficial	36.21 ± 7.2	-5.67 ± -2.2*	0.016	30.13 ± 10.3	-1.27 ± 2.1	0.183
	Healthy weight-bearing deep	28.42 ± 5.2	-0.78 ± -1.9	0.318	21.12 ± 5.2	-0.35 ± -1.8	0.340
	Healthy weight-bearing superficial	34.10 ± 6.2	-0.80 ± -1.5	0.325	24.22 ± 3.6	0.76 ± -2.4	0.454
	Healthy non-weight-bearing deep	27.09 ± 5.6	2.06 ± 0.3	0.493	24.34 ± 4.2	0.58 ± -0.5	0.203
	Healthy non-weight-bearing superficial	36.80 ± 5.9	-0.14 ± 0.4	0.221	30.87 ± 3.1	-1.45 ± -5.9	0.408
Month 12	Lesion deep	27.31 ± 3.7	-4.52 ± -6.9	0.052	21.12 ± 3.4	-3.97 ± -1.7	0.270
	Lesion superficial	35.28 ± 4.9	-6.60 ± -4.4*	0.020	30.08 ± 4.4	-1.32 ± -2.1	0.416
	Healthy weight-bearing deep	29.81 ± 3.5	0.61 ± -3.6	0.088	20.42 ± 2.5	-1.05 ± -4.5	0.428
	Healthy weight-bearing superficial	31.99 ± 2.3	-2.91 ± -5.5	0.365	26.01 ± 5.5	2.55 ± -0.5	0.189
	Healthy non-weight-bearing deep	27.92 ± 1.4	2.90 ± -3.9	0.104	22.84 ± 3.1	-0.92 ± -1.6	0.048
	Healthy non-weight-bearing superficial	39.79 ± 2.8	2.85 ± -2.7	0.201	26.42 ± 5.6	-5.90 ± -3.4	0.158

The T₂ values are presented as mean values (standard deviation) in milliseconds.

* In bold, significantly different from the baseline, p < 0.05.

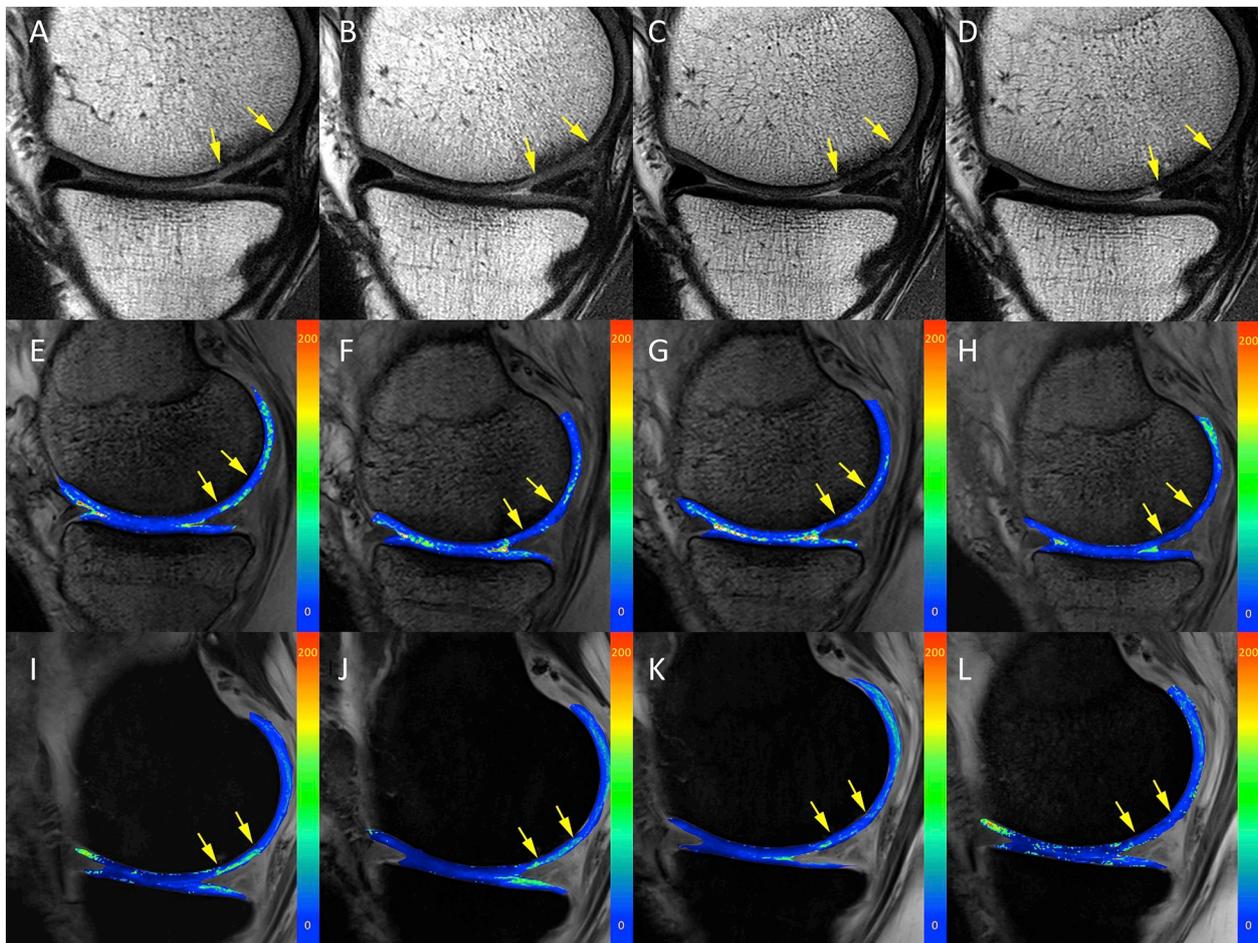


Fig. 3. An example of a patient with a traumatic cartilage lesion on a femoral condyle, where the hyper-intense region became hypo-intense over the course of four time-points, suggesting the disappearance of edema (depicted by the arrowheads). A to D) morphological images acquired by sagittal intermediate-weighted turbo-spin echo at baseline, three months, six and twelve months follow-up, respectively; E to H) the T_2 maps acquired with a 3D-TESS sequence at 3 T at the corresponding time-points; and I to L) the T_2 maps acquired with a 3D-TESS sequence at 7 T at the corresponding time-points. The values of the color bars are T_2 in milliseconds.

to 35.28 ± 2.3 ms, which was a difference of 6.6 ± 4.4 ms ($p = 0.044$).

At 7 T, no significant differences were observed for any of the time-points, although the continuous decrease in T_2 values of patients with lesions was also observed between baseline and six months in the superficial layer. The T_2 value decreased from 31.4 ± 8.6 ms to 30.13 ± 10.3 ms, which was a difference of 1.27 ± 2.1 ms ($p = 0.083$). A non-significant decrease in T_2 values was also observed between baseline and twelve months in the superficial layer, where the T_2 value decreased from 31.4 ± 8.6 ms to 30.08 ± 4.4 ms, which was a difference of 1.32 ± 2.1 ms ($p = 0.521$) (Fig. 3).

4. Discussion

The results of this study showed that the cartilage structure can be detected in patients with low-grade lesions and followed-up over time. The results also suggest that the T_2 values at 3 T might be more beneficial for detecting collagen organization than those obtained at 7 T. It is generally accepted that T_2 values slightly decrease as the field-strength increases [32]. Indeed, T_2 values in this study appeared lower when measured at 7 T compared to 3 T.

Conventional MR sequences typically used for the evaluation of cartilage can identify mostly morphological changes, such as partial- and full-thickness defects, cracks, fissures, and fibrillations; however, they are not capable of detecting any early stage alterations [1]. Recently, there has been an increasing effort to employ quantitative MR

approaches to assess the composition of cartilage. These methods are either proteoglycan-specific (sodium imaging [33], dGEMRIC [34]), collagen-specific (T_2 and T_2^* mapping [9]), or a mixture of methods (diffusion-weighted imaging [35], $T_1\rho$ mapping [36]). To date, the most often used quantitative MR technique is T_2 mapping for its relative uncomplicated use and no requirements for special hardware or for high magnetic field. The T_2 value itself provides information about the collagen fiber content and orientation, as well as water distribution. One of the earliest pathologic changes in cartilage degeneration is the elevated matrix permeability, leading to increased water content and faster motion of water molecules resulting in an increased stress on cartilage because the hydrodynamic pressure is not sustained by the matrix [1]. As the T_2 value is strongly dependent on collagen orientation, this value decreases from the superficial cartilage toward the deep zone and also varies between condyles and regions within the condyles [37,38]. Based on these assumptions, the reference cartilage in this study was selected in both weight-bearing and non-weight-bearing regions. However, due to potentially confounding magic angle effect, i.e., the T_2 dependence on the angle between the fibers and the static magnetic field resulting in a substantial T_2 increase at 55° , none of the regions-of-interest were selected in this region.

In this study, a statistically significant decrease in T_2 values acquired at 3 T was observed in the superficial zone of the lesion after one year; a decrease in T_2 values was observed in the deep zone of the lesion, too, although not a statistically significant decrease. In the degenerative patients, no statistically significant change in T_2 over time

was recorded. Desrochers et al. studied structural and biochemical changes in degenerated articular cartilage and concluded that the early changes include proteoglycan loss and collagen network disorganization at or near the articular surface [39]. This is in agreement with our results, as we observed substantial T_2 alterations predominantly in the superficial zone. Interestingly, T_2 values at 7 T did not demonstrate the same trend as seen at 3 T, which might be due to a multi-component T_2 relaxation. Previously, several studies have shown a multi-component T_2 decay in cartilage. Reiter et al. observed three-component T_2 decay in cartilage $T(2,1) = 2.3$ ms, $T(2,2) = 25.2$ ms, and $T(2,3) = 96.3$ ms, with fractions 6.2%, 14.5%, and 79.3%, respectively [19]. In another study, Liu et al. determined only two-components of T_2 in the knee cartilage: a short component ranging from 13.6 ms to 22.3 ms and a long component ranging from 63.8 ms to 75.4 ms, using the multi-component-driven equilibrium, single-shot observation of T_1 and T_2 (mcDESPOT) [40]. Qian et al. found two components of T_2^* in articular cartilage, a short component ranging from 1.5 to 3.6 ms in diseased cartilage and from 4.4 to 4.9 ms in healthy cartilage, while the long component had a mixed distribution between the healthy and diseased cartilage, with values ranging from 7.3 to 23.4 ms [21]. In this study, the echo time used in 3D-TESS T_2 mapping was 5.53 ms (at 3 T) and 5.1 ms (at 7 T). Thus, assuming the short component to be around 3 ms at 3 T, but much shorter at 7 T, the contribution of the short component to the ‘averaged’ T_2 value at 3 T might be much more substantial than that at 7 T at the given echo time. Different outcome at 3 and 7 T might be also caused by different in-plane resolution of TESS (0.5×0.5 mm at 3 T vs 0.37×0.37 mm at 7 T) leading to increased measurement error at 7 T due to lower signal gain. Also, the contribution of diffusion is higher at 7 T resulting in lower sensitivity of T_2 change. Comparing our 3 T results with the previously conducted longitudinal studies, such as [16,17,41], we were not able to observe any changes in the whole cartilage since the follow-up delay was too short to capture the slowly progressing cartilage degeneration.

In our study, 3D-TESS was used rather than conventional multi-echo spin echo (CPMG). The 3D-TESS relaxometry method was introduced to enable fast and accurate T_2 and T_1 mapping. This sequence has several advantages over the conventional T_2 mapping: it is very fast, the data are acquired in a single scan, and the quantification of T_2 is markedly insensitive to B_1 . In addition, due to the low excitation flip angles (in this study 15°), TESS imaging is not affected by SAR constraints making it suited to be applied at ultra-high-field strength. It has also been shown previously that the T_2 values acquired with 3D-TESS strongly correlate with those acquired with CPMG sequences, with the same regional and zonal distribution [14]. However, since multi-echo spin-echo techniques like CPMG tend to overestimate T_2 due to stimulated echo contributions, 3D-TESS T_2 values were found to be generally lower in comparison to CPMG-based T_2 quantification [14,15]. For T_2 mapping, 3D-TESS uses a thresholding based on the second (F_0) contrast images. This allows for a robust cartilage segmentation due to elimination of the partial volume effect from the bone and synovial fluid. A good reproducibility of 3D-TESS T_2 mapping was demonstrated in this study: the coefficient of variation between baseline and the eight-day re-test was on average as low as $7.8 \pm 2.0\%$ and $11.0 \pm 1.5\%$ at 3 T and 7 T, respectively.

This study has some limitations. Not all patients were scanned at all time-points due to either defective coil, drop-outs, or data reconstruction failure. From the total of 21 patients, the total number of full scans (morphological + T_2 mapping) at baseline, 8D, 3 M, 6 M, and 12 M was 17, 16, 16, 17, and 8, respectively (3 T) and 20, 20, 18, 18, and 10 (7 T). However, as we pooled all values through the time-points, we consider our results to be valid and conclusive. Second, although 3D-TESS T_2 mapping is B_1 -insensitive by its nature, in some cases of extreme B_1 (and/or B_0) imperfections, the signal drops so much that the reconstruction could not iterate to reasonable T_2 values. These artefacts occurred mostly in outer slices that were not used for the evaluation. In cases where the slices of interest were affected, the pixels with obvious

alterations were omitted. These cases, however, were rather rare and did not affect the overall evaluation.

5. Conclusion

3D-TESS T_2 mapping is highly sensitive for the detection of the status of low-grade lesions in human articular cartilage and for observing the development of the lesions over time. 3 T T_2 mapping appears to be more sensitive to subtle alteration in cartilage tissue due to residuals of short T_2 component (usually attributed to bound water molecules) which is mostly decayed at 7 T. In the future, T_2 mapping might be a valuable marker for monitoring cartilage development after regenerative therapy. Using 3D-TESS for obtaining T_2 values in human articular cartilage demonstrates many benefits in comparison with conventional techniques, i.e., a decrease of the scan time, lower SAR demands and an increase of the reliability and reproducibility of T_2 mapping on both high-field and ultra-high-field MR scanners.

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