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Cartilage repair of the ankle: first results of T2 mapping at 7.0 T after microfracture and matrix associated autologous cartilage transplantation

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SUMMARY

Background: Both microfracture (MFX) and matrix associated autologous cartilage transplantation (MACT) are currently used to treat cartilage defects of the talus. T2 mapping of the ankle at 7 T has the potential to assess the collagen fibril network organization of the native hyaline cartilage and of the repair tissue (RT). This study provides first results regarding the properties of cartilage RT after MFX (mean follow-up: 113.8 months) and MACT (65.4 months).

Methods: A multi-echo spin-echo sequence was used at 7 T to assess T2 maps in 10 volunteer cases, and in 10 cases after MFX and MACT each. Proton weighted morphological images and clinical data were used to ensure comparable baseline criteria.

Results: A significant zonal variation of T2 was found in the volunteers. T2 of the superficial and the deep layer was 39.3 ± 5.9 ms and 21.1 ± 3.1 ms (zonal T2 index calculated by superficial T2/deep T2: 1.87 ± 0.2, $P < 0.001$). In MFX, T2 of the reference cartilage was 37.4 ± 5.0 ms and 25.3 ± 3.5 ms (1.51 ± 0.3, $P < 0.001$). In the RT, T2 was 43.4 ± 10.5 ms and 36.3 ± 7.7 ms (1.20 ± 0.2, $P = 0.009$). In MACT, T2 of the reference cartilage was 39.0 ± 9.1 ms and 27.1 ± 6.6 ms (1.45 ± 0.2, $P < 0.001$). In the RT, T2 was 44.6 ± 10.4 ms and 38.6 ± 7.3 ms (1.15 ± 0.1, $P = 0.003$). The zonal RT T2 variation differed significantly from the reference cartilage in both techniques (MFX: $P = 0.004$, MACT: $P = 0.001$).

Conclusion: T2 mapping at 7 T allows for the quantitative assessment of the collagen network organization of the talus. MACT and MFX yielded RT with comparable T2 properties.

Introduction

Defects of the talar cartilage layer are frequent; one has to expect a high incidence of osteochondral lesions after ankle joint fractures, and magnetic resonance imaging (MRI) results suggest that as many as 50% of patients with twisted ankles and associated ligament damage will have concomitant cartilage lesions[1,2]. Conversely, up to 15% of cases with osteochondral defects have no history of trauma[1], so that the incidence of cartilage damage in the ankle often is underestimated[3]. In symptomatic patients, the surgical treatment is considered the gold standard in therapy; various techniques have been used in the ankle, however, the microfracture technique (MFX) is considered the most effective option at this time[4]. MFX introduces pluripotent cells from the bone marrow into the defect that form a blood clot which will eventually form repair tissue (RT), filling and stabilizing the defect[5]. High rates of excellent outcome at short term, as well as stable mid-term results have been reported after MFX in the ankle[6,7]. Still, there is concern if the RT quality is sufficient in the long term[8], as histological analyses in the knee and in animal models indicate that MFX mainly results in fibrous RT[9–13].

In the knee, several studies demonstrate that autologous chondrocyte transplantation (ACT) techniques are more likely to result in hyaline-like RT than MFX, and that this leads to better clinical outcome at mid-term[9,14–16]. Based on this rationale, there is an incentive to apply ACT and matrix associated autologous cartilage transplantation (MACT) to the ankle[4,17–20].

It should be noted that talar cartilage is generally deemed to have a better potential to regenerate than knee cartilage[21]. At this

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time, there is not sufficient evidence available to determine if the higher morbidity associated with ACT techniques in the ankle is actually warranted by a clinically relevant superiority when compared to MFX in the long term.

Histology remains the gold standard for RT quality assessment, however, recent advance in MRI has yielded techniques that allow for the quantitative measurement of specific components of the cartilage and RT ultra-structure[22].

T2 mapping has been demonstrated to be valuable for the evaluation of cartilage RT in several studies. Briefly, both free water and water molecules bound to cartilage collagen fibers contribute to T2[23]. Whereas increased free water leads to a general increase of T2, the orientation dependent relaxation component of T2 allows for the visualization of the collagen fibril arrangement both in articular cartilage and in cartilage RT[13,24].

In the knee, MFX RT has lower T2 than native hyaline reference cartilage, and that there is a lack of T2 variation across the layer when compared to reference cartilage and to MACT RT, suggesting that MACT yields RT with a higher degree of collagen fibril organization[25].

In contrast, the first measurements at 3 T in the ankle showed the mean T2 of RT was comparable to that of the reference cartilage both after MFX and after MACT[26,27], albeit the resolution and signal-to-noise (SNR) achieved at 3 T allowed for a global assessment of the whole extent of the cartilage layer only. At this time, there are no quantitative data on the zonal organization of cartilage RT after either technique in the ankle.

With the introduction of 7 T ultra-high field whole body MR units and dedicated multi-channel surface coils into clinical research, a considerably higher SNR and resolution is achievable within clinically feasible scan times. The aim of this study was to use an optimized T2 mapping protocol to assess healthy talar cartilage in volunteers, and to acquire first data on the collagen organization of cartilage RT after MFX and after MACT in the ankle.

Materials and methods

Study participants and clinical evaluation

The study protocol was approved by the local Ethics Committee, and informed consent was obtained from all participants prior to inclusion into the study. Ten asymptomatic ankles of eight volunteers with 100 points in the American Orthopaedic Foot and Ankle Society (AOFAS) score, without any history of trauma, surgery or malalignment in the clinical examination were recruited for the optimization of the T2 mapping protocol and to obtain baseline T2 values for healthy talar cartilage[7]. The mean age at MRI was 30.2 ± 6.1 years, the body mass index (BMI) was 24.2 ± 3.3 kg/m^2, two were female and six male.

Between 1997 and 2006 39 patients with symptomatic osteochondral defects of the talus were treated with MFX or drilling at the Department of Orthopaedics of the Medical University of Vienna. Additionally, several different autologous chondrocyte transplantation techniques (autologous chondrocyte transplantation with a periosteal flap – ACT, matrix augmented autologous chondrocyte transplantation – MACT: Hyalograft C, CaRes) were used between 1998 and 2009 for singular talar defects in 23 cases.

The inclusion criteria both for MFX and for MACT were symptomatic deep chondral singular defects (Outerbridge Grade 3 or 4) or singular osteochondral defects (Hepple 3 and 4) with stable adjacent cartilage.

The exclusion criteria were: rheumatoid arthritis, progressed osteoarthritis, kissing lesions, malalignment or instability of the joint.

From this patient collective, we were able to recruit 18 patients (20 cases of ankles after cartilage repair) that were comparable in age, BMI, sex and defect size (10 MFX, 10 MACT).

The surgical procedures used in these cases have been described in detail[26,27]. Briefly, MFX was carried out as recommended by Steadman[5], and all MACT cases included in this study were treated with a hyaluronan matrix (Hyalograft C™, Fidia Advanced Biopolymer, Abbano, Italy): after a biopsy in first-look arthroscopy and subsequent *in vitro* expansion, the graft was implanted in mini-arthrotomy[28–31].

In the MFX cases, the mean age at surgery was 30.8 ± 9.7 years, the BMI was 25.9 ± 4.3 kg/m^2, five were female and four male, the defect size was 1.16 ± 0.49 cm^2, and the follow-up period was 113.8 ± 28.8 months.

In the MACT cases, the mean age at surgery was 25.4 ± 5.6 years, the BMI was 27.1 ± 4.3 kg/m^2, six were female and three male, the defect size was 1.39 ± 0.33 cm^2, and the follow-up period was 65.4 ± 34.1 months.

The evaluation of clinical outcome was carried out with the AOFAS score[7]. The AOFAS score is a numerical system which emphasizes the patient's perception of function and pain. The maximum is 100 points (50 function, 40 pain, 10 alignment). We considered 100–90 points excellent, 89–80 good, 79–60 fair and below 59 poor[17].

There were no significant differences between the two groups in the *t*-test and chi-square test except the follow-up intervals due to the fact that the treatment with cell-based techniques has become the preferred treatment option at the department.

MRI technique

All examinations were carried out with a 7 T MR whole body system (Magnetom, Siemens Healthcare, Erlangen, Germany) using a 28-channel array-coil (Quality Electrodynamics LLC, Cleveland, OH). Each case was measured in one session that consisted both of morphological sequences and the T2 mapping sequence: for the standard morphological assessment, we used a proton density (PD) weighted two-dimensional turbo spin-echo (2D-TSE) sequence with fat suppression (fs) in sagittal and coronal planes (Fig. 1). The in-plane resolution in the sagittal and coronal orientation was both 0.31 × 0.31 mm [448 × 448 matrix in a 140 mm × 140 mm field-of-view (FOV)], with a slice thickness of 3 mm, repetition time / echo time was 4,000/26 ms and 3,000/25 ms, respectively, and the flip angles were 170° and 180°. One average was sufficient and the bandwidth was 243 Hz/pixel. Fifteen slices were measured in each orientation with a distance factor of 10%, resulting in total scan times of 3 min 14 s in the sagittal orientation, and in 2 min 26 s in the coronal orientation.

For the calculation of the T2 maps, we used a multi-echo spin-echo sequence. The planning was based on the morphologic PD images, and the slices were oriented in the sagittal plane so that the slab covered the entire repair site. The FOV was 140 mm × 140 mm and the matrix was 320 × 320, resulting in an in-plane resolution of 0.4 × 0.4 mm with a slice thickness of 3 mm and distance factor of 0%. TR was 3,830 ms, and six different echo times were measured: 11.9/23.8/35.7/47.6/59.5 and 71.4 ms. The bandwidth was 252 Hz/pixel, one average was used and seven slices were acquired, resulting in a scan time of 13 min 7 s. The T2 maps were then calculated on the workstation with a pixel wise, mono-exponential non-negative least squares (NNLS) fit analysis (MapIt, Siemens).

The following morphologic criteria were systematically assessed by the senior author (ST, 20 years of experience in musculo-skeletal MR) in the morphological MR images: filling of the defect, cartilage interface, surface of the RT, structure, adjacent bone marrow, signal intensity, effusion (Table I).

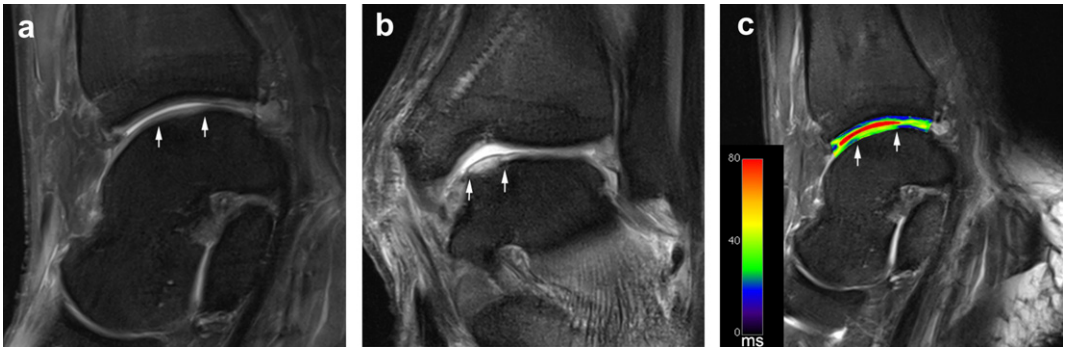

Fig. 1. Proton weighted sagittal (a) and coronal (b) images and corresponding T2 map (c) of a case after MACT. The repair site is marked with white arrows. The superficial T2 values of the repair tissue are comparable to those of the adjacent cartilage, whereas there is prolonged T2 in the deep layer.

Region of interest (ROI) analysis

In consensus with the morphological images (Fig. 1), two contiguous slices covering the cartilage RT, and two contiguous slices of intact reference cartilage of the talus in the same orientation to the static magnetic field were selected for the ROI analyses by the senior author. The T2 ROI analyses were carried out independently by two trained readers (SD and SA).

A deep and a superficial ROI were placed in each slice covering half the thickness of the reference cartilage or of the RT layer, respectively (Fig. 2). Subchondral bone and synovial fluid were carefully excluded. By definition, the minimum ROI size to be considered acceptable was 30 pixels.

The ROIs from all slices in each individual case were then used to calculate the mean deep and superficial T2 of RT and reference cartilage, respectively, as well as the mean global (average of deep and superficial) T2 of the RT and reference cartilage in each individual.

In the volunteers, we obtained 20 mean T2 values in a sample size of 10 (40 ROIs in 10 cases, 10 mean deep and 10 mean superficial T2 of the healthy control cartilage).

In the patient groups, we obtained 40 mean T2 values in a sample size of 10 each (80 ROIs in 10 cases, 10 mean deep and 10 mean superficial T2 values each in the RT and in the reference cartilage).

The relative T2 (rT2) was calculated from the global T2 values to compare the surgical techniques (rT2 = T2 of RT/T2 of reference cartilage)[32].

Finally, we calculated superficial T2 over deep T2 in order to obtain a zonal T2 index for the distribution of T2 between deep and superficial in healthy control cartilage, reference cartilage and RT.

Table I
Morphological evaluation. Comparable results were after both surgical techniques. The vast majority of the cases had alterations of the subchondral bone, whereas good defect filling was found in most cases

	MFX (N = 10)	MACT (N = 10)
1. Filling of the defect		
Complete	7	9
Hypertrophy	1	1
Incomplete		
>50%	2	
<50%		
0%		
2. Cartilage interface lengths (filling parallel to cartilage surface)		
Complete (integration with surrounding cartilage)	7	7
Incomplete (integration with surrounding cartilage)	1	3
Demarcation border visible (split like)		
Defect visible		
<50% of length of the RT	2	
>50% of length of the RT		
3. Surface of the RT		
Surface intact	7	7
Surface damaged: fibrillations/fissures/ulcerations		
<50% of RT depth	3	3
>50% of RT depth/total degeneration		
4. Structure		
Homogenous	7	6
Inhomogenous	3	4
5. Adjacent bone marrow		
Normal	1	1
Edema, granulation tissue, cyst, sclerosis	9	9
6. Signal intensity		
PD TSE		
Isointense	9	6
Hyperintense	1	4
Hypointense		
7. Effusion		
No	4	4
Yes	6	6

Statistical analyses

Statistical analyses were carried out with SPSS 14.0 (SPSS Institute, Chicago, IL, USA) and in Microsoft Excel on a Windows XP platform (Microsoft, Redmont, WA, USA).

We used an unpaired, two-sided *t*-test to detect statistically significant differences between the AOFAS score of the MFX and MACT cases.

The quality of the T2 ROI readings was validated with the intraclass co-efficient (ICC).

Normal distribution of the data (T2 values in ms) was assumed and verified in Shapiro–Wilk tests. We used paired, two-sided Student's *t*-tests to compare the deep and superficial T2 values within the tissue types (healthy control cartilage, reference cartilage and RT), and to test for differences between the layers of the RT and the reference cartilage as well as between the global T2 of the reference cartilage and the RT within groups.

To compare of the deep and superficial T2 values among the groups, we used unpaired two-sided Student's *t*-tests.

We tested for differences in the zonal organization between the cartilage of the healthy control of the volunteers and the reference cartilage of the patients under consideration of the Bonferroni correction. Finally, we tested for differences between the zonal organization of the RT after MFX and MACT. The same tests were used to compare the zonal indices of the tissue types and rT2.

$P < 0.05$ was considered significant (Bonferroni: $P < 0.025$), and $P < 0.001$ was considered highly significant.

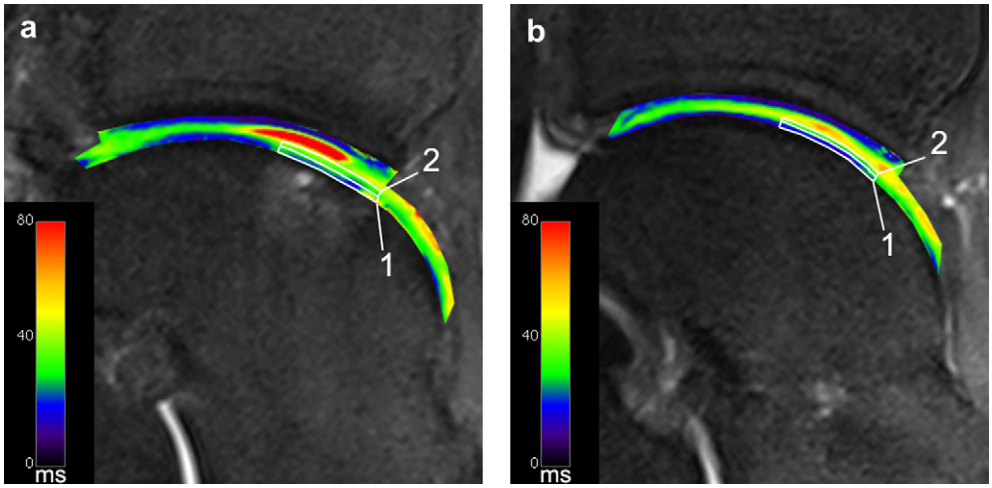

Fig. 2. Example of the ROI setting in a case after MACT in the repair site (a) and the reference (b). Both ROIs are set at the same orientation to the static magnetic field. The deep (1) and superficial (2) ROIs are indicated by the white boxes. This case shows T2 values in the repair tissue that are comparable to the articular cartilage both in the deep and the superficial layer.

Results

The morphological outcome was comparable in both groups (see Table I for details). The majority of cases had complete defect filling and good integration of the RT, however, interestingly almost all cases had alteration of the subchondral bone.

The mean AOFAS score at follow-up was 88.3 ± 8.5 (excellent in 35.7%, good in 35.7%, fair in 14.3% and poor in 14.3%). There was no significant difference between the MFX (91.3 ± 6.2) and the MACT cases (85.3 ± 9.8, $P = 0.119$, see Tables I and II).

The inter-observer evaluation analysis yielded an excellent agreement for the T2 readings; the ICC was 0.932 for the deep and 0.914 for the superficial ROIs.

Please see the detailed results of the T2 analyses in Table II and Fig. 3.

In the volunteers, we observed a highly significant increase from deep to superficial T2 (21.1 ± 3.1 ms vs 39.3 ± 5.9 ms, $P < 0.001$, zonal T2 index = 1.87).

The reference cartilage both of the MFX and of the MACT cases yielded comparable ranges of T2 and a highly significant variation of T2, however, we found small, yet significant differences between the deep T2 layers of the healthy control and the MFX and MACT cases ($P = 0.012$ for MFX and 0.018 for MACT). This did however not lead to significant differences in global T2. Furthermore, no significant differences were found between MFX and MACT reference cartilage.

The analysis of the RT demonstrated there was a significant variation in T2 after both techniques (MFX: $P = 0.009$; MACT: $P = 0.003$). With regard to the comparison of the RT to the reference cartilage, it may be of particular interest to note that there were no

Table II
Statistical results of the T2 mapping analyses

Study-group		Deep T2	Superficial T2	*P*-value*	Zonal T2 index	Global T2	rT2
Volunteers ($N = 10$)	Healthy control	21.1 ± 3.1 (18.9/23.4)	39.3 ± 5.9 (35.1/43.6)	<0.001	1.87 ± 0.2 (1.7/2.0)	30.1 ± 4.2 (27.1/33.1)	
	P-value† healthy control vs reference MFX	0.012	0.443		0.004	0.471	
	P-value† healthy control vs reference MACT	0.018	0.928		0.001	0.294	
MFX ($N = 10$)	Reference cartilage	25.3 ± 3.5 (22.7/27.8)	37.4 ± 5.0 (33.9/41.0)	<0.001	1.51 ± 0.3 (1.3/1.7)	31.4 ± 3.1 (29.1/33.6)	1.29 ± 0.4 (1.0/1.5)
	RT	36.3 ± 7.7 (30.8/41.8)	43.4 ± 10.5 (35.9/50.9)	0.009	1.20 ± 0.2 (1.1/1.3)	39.8 ± 8.6 (33.7/46.0)	
	P-value*	0.004	0.159		0.011	0.025	
MACT ($N = 10$)	Reference cartilage	27.1 ± 6.6 (22.4/31.8)	39.0 ± 9.1 (32.5/45.5)	<0.001	1.45 ± 0.2 (1.3/1.6)	33.1 ± 7.5 (27.7/38.5)	1.29 ± 0.3 (1.1/1.5)
	RT	38.6 ± 7.3 (33.4/43.9)	44.6 ± 10.4 (37.2/52.0)	0.003	1.15 ± 0.1 (1.1/1.2)	41.6 ± 8.6 (35.4/47.8)	
	P-value*	0.001	0.155		0.002	0.015	
MFX vs MACT	*P*-value† Reference cartilage	0.444	0.632		0.691	0.512	
	P-value† RT	0.507	0.796		0.500	0.656	
	P-value† rT2						0.993

± = standard deviation; 95% confidence interval in parentheses (lower/upper limit), T2 values in ms, N = number of subjects.
* Paired, two-sided *t*-test.
† Unpaired, two-sided *t*-test.

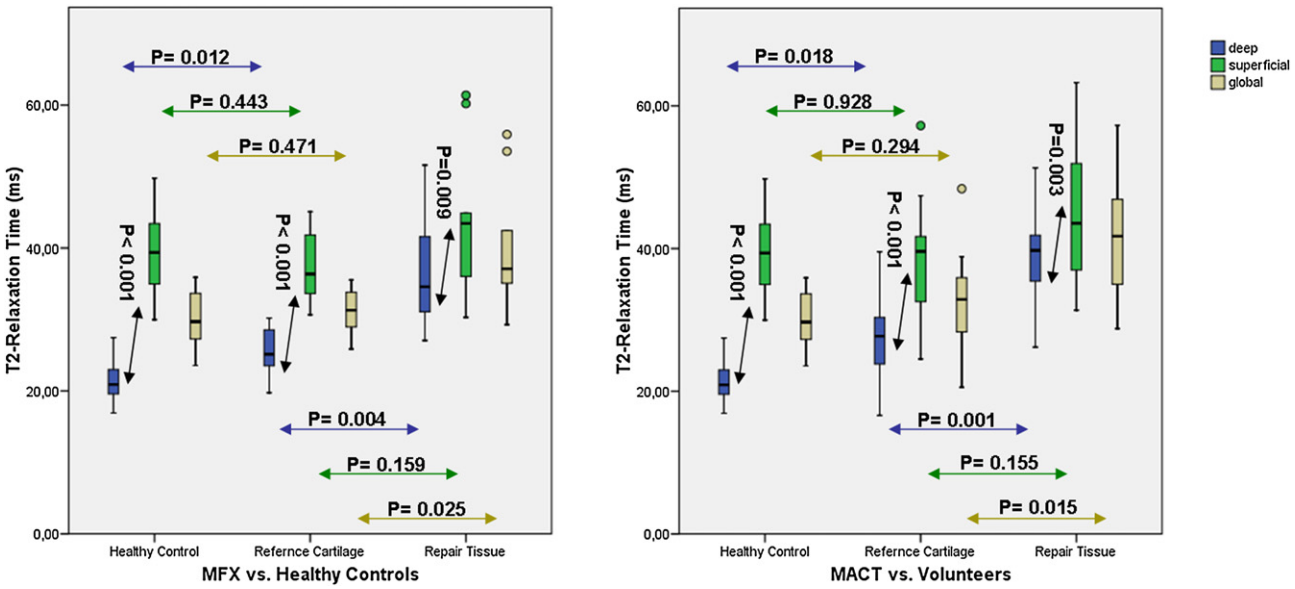

Fig. 3. Boxplots of the T2 values after MFX and matrix associated autologous chondrocyte implantation (MACT) in cartilage RT and reference cartilage. Both treatment groups show a significant increase of T2 in the superficial layer of the RT similar to the hyaline reference cartilage (blue and green boxes), however, T2 of the deep layers differs significantly between RT and reference cartilage (blue boxes). In contrast, T2 of the superficial layers is comparable between RT and reference cartilage (green boxes). The *P*-values refer to Student's *t*-tests.

significant differences between the superficial layers (MFX: $P = 0.159$; MACT: $P = 0.155$). In contrast, both patient groups had significantly (MFX: $P = 0.004$; MACT: $P = 0.001$) increased T2 in the deep layers of RT when compared to the reference cartilage, which led to a significant difference between global RT and global reference cartilage T2 (MFX: $P = 0.025$; MACT: $P = 0.015$).

The direct comparison of the absolute RT T2 values yielded no significant differences between MFX and MACT RT (deep T2: $P = 0.507$; superficial T2: $P = 0.796$). As a consequence, rT2 was almost identical for the MFX and MACT cases ($P = 0.993$).

Discussion

This study reports on the first utilization of T2 mapping in the ankle at 7 T in a clinical setting, and yields new knowledge regarding the T2 properties of the articular cartilage and cartilage RT after MFX and MACT.

We found that the zonal T2 variation of RT after both surgical procedures differed significantly from that of adjacent articular reference cartilage. T2 was comparable in the superficial layers, however, in the deep layers we found increased T2 when compared to the articular cartilage both of patients and healthy controls. The T2 properties of MFX and of MACT RT did not differ significantly.

At this time, no randomized control trial has been published to directly compare if MFX and MACT of the ankle lead to significantly different clinical outcome. The current knowledge regarding the surgical treatment of osteochondral lesions is based on case series than mainly report short- and mid-term results and use clinical scores as outcome measure; based on a systematic review, bone marrow stimulation is considered the best treatment option[4]. The analysis yielded a study weighted success rate of 85% (46–100%) under consideration of 388 cases deriving from 18 studies. In contrast, for classical ACT with a periosteal flap, a successful result was found only in 76% (70–92%) in 59 cases from four studies. No matrix associated ACT techniques were included in the review.

With regard to the overall success of MFX it should however be noted that there are not sufficient study results available to estimate the long-term efficiency of the technique; Ferkel *et al.*[33] report a deterioration of clinical outcomes at 71 months, and Hunt and Sherman found 54% of the cases had fair or poor results at 66 months[34]. Also, first second-look arthroscopy findings indicate that despite good and excellent clinical outcome, visible cracks and fissuring of the RT are present 1 year after treatment[35].

As a consequence, there remains a need to improve cartilage repair in the ankle. The major advantage of matrix associated ACT (MACT) in the ankle is that malleotomy is often not necessary, which considerably decreases the morbidity of the procedure[18]. With regard to the clinical outcome the first short- and mid-term results are comparable to those reported after ACT, albeit of limited level of evidence; Giannini *et al.*[18] report good and excellent outcome in more than 80% at 36 months in a series of 46 cases treated with Hyalograft C. Nehrer *et al.*[27] report stable clinical outcome in 13 cases after MACT with Hyalograft C after 1–6 years (76.9% good-to-excellent).

The histological evidence on the RT composition after Hyalograft C in the ankle is currently limited to three cases; hyaline-like quality was reported in all cases and the international cartilage repair society repair categories were rated normal, nearly normal and nearly normal, respectively[18]. A series of 10 cases that were evaluated with delayed Gadolinium Enhanced MRI of Cartilage (dGEMRIC) at 3.0 T yielded relatively high glycosaminoglycan (GAG) content, still, we do not know at this time if the RT quality is actually better than after MFX[36].

It is therefore of substantial interest to optimize quantitative MR mapping protocols for the assessment of cartilage RT quality in the ankle. Among other techniques such as dGEMRIC and diffusion weighted imaging[36,37], T2 mapping remains the most promising approach to integrate biochemical cartilage imaging into a clinical setting.

Both in cartilage and RT, there are two major mechanisms that influence T2: free water increases T2 independently from the orientation to the static magnetic field, and additionally there is an orientation dependent relaxation component of macromolecule-associated water[38,39]. The collagen fibers running anisotropically perpendicular to the cortical bone in the deep zone of normal hyaline cartilage reduce the mobility of water protons and thus reduce T2 relaxation time values in the deep zone of hyaline

cartilage, which is not present in the superficial zone of cartilage where the collagen fibers are randomly oriented. This different orientation of the collagen fiber network explains the increase of T2 values from the deep to superficial cartilage zone in normal hyaline cartilage and is a marker for collagen fiber network organization. Another factor is the dipolar coupling of collagen associated water is minimum at 54.7° to the static magnetic field, which leads to increased T2 (magic angle effect)[13,32,40].

In the knee joint, the T2 and dGEMRIC properties of the RT after MACT were closer to those of native cartilage than after MFX[32,41–46], albeit not comparable. The global T2 of the RT after MFX was lower than after MACT and lower than the reference cartilage, indicating lower water content. Also, there was a lack of zonal organization after MFX, whereas MACT RT yielded a similar variation of T2 across the layers like native cartilage[37].

In the ankle, the first results of T2 mapping at 3 T yielded differing results: rT2 was 1.00 ± 0.20 (0.72–1.36) in a series of 14 cases after MFX and 0.85 ± 0.21 (0.49–1.26) in a series of eight cases after Hyalograft C, and in another series of 12 cases after MACT rT2 was 1.05 (50.1 ± 8.0 ms in the RT and 47.6 ± 9.3 ms in the reference cartilage)[26,27]. Based on these results, the water and collagen content was similar to the reference cartilage after both treatment modalities. It should however be noted that a zonal analysis was not feasible at 3 T, mainly due to the lower SNR.

The aim of this study was to attain additional data on the collagen fibril arrangement in the RT after either technique. With regard to the use of the T2 mapping protocol in a clinical setting, the potential of the 7 T system could be used to achieve excellent SNR and resolution within a reasonable scan time. T2 mapping is generally considered a reliable modality, as it is fast, reproducible and does not require the use of contrast agent[47]. A possible source of bias is the magic angle effect, which may cause higher T2 of the cartilage because of the orientation to the static magnetic field depending on the anatomical properties of the joint[48]; regarding the ankle, T2 may be influenced in the coronal plane, as the cartilage of the talar shoulder will be oriented around 55° to the static magnetic field. In contrast, this should not occur in the sagittal plane as the orientation of the talar cartilage will be more perpendicular. This was the main reason to perform the T2 mapping protocol in the sagittal plane and to choose the ROI for the reference cartilage in the same orientation as the repair site in parallel slices (see Fig. 2).

We are aware of the limited level of evidence that is associated with the study design and also note that the differing follow-up intervals are a possible source of bias to our results; still, we find it worth to report that both surgical techniques resulted in RT with a comparable degree of organization in T2 mapping.

T2 of the deep layer was higher than in the reference cartilage in both groups, indicating a higher ratio of free water. This may result both from a lower concentration in collagen and from lower GAG content. Still, there was a significant increase of T2 towards the surface in MFX RT, which has not been found in the knee or in animal models; the organization of the RT fibrils was not adequate to hyaline cartilage, but within the range that has been found for MACT RT in the knee[25,41]. It should be noted that the MFX cases were mid- and long-term results, and that these cases should be particularly prone to degeneration; even more, the clinical outcome was good-to-excellent in all cases. The zonal variation of the reference cartilage of the patients was comparable to the healthy control cartilage, albeit there was a small but significant difference in the deep layer (21.1 ms vs 25.3 ms in MFX, and 27.1 ms in MACT; see Fig. 3 and Table II). We believe this indicates there remains a detectable alteration of the adjacent cartilage after surgery, however, the current data do not allow to conclude if this is clinically relevant.

With regard to the global T2 values, there was a considerable range of T2 within each treatment group. This agrees well with findings at 3 T both in the ankle and in the knee[25–27,32,45], and confirms there is a wide variation of RT quality within treatment groups, as has been described in histological analyses[14,16]. Still, these first results further substantiate the notion that other than in the knee, MFX results in organized RT and may be particularly suited for the treatment of cartilage defects of the ankle[4,10,21,25,26,36]. Further studies with T2 mapping will however be needed to enable clinical investigators to draw conclusions for the treatment algorithms in clinical routine.

In summary, T2 mapping at 7 T allows for the quantitative assessment of the collagen network organization of the talus both in native cartilage and in cartilage RT. In contrast to the knee, both MACT and MFX result in RT with a similar degree of T2 variation, however different from that of native hyaline cartilage.

Author contributions

Stephan Domayer: Conception and design of the study, data acquisition and analysis, interpretation of the results, drafting and revising of the article and final approval.

Sebastian Apprich: Design of the study, data analysis, interpretation of the results, drafting and revising of the article and final approval.

David Stelzeneder: Data acquisition, revising of the article and final approval.

Clemens Hirschfeld: Data acquisition, revising of the article and final approval.

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Reinhard Windhager: Design of the study, interpretation of the results, revising of the article and final approval.

Siegfried Trattnig: Design of the study, development and optimization of the MR techniques used for this study, interpretation of the results, drafting and revising of the article and final approval.

Conflicts of interest

No conflict of interest existed with regard to affiliations with any organization or entity with interest in the outcome of this study.

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