Quantitative T2 Mapping during Follow-up after Matrix-Associated Autologous Chondrocyte Transplantation (MACT): Full-Thickness and Zonal Evaluation to Visualize the Maturation of Cartilage Repair Tissue

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ABSTRACT: The purpose of this article was to evaluate the potential of in vivo zonal T2-mapping as a noninvasive tool in the longitudinal visualization of cartilage repair tissue maturation after matrix-associated autologous chondrocyte transplantation (MACT). Fifteen patients were treated with MACT and evaluated cross-sectionally, with a baseline MRI at a follow-up of 19.7 ± 12.1 months after cartilage transplantation surgery of the knee. In the same 15 patients, 12 months later (31.7 ± 12.0 months after surgery), a longitudinal 1-year follow-up MRI was obtained. MRI was performed on a 3 Tesla MR scanner; morphological evaluation was performed using a double-echo steady-state sequence; T2 maps were calculated from a multiecho, spin-echo sequence. Quantitative mean (full-thickness) and zonal (deep and superficial) T2 values were calculated in the cartilage repair area and in control cartilage sites. A statistical analysis of variance was performed. Full-tickness T2 values showed no significant difference between sites of healthy cartilage and cartilage repair tissue ($p < 0.05$). Using zonal T2 evaluation, healthy cartilage showed a significant increase from the deep to superficial cartilage layers ($p < 0.05$). Cartilage repair tissue after MACT showed no significant zonal increase from deep to superficial cartilage areas during baseline MRI ($p > 0.05$); however, during the 1-year follow-up, a significant zonal stratification could be observed ($p < 0.05$). Morphological evaluation showed no significant difference between the baseline and the 1-year follow-up MRI. T2 mapping seems to be more sensitive in revealing changes in the repair tissue compared to morphological MRI. In vivo zonal T2 assessment may be sensitive enough to characterize the maturation of cartilage repair tissue. J Orthop Res 27:957–963, 2009

Keywords: articular cartilage repair techniques; quantitative T2 mapping; MACT

Surgical articular cartilage repair techniques, such as microfracture therapy (MFX), osteochondral autologous transplantation (OAT), autologous chondrocyte transplantation (ACT), or matrix-associated ACT (MACT), are becoming increasingly important.[1–3] Compared to bone marrow-stimulating techniques, such as MFX, cartilage transplantation procedures like MACT, as a result of technological advances, provide the possibility of redifferentiation of the cartilage repair tissue, and thus, the reformation of hyaline or hyaline-like cartilage.

In the noninvasive postoperative evaluation after cartilage repair procedures, morphological magnetic resonance imaging (MRI) has been reported as the method of choice.[4,5] To obtain a better insight into the ultrastructural composition of the cartilage repair tissue, biochemical MRI techniques have shown promising results in recent studies.[6–8] For the assessment of the constitution and organization of healthy articular cartilage as well as cartilage repair tissue, delayed gadolinium-enhanced MRI of cartilage (dGEMRIC) and the mapping of transverse relaxation times (T2-mapping) are most often utilized. Whereas the dGEMRIC technique can visualize the glycosaminoglycan (GAG) component of articular cartilage, T2 mapping focuses on changes in water and collagen content and tissue anisotropy.

The composition of articular cartilage is mainly attributable to collagen fibril orientation, and this composition affects its MR appearance.[9] The organization of the collagen matrix in repair tissue over time is important, as a failure in the collagenous fiber network is considered indicative of further cartilage breakdown. In cartilage repair, it would therefore be of immense interest to visualize this organization as it relates to the maturation of cartilage repair tissue over time. In an in vitro study, MRI was proven to be able to detect histological differences in healthy articular cartilage collagen architecture among species, which is likely to be strongly related to the differences in maturation of the tissue.[10] In vivo, the visualization of collagen architecture, and possibly the maturation of this architecture over time in cartilage repair tissue, can be seen when assessing the spatial variation of T2 values. In healthy cartilage, T2 relaxation times increase from the cortical bone to the articular surface.[11] In cartilage repair tissue, histologically validated animal studies report this increase in zonal T2 as an indicator of hyaline or "hyaline-like" cartilage composition.[12,13]

The aim of this study was to evaluate if in vivo mean (full-thickness) as well as zonal (deep and superficial) quantitative T2 assessment in patients after MACT is capable to visualize the maturation of the cartilage repair tissue.

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MATERIALS AND METHODS

Patient Population

Institutional review board approval and written, informed consent to collect data on the study population were obtained. Fifteen patients (2 females, 13 males; mean age, 37.8 ± 8.8 years; age range, 21–54 years) who had undergone MACT of the knee joint were included into the study out of a larger cohort. Patient selection was based on the inclusion of patients of different follow-up intervals form very early (3 months) to latest possible (42 months) to have the possibility to visualize cartilage repair tissue maturation. Within this group of 15 patients, MRI was performed longitudinally over time at two time points; a baseline MRI 19.7 ± 12.1 months after cartilage transplantation and a follow-up MRI 12 months later (1-year follow-up scan) 31.7 ± 12.0 months postoperatively. Further inclusion criteria were MACT due to a single full-thickness cartilage defect on the femoral condyle; no advanced osteoarthritis, instability, or deformity. The grafts were located on the medial femoral condyle in 12 patients, and on the lateral femoral condyle in 3 patients. Cartilage defect mean size was 5.8 cm^2 (range: 2.6–12.4 cm^2). A hyaluronan-based scaffold was used (Hyalograft®C, Fidia Advanced Biomaterials, Abano Terme, Italy). All patients received the same postoperative rehabilitation program. For further evaluation in terms of postoperative interval (delay between operation and initial MR scan), the patients were divided into two groups: one group with a shorter postoperative interval (group 1; six patients; mean age, 37.0 years; postoperative interval 8.2 months, ranging from 3–13 months) and a longer postoperative interval (group 2; nine patients; mean age, 38.3 years; postoperative interval 27.3 months, ranging from 19–42 months). In the 1-year follow-up MRI, the same patients were examined at a postoperative interval (delay between operation and follow-up MR scan) of 20.2 months for group 1 and 38.9 months for group 2.

Image Acquisition

All MR examinations were performed on a 3.0 Tesla MR scanner (Magnetom Trio, Siemens Medical Solutions, Erlangen, Germany) using an eight-channel knee coil (Invivo, Gainesville, FL). The patients were positioned consistently with the knee extended, the joint space in the middle of the coil, and, to avoid differences in T2 relaxation caused by different loading before the MR examination, after half an hour of rest.

After a set of localizers, a three-dimensional Double Echo Steady-State (3D-DESS) sequence was acquired for morphological evaluation, with a repetition time (TR) of 15.1 ms, an echo time (TE) of 5.11 ms, and a flip angle of 25°. The field of view (FoV) was 150 × 150 mm, the pixel matrix was 250 × 250, the bandwidth was 220 Hz/pixel, and the slice thickness was 0.6 mm with an in-plane resolution of 0.6 × 0.6 mm. A total of 192 slices were obtained in 5:39 min. One exemplary reconstructed 3D-DESS data set is given in Figure 1 and Figure 2 for the same patient at the baseline and 1-year follow-up MRI. After the 3D-DESS sequence and after multiplanar reconstruction using a built-in 3D viewing tool, and together with the provided surgical reports, the cartilage repair area was identified, and subsequenty, thickness measurements as well as the quantitative T2 sequence were planned in the sagittal direction. To assure the similar localization of the quantitative T2 measurements between the baseline and the 1-year follow-up MRI, the 3D planning procedure based on the isotropic 3D-DESS data set was saved and available at the time point of 1-year follow-up MRI. The T2 relaxation times were calculated from T2 maps using a multiecho, spin-echo (SE) technique with a TR of 2.060 s and six TEs of 16.4, 32.8, 49.2, 65.6, 82.0, and 96.4 ms. The FoV was 180 × 200 mm, the pixel matrix was 320 × 288, the bandwidth was 240 Hz/pixel, and the slice thickness was 1 mm, with an in-plane resolution of 0.6 × 0.6 mm. Eighteen slices were obtained in 6:43 min. Figures 3 and 4 give exemplary T2 maps of patients for the baseline (a) and the follow-up (b) MRI.

Data Analysis

All evaluations were performed by an experienced senior musculoskeletal radiologist in consensus with an orthopedic surgeon with a special interest in musculoskeletal MRI. Morphological evaluation was realized using the isotropic 3D-DESS sequence for the magnetic resonance observation of cartilage repair tissue (MOCART) scoring system.[14] This point-scoring system was designed to systematically record the constitution of the area of cartilage repair and surrounding tissues, and has been shown to be reliable and reproducible and can be applied to different surgical cartilage repair techniques.[4,15] The maximum score achievable in the evaluation of nine variables is 100. MOCART scoring was performed at the baseline and at the 1-year follow-up MR scan to confirm the morphological condition of the cartilage repair tissue over time. Furthermore, based on the 3D-DESS sequence, the cartilage repair tissue as well as the selected region of healthy seen cartilage was analyzed using thickness measurements. Thickness measurements were achieved along both cartilage

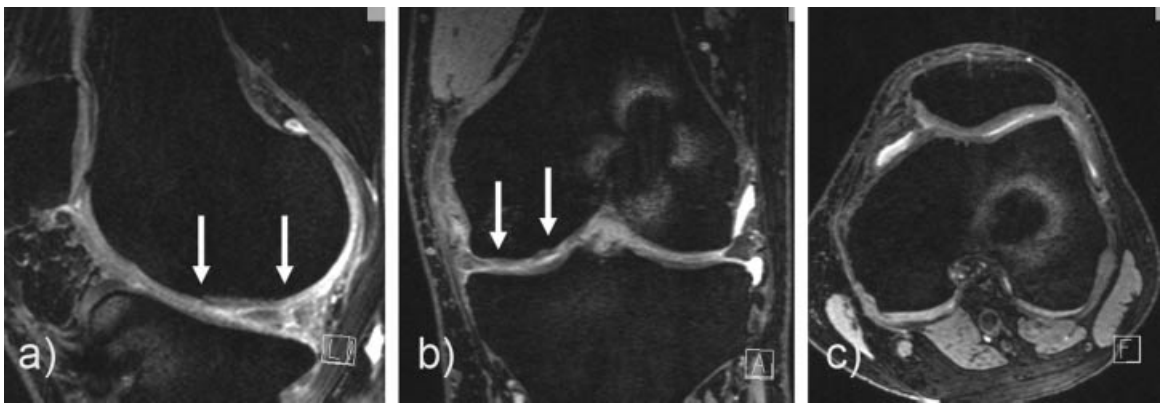

Figure 1. Morphological, isotropic, 3D double-echo, steady state (DESS) sequence from one patient 3 months after MACT surgery (baseline MRI). Multiplanar reconstruction of sagittal (a), coronal (b), and axial (c) plane; arrows mark the area of cartilage repair.

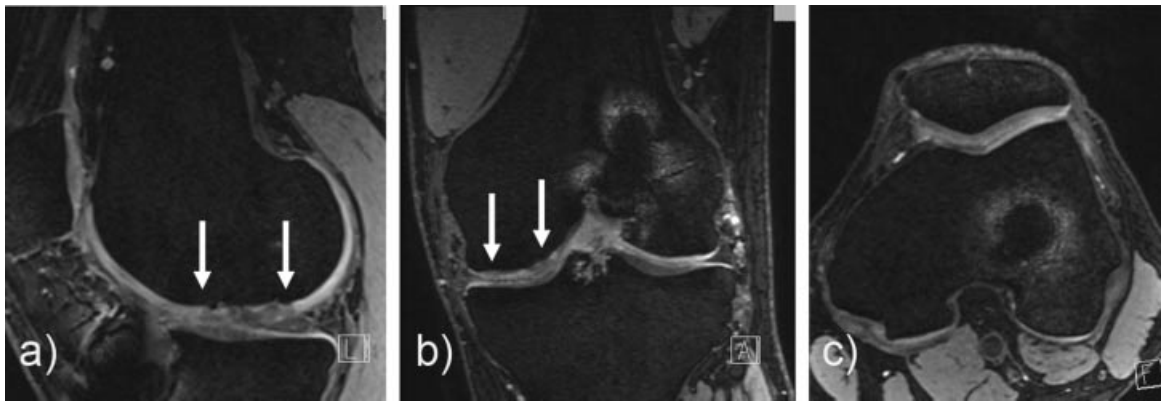

Figure 2. Morphological, isotropic, 3D-DESS sequence of the same patient 15 months after MACT surgery (1-year follow-up MRI). Multiplanar reconstruction of sagittal (a), coronal (b), and axial (c) plane; arrows mark the area of cartilage repair.

sites with four measurements at each site on three consecutive sagittal sections.

The assessment of the T2 values was based on a region-of-interest (ROI) evaluation. The area of cartilage repair and an area of healthy cartilage (as an internal control) were selected using the isotropic 3D-DESS dataset and the surgical reports as verification. The area seen as healthy hyaline articular cartilage, was seen as healthy during initial surgery and had to have a normal MR appearance on the 3D-DESS sequence at the follow-up examination. The similar localizing of the baseline and the 1-year follow-up T2 measurements, based on the isotropic 3D-DESS data set as mentioned above, ensured their crossregistration. Furthermore, the ROIs were evaluated side by side; however, the follow-up time point was blinded. The selection of the ROIs was made on the same three consecutive slices covering the area of cartilage repair. The ROIs for cartilage repair tissue and healthy hyaline cartilage had to cover the full thickness of cartilage for the full-thickness evaluation of T2 values. Numbers of pixels were 127 ± 61 for cartilage repair tissue and 120 ± 52 for healthy cartilage. For the zonal assessment, these ROIs were divided into an equal (50%) deep and a superficial half (Figs. 3 and 4). As all areas of cartilage repair were located within the femoral weight-bearing zone, also all control cartilage sites were located within the weight-bearing zone, mostly anterior to the MACT and away from a potential magic angle effect. T2 maps were calculated using a pixel-wise, mono-exponential, nonnegative least-squares (NNLS) fit analysis.

Concerning morphological MR images, comparison using the MOCART scoring system was performed between the baseline examination and the 1-year follow-up. Then biochemical T2 evaluation was completed as follows. Comparison was achieved initially for full-thickness T2 values. First, T2 values of healthy articular cartilage were compared between the baseline MRI exam and the 1-year follow-up for all patients and afterward with respect to the postoperative follow-up group. Second, T2 values of cartilage repair tissue were compared between the baseline MRI exam and the 1-year follow-up for all patients and afterward with respect to the postoperative follow-up group. Third, T2 values of healthy cartilage were compared to T2 values of cartilage repair tissue at the baseline MRI exam and the 1-year follow-up. Comparison was furthermore achieved for zonal (deep and superficial) T2 values by assessing deep and superficial cartilage areas in healthy cartilage sites as well as in cartilage repair tissue.

Statistical tests were used to perform the data analyses. Quantitative evaluation was accomplished by analyses of variance using a three-way ANOVA with a random factor, considering the fact of different measurements within each patient. For the trend between the cartilage layers, a three-way analysis of variance with random effects and two repeated measures factors was performed. Additionally,

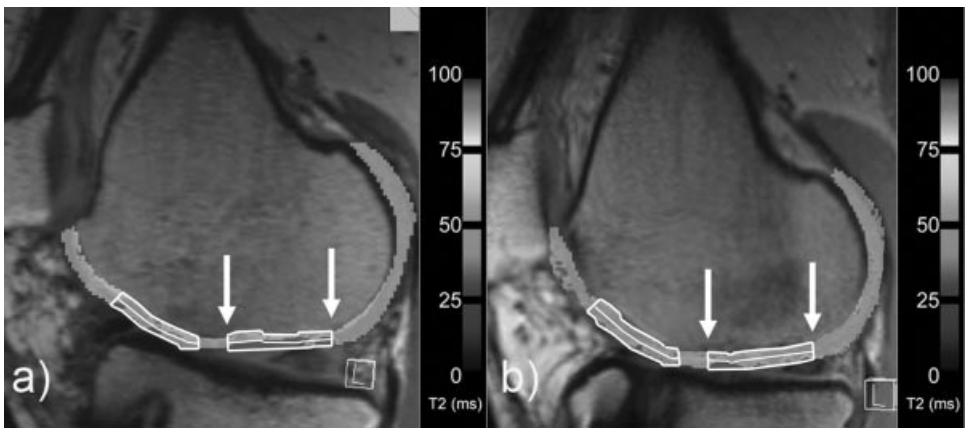

Figure 3. T2 map of the same patient 3 months (a) and 15 months (b) after MACT surgery. Arrows mark the area of cartilage repair; ROIs are displayed for the cartilage repair tissue (arrows) and healthy seen control cartilage. Visible reduction in T2 values in the cartilage repair area over time.

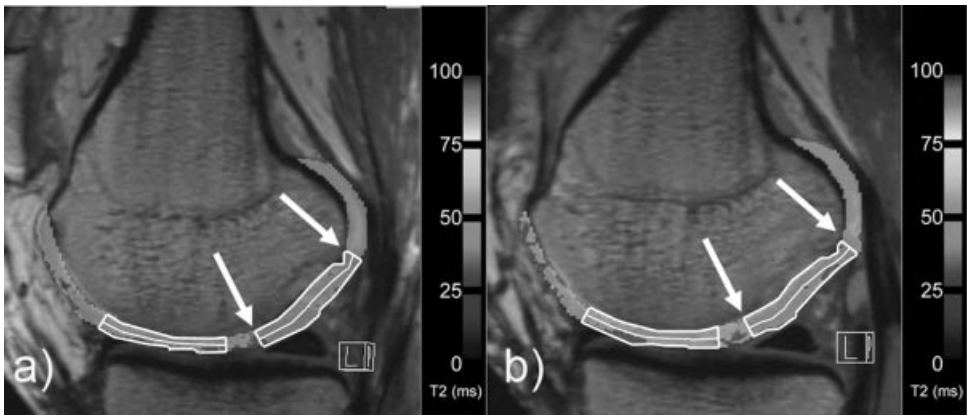

Figure 4. T2 map of one patient 22 months (a) and 34 months (b) after MACT surgery. Arrows mark the area of cartilage repair; ROIs are displayed for the cartilage repair tissue (arrows) and healthy seen control cartilage.. No visible change in T2 values in the cartilage repair area over time.

Pearson correlation was performed between graft T2 and time from surgery. SPSS version 15.0 (SPSS Institute, Chicago, IL) for Windows (Microsoft, Redmond, WA) was used. Differences with a p-value <0.05 were considered statistically significant.

RESULTS

Morphological Evaluation

Morphological MR measurements evaluated using the MOCART scoring system showed a slight, but not significant, increase from the baseline scan, with 70.5 ± 12.3 (ranging from 45 to 90) to the 1-year follow-up, with 75.7 ± 9.2 (ranging from 60 to 90) ($p = 0.217$).

Cartilage thickness measurements showed comparable results for healthy seen control cartilage (baseline: 0.327 cm; 1-year follow-up: 0.324 cm) and cartilage repair tissue (baseline: 0.328 cm; 1-year follow-up: 0.331 cm) with no change between the baseline scan and the 1-year follow-up (control cartilage; $p = 0.819$; MACT, $p = 0.849$).

Full-Thickness T2 Evaluation

The full-thickness T2 values (ms) for all patients in healthy articular cartilage showed stable results over time between the baseline scan, with 56.2 ± 5.2 (ranging from 45 to 69) and the 1-year follow-up, with 56.7 ± 6.1 (ranging from 42 to 68) ($p = 0.759$). In addition, there was no significant difference between the follow-up groups ($p < 0.05$) (Table 1).

The full-thickness T2 values for all patients showed a decrease between the baseline scan, with 59.8 ± 11.6 (ranging from 40 to 84) and the 1-year follow-up, with 56.7 ± 6.9 (ranging from 45 to 70). This decrease, however, was not statistically significant ($p = 0.339$). With regard to postoperative interval, full-thickness T2 values for cartilage repair tissue in patients from group 1 showed a significant decrease between the baseline and the 1-year follow-up scan ($p = 0.027$); patients from group 2, on the other hand, showed no significant change between the baseline and the 1-year follow-up evaluation ($p = 0.673$) (Table 1).

When comparing healthy cartilage and cartilage repair tissue, there was no significant difference between the baseline evaluation (control cartilage: 56.2 ± 5.2; MACT: 59.8 ± 11.6) ($p = 0.760$) and the 1-year follow-up examination (control cartilage: 56.7 ± 6.1; MACT:

Table 1. Zonal (Deep and Superficial) as Well as Mean (Full Thickness) T2 values (ms) for the Two Groups Concerning Postoperative Follow-up

MRI	Group		Control Deep	Control Superficial	Control Mean	MACT Deep	MACT Superficial	MACT Mean
Baseline scan	1	Mean	51.4[a]	59.1[a]	55.2[d]	66.9[b]	67.3[b]	67.1[d]
		SD	5.4	5.6	5.1	12.5	12.4	11.3
	2	Mean	52.7[a]	61.1[a]	56.9[e]	54.1[b]	55.8[b]	54.9[e]
		SD	4.8	6.6	5.2	9.0	10.1	9.0
One-year follow-up scan	1	Mean	49.6[a]	59.3[a]	54.4[e]	54.7[c]	59.2[c]	57.0[e]
		SD	6.5	7.1	6.5	6.2	7.7	5.9
	2	Mean	53.3[a]	63.0[a]	58.2[e]	53.9[c]	59.0[c]	56.5[e]
		SD	4.7	6.9	5.4	7.7	8.2	7.6

Signances are given tor zonal variation as a trend tor T2 values from deep to superficial (footnotes a–c); as well as tor differences in global mean values between control cartilage sites and cartilage repair tissue (footnotes d + e). [a]Significant increase from deep to superficial for all healthy control cartilage sites ($p < 0.05$). [b]No significant increase from deep to superficial for cartilage repair sites ($p < 0.05$). [c]Significant increase from deep to superficial for cartilage repair sites ($p < 0.05$). [d]Significant difference in mean values between control cartilage and cartilage repair tissue ($p < 0.05$). [e]No significant difference in mean values between control cartilage and cartilage repair tissue ($p < 0.05$).

56.7 ± 6.9) ($p = 0.512$). The values for the different groups with regard to follow-up can be seen in Table 1.

Correlation between the full-thickness T2 values and the postoperative follow-up showed a significant negative correlation for the baseline evaluation with a Person coefficient of -0.480 ($p = 0.001$) and no significant correlation for the 1-year follow-up MRI with a Pearson coefficient 0.073 ($p = 0.635$).

Zonal T2 Evaluation

For the zonal evaluation of healthy cartilage sites, zonal mean T2 values (ms) revealed that all healthy cartilage sites showed a highly significant increase between the deep and superficial layers of articular cartilage at the baseline scan (deep: 52.2 ± 5.0; superficial:60.2 ± 6.2) ($p < 0.001$) as well as at the 1-year follow-up examination (deep: 51.8 ± 5.7; superficial: 61.6 ± 7.1) ($p < 0.001$). With regard to the group divisions, the results for healthy cartilage sites for group 1 and group 2 are documented in Table 1 and Figure 5.

The zonal evaluation of cartilage repair tissue, however, showed varying results with regard to the zonal assessment. In the cartilage repair tissue of all patients at the baseline scan, T2 values varied from 59.2 ± 12.2 for the deep to 60.4 ± 12.3 for the superficial aspect. This zonal variation was not significant ($p = 0.105$). One year later, the cartilage repair tissue of all patients at the 1-year follow-up examination showed an increase from 54.2 ± 7.0 for the deep to 59.1 ± 7.9 for the superficial cartilage layer. This increase was statistically significant ($p = 0.025$). For follow-up intervals based on the group divisions, Table 1 and Figure 5 are showing the results for cartilage repair tissue from group 1 and 2.

Correlation between zonal T2 values of the repair tissue and the time interval after surgery, showed a significant correlation for deep and superficial T2 values within the baseline MRI ($p < 0.05$) with a slightly higher Pearson coefficient of the deep cartilage layer (-0.504) compared to the superficial (-0.402); however, no significant correlation for the 1-year follow-up ($p > 0.05$) was found.

DISCUSSION

Because fibrocartilage lacks the properties of hyaline cartilage for optimal joint function, such as resistance to compressive shear strains, after cartilage repair, the formation of hyaline or "hyaline-like" repair tissue would be of utmost importance.[15,16] MACT, as a result of technological advances, uses biomaterials seeded with chondrocytes as carriers and scaffolds for cell growth. In this study, the Hyalograft®C we used is composed of autologous chondrocytes grown on a 3D HYAFF 11 scaffold that promotes an in vitro proliferation of chondrocytes and favors the expression and maintenance of a cell-differentiated phenotype.[17] Thus, the created repair tissue may have the ability to produce an organized collagen network over time. A highly organized collagen structure is the basis for histological zonal characterization of normal hyaline articular cartilage as well as cartilage repair tissue.[18,19] Under ideal circumstances, cartilage repair tissue should, over time, develop a collagen network with a similar shape, collagen concentration, and in particular, a zonal organization similar to normal hyaline cartilage.

Based on our results, we believe that T2 relaxation may be more sensitive in the evaluation of cartilage repair tissue than morphological MR measurements. Thickness measurements seemed to be unable to reflect any changes in the repair tissue over time. The MOCART scoring system, nevertheless, showed increasing values between the baseline scan and the 1-year follow-up MRI possibly reflecting a better constitution of the repair tissue; this increase, however, was not statistically significant. Considering all patients together, full-thickness T2 values also revealed no significant differences between healthy articular cartilage and cartilage repair tissue after MACT. However, considering the two groups in terms of follow-up, it was possible to detect differences because of high T2 relaxation times in the early follow-up

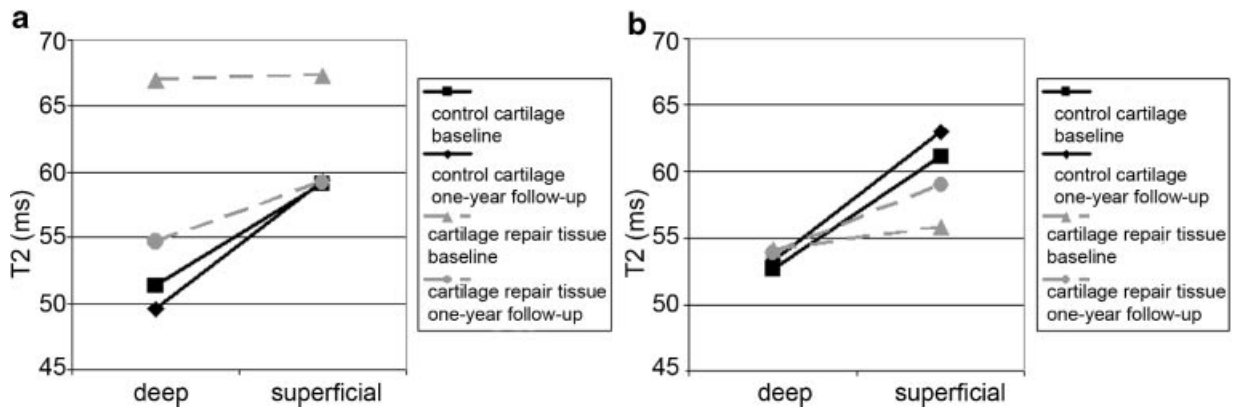

Figure 5. For visualization of Table 1, graphs showing zonal T2 (ms) values for patients from group 1 (a) and group 2 (b) with the statistical significance of the zonal increase from the deep to superficial layers. Within the groups, for group 1 (a) baseline scan was 8.2 months postoperatively, and 1-year follow-up scan was 20.2 months postoperatively. For group 2 (b) baseline scan was 27.3 months postoperatively, and 1-year follow-up scan was 39.3 months postoperatively.

period. The significantly higher T2 values in the follow-up period from 3 to 13 months may be attributable to greater hydration or metabolic rate of the newly built cartilage repair tissue. For all longer follow-up intervals, full-thickness T2 repair tissue values approached those of control sites, as has been shown previously.[20] The present results indicate that the decrease in full-thickness T2 values over time and its adaption to T2 values of control cartilage mirrors the cartilage repair tissue maturation. This proposition is furthermore confirmed when looking at the negative correlation between the T2 values of the cartilage repair tissue and the postoperative follow-up period visible during baseline MRI. For the 1-year follow-up, however, no correlation could be found, indicating that full-thickness T2 values are not changing any more and the maturation process might be over.

Concerning quantitative T2 mapping, few studies are available in the follow-up after cartilage repair. Besides full-thickness evaluation, the importance of a zonal T2 assessment has been emphasized by Mosher et al.[21] for cartilage degeneration, where preliminary results indicated a focal increase in T2 values within the transitional zone of articular cartilage, which would indicate focal defects. A more general degeneration would presumably be reflected in an overall increase of T2, possibly beginning at the surface. Although the mechanisms of cartilage degeneration in osteoarthritis and cartilage maturation of cartilage repair tissue are different, zonal evaluation may present additional information about the constitution of cartilage architecture.

In the present study, besides the full-thickness evaluation, the zonal assessment provides a possible insight into the maturation of cartilage repair tissue after MACT. In the longitudinal follow-up of the same patients, from the baseline MRI examination to the 1-year follow-up, an increase between the deep and the superficial cartilage layer becomes apparent and statistically significant, possibly indicating a still ongoing maturation process, also when full-thickness T2 values are not changing any more. Although histological validation is missing, as follow-up arthroscopy was not required because of satisfactory clinical outcomes, the trend of increasing T2 values from the deep to superficial cartilage layers could be interpreted as maturation of cartilage repair tissue toward a "hyaline-like" ultrastructure. This "hyaline-like" character of cartilage repair tissue after cartilage transplantation has been detailed by the histological biopsies of other studies.[15,22] Nevertheless, histological outcome after cartilage repair procedures has been a subject of controversy,[23,24] and thus, the increase in T2 in the superficial cartilage layer could be only a product of hydration and not of a redifferentiation of the collagen fiber network. Nevertheless, the interpretation of our results could be that there may be a maturation process. As illustrated in Table 1, the difference in T2 between the superficial and the deep layer is caused by a stronger decrease of superficial T2 in the follow-up scan. This would fit the picture of reduced water content, and possibly, stronger anisotropy in the deep layer.

As the T2 values are quite dependent on this laminar appearance of articular cartilage in MRI, the magic angle effect may also cause this increase in superficial T2 values.[25,26] However, the magic angle is usually seen at about 55° to the orientation of the magnetic field, and may, therefore, not alter the reported results as the area of cartilage repair was within the weight-bearing zone of the femoral condyle in all patients.

The results of White et al.[13] were encouraging. These investigators performed OAT and MFX in horses, and were able to correlate a zonal increase in cartilage T2 values from near the subchondral bone to near the cartilage surface to histology and collagen structural anisotropy, as assessed by polarized light microscopy. Their results showed that, after OAT, "hyaline-like" cartilage structure and zonal collagen organization was correlated to a significant zonal increase in T2 from the deep to superficial layers in T2 relaxation times, whereas, after MFX, only disorganized fibrous reparative cartilage repair tissue was visible, with no zonal variation in T2 values.

Nevertheless, the supposition that the increase of zonal variation within cartilage repair tissue over time may reflect the maturation of cartilage repair tissue toward zonal collagen architecture and "hyaline-like" cartilage composition is somewhat questionable. However, excepting the limitations of this study, such as the missing histological proof, the small number of patients, the cross-sectional study character, and the high heterogeneity in the postoperative time delays, zonal T2 evaluation could be shown to provide additional information about the cartilage repair tissue compared to full-thickness assessment.

In the postoperative evaluation after MACT, the present study shows that quantitative full-thickness T2 evaluation shows significantly increased T2 values within the first year after surgery, and then, returning to the T2 values of healthy cartilage at a longer follow-up. The zonal variation, as reflected by the zonal differences in T2, increases in the cartilage repair tissue over time and shows significantly higher T2 values for superficial compared to deep cartilage layers. However, this zonal variation is still far from that of healthy control cartilage sites. Thus both, full-thickness and zonal T2 evaluation may be able to visualize the maturation of cartilage repair tissue.

Our study results are compatible with the maturation process of cartilage repair tissue as shown by Watrin-Pinzano et al.,[12] which has recently been demonstrated in humans in an initial pilot study with preliminary results. Watrin-Pinzano et al.[12] first described the ability of MR T2 mapping to characterize cartilage maturation longitudinally in an ex vivo rat model at 8.5 Tesla. Animals were sacrificed at different time points after cartilage repair with biomaterial implantation, and MRI was compared to the histological assessment. At the longest follow-up time point after 60 days, zonal

variation as a significant increase from the deep to superficial aspects was apparent, and could be histologically proven to reflect collagen network organization. T2 maps were seen to characterize chondral repair tissue as a virtual biopsy, which shown in the present study initially in vivo.

In summary, the data from the present study strongly emphasizes that T2 evaluation is more sensitive in revealing changes in articular cartilage and cartilage repair tissue compared to morphological analysis using thickness measurements or the MOCART score. Therefore, full-thickness as well as zonal T2 analysis may provide additional information concerning the maturation of cartilage repair tissue. Thus, the results should be carefully interpreted, but encourage future studies to use quantitative zonal T2 evaluation to follow-up cartilage repair procedures. Therefore, studies on larger patient groups, with longer follow-up intervals, and after different cartilage repair procedures, will show the possible predictive value of zonal variation for cartilage repair tissue.

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REFERENCES

1. Brittberg M. 1999. Autologous chondrocyte transplantation. Clin Orthop Relat Res 367(Suppl):S147–S155.
2. Minas T, Peterson L. 2000. Autologous chondrocyte transplantation. Oper Tech Sports Med 8:144–157.
3. Steadman JR, Rodkey WG, Rodrigo JJ. 2001. Microfracture: surgical technique and rehabilitation to treat chondral defects. Clin Orthop Relat Res 391(Suppl):S362–S369.
4. Trattnig S, Millington SA, Szomolanyi P, et al. 2007. MR imaging of osteochondral grafts and autologous chondrocyte implantation. Eur Radiol 17:103–118.
5. Winalski C, Minas T. 2000. Evaluation of chondral injuries by magnetic resonance imaging: Repair assessments. Oper Tech Sports Med 8:108–119.
6. Trattnig S, Mamisch TC, Welsch GH, et al. 2007. Quantitative T2 mapping of matrix-associated autologous chondrocyte transplantation at 3 Tesla: an in vivo cross-sectional study. Invest Radiol 42:442–448.
7. Trattnig S, Marlovits S, Gebetsroither S, et al. 2007. Three-dimensional delayed gadolinium-enhanced MRI of cartilage (dGEMRIC) for in vivo evaluation of reparative cartilage after matrix-associated autologous chondrocyte transplantation at 3.0T: preliminary results. J Magn Reson Imaging 26:974–982.
8. Watanabe A, Wada Y, Obata T, et al. 2006. Delayed gadolinium-enhanced MR to determine glycosaminoglycan concentration in reparative cartilage after autologous chondrocyte implantation: Preliminary results. Radiology 239: 201–208.
9. Goodwin DW, Zhu H, Dunn JF. 2000. In vitro MR imaging of hyaline cartilage: correlation with scanning electron microscopy. AJR Am J Roentgenol 174:405–409.
10. Nissi MJ, Rieppo J, Toyras, et al. 2006. T(2) relaxation time mapping reveals age- and species-related diversity of collagen network architecture in articular cartilage. Osteoarthritis Cartilage 14:1265–1271.
11. Smith HE, Mosher TJ, Dardzinski BJ, et al. 2001. Spatial variation in cartilage T2 of the knee. J Magn Reson Imaging 14:50–55.
12. Watrin-Pinzano A, Ruaud JP, Cheli Y, et al. 2004. Evaluation of cartilage repair tissue after biomaterial implantation in rat patella by using T2 mapping. Magn Reson Mater Phys 17: 219–228.
13. White LM, Sussman MS, Hurtig M, et al. 2006. Cartilage T2 assessment: differentiation of normal hyaline cartilage and reparative tissue after arthroscopic cartilage repair in equine subjects. Radiology 241:407–414.
14. Marlovits S, Striessnig G, Resinger CT, et al. 2004. Definition of pertinent parameters for the evaluation of articular cartilage repair tissue with high-resolution magnetic resonance imaging. Eur J Radiol 52:310–319.
15. Marlovits S, Zeller P, Singer P, et al. 2006. Cartilage repair: generations of autologous chondrocyte transplantation. Eur J Radiol 57:24–31.
16. Marcacci M, Berruto M, Brocchetta D, et al. 2005. Articular cartilage engineering with Hyalograft C: 3-year clinical results. Clin Orthop Relat Res 435:96–105.
17. Gobbi A, Kon E, Berruto M, et al. 2006. Patellofemoral full-thickness chondral defects treated with Hyalograft-C: a clinical, arthroscopic, and histologic review. Am J Sports Med 34:1763–1773.
18. Buckwalter JA, Mankin HJ. 1998. Articular cartilage: degeneration and osteoarthritis, repair, regeneration, and transplantation. Instr Course Lect 47:487–504.
19. Grigolo B, Lisignoli G, Piacentini A, et al. 2002. Evidence for redifferentiation of human chondrocytes grown on a hyaluronan-based biomaterial (HYAFF (R) 11): molecular, immunohistochemical and ultrastructural analysis. Biomaterials 23: 1187–1195.
20. Trattnig S, Mamisch TC, Welsch GH, et al. 2007. Quantitative T2 mapping of matrix-associated autologous chondrocyte transplantation at 3 Tesla—an in vivo cross-sectional study. Invest Radiol 42:442–448.
21. Mosher TJ, Dardzinski BJ, Smith MB. 2000. Human articular cartilage: influence of aging and early symptomatic degeneration on the spatial variation of T2—preliminary findings at 3 T. Radiology 214:259–266.
22. D'Anchise R, Manta N, Prospero E, et al. 2005. Autologous implantation of chondrocytes on a solid collagen scaffold: clinical and histological outcomes after two years of follow-up. J Orthopaed Traumatol 6:36–43.
23. Knutsen G, Drogset JO, Engebretsen L, et al. 2007. A randomized trial comparing autologous chondrocyte implantation with microfracture. Findings at five years. J Bone Joint Surg Am 89:2105–2112.
24. Knutsen G, Engebretsen L, Ludvigsen TC, et al. 2004. Autologous chondrocyte implantation compared with microfracture in the knee. A randomized trial. J Bone Joint Surg Am 86-A:455–464.
25. Goodwin DW, Wadghiri YZ, Dunn JF. 1998. Micro-imaging of articular cartilage: T2, proton density, and the magic angle effect. Acad Radiol 5:790–798.
26. Xia Y. 2000. Magic-angle effect in magnetic resonance imaging of articular cartilage—a review. Invest Radiol 35: 602–621.