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# T2 mapping in the knee after microfracture at 3.0 T: correlation of global T2 values and clinical outcome – preliminary results

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## Summary

*Objective*: The aim of our study was to correlate global T2 values of microfracture repair tissue (RT) with clinical outcome in the knee joint.

*Methods*: We assessed 24 patients treated with microfracture in the knee joint. Magnetic resonance (MR) examinations were performed on a 3 T MR unit, T2 relaxation times were obtained with a multi-echo spin-echo technique. T2 maps were obtained using a pixel wise, mono-exponential non-negative least squares fit analysis. Slices covering the cartilage RT were selected and region of interest analysis was done. An individual T2 index was calculated with global mean T2 of the RT and global mean T2 of normal, hyaline cartilage. The Lysholm score and the International Knee Documentation Committee (IKDC) knee evaluation forms were used for the assessment of clinical outcome. Bivariate correlation analysis and a paired, two tailed *t* test were used for statistics.

*Results*: Global T2 values of the RT [mean 49.8 ms, standards deviation (SD) 7.5] differed significantly ($P < 0.001$) from global T2 values of normal, hyaline cartilage (mean 58.5 ms, SD 7.0). The T2 index ranged from 61.3 to 101.5. We found the T2 index to correlate with outcome of the Lysholm score ($r_s = 0.641$, $P < 0.001$) and the IKDC subjective knee evaluation form ($r_s = 0.549$, $P = 0.005$), whereas there was no correlation with the IKDC knee form ($r_s = -0.284$, $P = 0.179$).

*Conclusion*: These findings indicate that T2 mapping is sensitive to assess RT function and provides additional information to morphologic MRI in the monitoring of microfracture.


*Key words*: Microfracture, Clinical radiodiagnostic correlation, T2 mapping, 3 T, Quantitative MRI, Cartilage repair.

## Introduction

Recent progress in cartilage repair has resulted in a diversity of approaches on the treatment of cartilage defects[1]. Bone marrow stimulating techniques such as microfracture (MFX) are considered as good first line treatment for the defects below 4 $cm^2$ [1,2]. Penetration of the subchondral bone and subsequent bleeding result in the formation of fibrocartilaginous repair tissue (RT). Improved knee function after MFX is reported in 70–95%[2–5], but there are also reports of knee function deterioration after 18 months[6,7]. Autologous cartilage transplantation techniques are hoped to provide more durable RT; a direct comparison of autologous chondrocyte transplantation and MFX did not demonstrate a significant difference between either techniques at 2 years[2]. However, both techniques do significantly differ with respect to costs, morbidity and surgical complexity. An objective assessment of cartilage repair efficacy therefore is of substantial interest.

MRI provides objective and reliable data on cartilage repair, in particular on defect filling, RT integration and surface, signal intensity and homogeneity, integrity of the subchondral lamina and bone, central osteophytes and effusion[8,9]. Defect filling and subchondral edema seem to correlate with clinical outcome[10]. Still, assessment of RT composition with standard MRI has demonstrated differing outcomes[10,11].

MRI of biochemical RT properties may provide valuable additional information on cartilage repair[12,13]. Presently, two different techniques to directly visualize the molecular structure of cartilage are considered to be of promise: delayed gadolinium-enhanced MRI of cartilage (dGEMRIC) and quantitative T2 mapping. dGEMRIC is considered to be specific for glycosaminoglycan (GAG) content, whereas quantitative T2 mapping provides information on cartilage collagen network organization and concentration[14].

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The dGEMRIC technique is based on i.v. contrast agent administration. Gd−DTPA2− distributes inversely to GAG concentration. A time delay of about 90 min from contrast agent administration to the MR examination is required to provide sufficient time for a homogeneous distribution of contrast agent in cartilage, which detracts from clinical use.

T2 mapping can be carried out in relatively short time if high field MRI units are available to ensure sufficient signal to noise and high resolution at reasonable scan times. There is no demand for a contrast agent, which is another advantage for clinical use. As 3.0 T units are gradually established in clinical routine, the integration of T2 mapping may be useful to gain further knowledge on the treatment of full thickness cartilage defects.

Based on a recent study on T2 mapping after MFX in an equine model[12], our hypothesis was that T2 mapping could be used to assess RT function. In this study we therefore aimed to correlate RT T2 values with clinical outcome in patients after MFX in the knee joint.

## Methods

### PATIENTS

Approval for this observational study was obtained from the Ethics Committee of the Medical University of Vienna. All patients signed an informed consent form before participation.

We assessed 24 patients treated with MFX in the knee joint. Mean age was 41 standards deviation (SD) 14 years, 17 patients were males and seven females. The repair site was located on the medial femoral condyle (MFC) in 19 cases, in five cases MFX had been carried out on the lateral femoral condyle (LFC).

Mean defect size was 2.0 SD 1.1 $cm^2$ (0.8−5.0 $cm^2$). The mean body mass index (BMI) was 27.2 SD 4.1 $kg/m^2$. The mean follow up period was 29 SD 14 months.

### EXCLUSION CRITERIA

Patients with trauma within the last 6 weeks, recent intra-articular injections and knee arthroscopy within the last 6 months were excluded. Furthermore we excluded patients with advanced osteoarthritis, ligament instability, genu varum or valgum malalignment and patients with no RT in the site of defect. Lesions had to be localized in one compartment of the knee only. Patients' age was limited to 18−65 years, surgery had to date back at least 12 months.

The filling of the defect was verified with morphologic MRI. Patients who had a filling grade below 25% of the total volume fill were excluded from quantitative T2 mapping analysis.

### SURGICAL TECHNIQUE AND REHABILITATION

MFX was carried out by two experienced surgeons as described by Steadman *et al.*[3]. During arthroscopy with a tourniquet, loose cartilage bodies were removed and marginally attached cartilage was debrided. After exact preparation of the bed, an arthroscopic 70° angled awl was used to penetrate the subchondral plate and to generate micro-holes in the exposed bone starting in the periphery of the lesion. Subchondral plate integrity was ensured by a minimum distance of 3 mm between the micro-holes. After release of the tourniquet bleeding from the perforations was ensured. A single drain without suction was placed suprapatellar medial in the outflow portal to reduce the risk of arthrofibrosis. The drain was removed 1 day after surgery.

Postoperative treatment was based on continuous passive motion (CPM) for a period of 6 weeks after surgery. Crutch assisted non-weight bearing ambulation was prescribed for 4 weeks, touch-down partial weight bearing up to 20 kg had to be kept for another 2 weeks. After 6 weeks patients progressed to full weight bearing, free or machine weights were not permitted before week 16. Sports that involve pivoting, cutting and jumping were interdicted until 6 months after surgery.

### MRI

MRI examinations were performed on a 3 T MR unit (Magnetom Trio, Siemens, Erlangen, Germany) with a gradient strength of 40 mT/m using an eight-channel (phased array) knee coil (In vivo, Gainesville, FL, USA).

For morphological evaluation we used an isotropic three-dimensional (3D)-Double echo steady state (DESS) sequence[15]. This sequence provides a high sensitivity for cartilage morphology due to heterogeneous cartilage signal and high cartilage to fluid contrast. Additionally, quantitative measurements due to the high resolution and isotropic signal acquisition are feasible whilst a short acquisition time is preserved. The DESS sequence in this study had a repetition time (TR) of 15.1 ms, echo time (TE) of 5.11 ms and a flip angle of 25°. The field of view (FOV) was 150 mm × 150 mm with a 250 × 250 pixel matrix and a slice thickness of 0.6 mm with an in plane resolution of 0.6 mm × 0.6 mm. An acceleration factor of 2 was applied; the scan time was 6 min 32 s.

The T2 relaxation times were obtained from T2 maps reconstructed using a custom programmed multi-echo spin-echo technique that has already found application in former studies on cartilage repair[16]. The TR was 1.650 s. Six TEs were collected (12.9 ms, 25.8 ms, 38.7 ms, 51.6 ms, 65.5 ms and 77.4 ms). A 20.0 cm × 20.0 cm FOV, 320 × 320 pixels matrix and a slice thickness of 1 mm, with an in plane resolution of 0.6 mm × 0.6 mm and a distance factor of 100% was used. The bandwidth was 240 Hz/pixel. The number of averages was 1 and the total scan time 8 min 46 s. Sixteen slices were measured in the relevant compartment for each patient. Images were acquired in the sagittal plane.

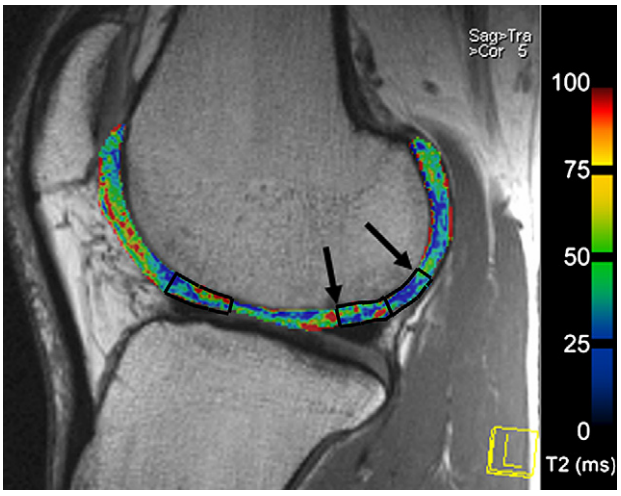


Fig. 1. Fused T2 map of a patient after MFX therapy (arrows) with two ROIs placed within the cartilage RT and one ROI placed within morphologically healthy articular cartilage.

### T2 MAPPING AND MORPHOLOGIC MRI EVALUATION

T2 maps were obtained using a pixel wise, mono-exponential non-negative least squares (NNLS) fit analysis. In combination with the morphological images provided by the DESS sequence and the intra-operative documentation, slices covering the cartilage RT were selected and region of interest (ROI) analysis was done by an experienced senior musculoskeletal radiologist in consensus with an orthopedic surgeon. The ROIs covered the full thickness of cartilage RT and were positioned on three contiguous sagittal slices to assess the whole repair site. In each slice three ROIs were defined, two ROIs were placed within the RT and one ROI comprised a cartilage region that appeared intact (preserved thickness and surface, no signal alterations) on the morphological DESS sequence (see Fig. 1). In each patient, T2 values of the two ROIs within the repair sites were compared and found not to differ beyond respective ROI SDs. Subsequently, global T2 values of the RT (RT T2) and normal, hyaline cartilage (NC T2) were calculated for each patient from the ROIs of all assessed slices.

In order to compare RT T2 among patients we aimed to express RT T2 relative to NC T2. Thus, we calculated a non-dimensional coefficient which we defined as T2 index:

Table I
*Defect volume filling*

| Volume fill % | *N* | % |
|---|---|---|
| 0−25 | 1 | 4.1 |
| 25−50 | 4 | 16.7 |
| 50−75 | 3 | 12.5 |
| 75−100 | 9 | 37.5 |
| 100 | 7 | 29.2 |
| >100 | 0 | 0 |

Table II
*T2 values of repair tissue (RT T2) and normal, hyaline cartilage (NC T2)*

| | RT T2 | NC T2 |
|---|---|---|
| Mean | 49.8 | 58.5 |
| SD | 7.5 | 7.0 |
| Median | 50.6 | 58.4 |
| Minimum | 33.0 | 40.0 |
| Maximum | 67.0 | 71.0 |
| *N* | 24 | 24 |

$$\text{T2 index} = \left(\frac{\text{RT T2}}{\text{NC T2}}\right) \times 100.$$

Repair site filling and subchondral edema were evaluated with the DESS sequence. Evaluation parameters were chosen with reference to the magnetic resonance observation of cartilage repair tissue (MOCART) classification system[10]. Defect filling volume was assessed with a 3D viewer and classified into seven categories (see Table I). Subchondral edema was described as absent, as moderate if below 2 cm in diameter or as severe if larger than 2 cm in diameter.

### CLINICAL EVALUATION

For assessment of the clinical outcome we used two established scoring systems: the Lysholm score[17], and the International Knee Documentation Committee (IKDC) knee evaluation forms[18,19]. The Lysholm score includes eight subcriteria, three of them functional and five subjective. A total of 100 points can be achieved, with 50% based on the symptoms of pain and instability.

The IKDC knee form describes four categories as follows: normal, nearly normal, abnormal and severely abnormal. There are four categories for evaluation, respectively, effusion, passive motion deficit, ligament examination and compartment findings. The worst single value defines the final result.

IKDC subjective knee evaluation form has been designed and validated to assess symptoms, function and sports activity in patients with knee disorders[19,20].

### STATISTICAL EVALUATION

For statistical analysis we used SPSS 14.0 (SPSS Institute, Chicago, IL, USA) and Microsoft Excel on a Windows XP platform (Microsoft, Redmond, WA, USA). We compared T2 values of repair sites and normal cartilage with a paired, double tailed student *t* test. The T2 index was calculated with Microsoft Excel. Bivariate correlation analysis (Spearman's rho, $r_s$) was carried out to determine correlations of respective parameters. The level of significance was $P < 0.05$.

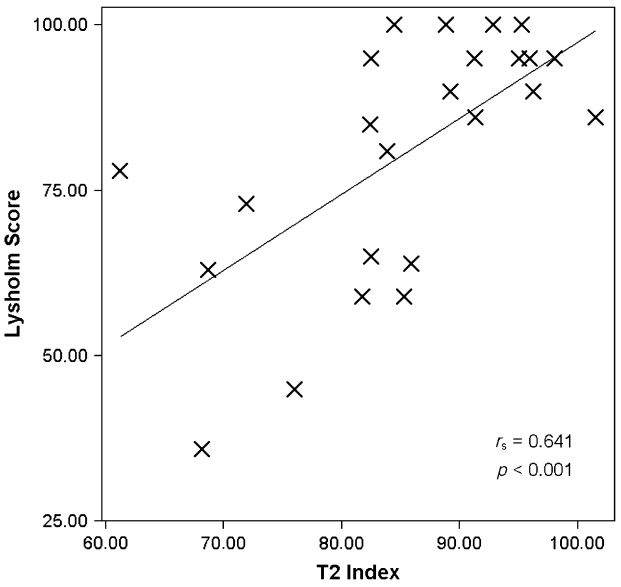


Fig. 3. Correlation of the T2 index and the Lysholm score.

## Results

Mean T2 values of the repair sites ranged from 33 to 67 ms (mean 49.8, SD 7.5), mean T2 values of normal, hyaline cartilage ranged from 40 to 71 ms (mean 58.5, SD 7.0, see Table II and Fig. 2). A significant difference between T2 values was found in the paired, double tailed *t* test ($P < 0.001$).

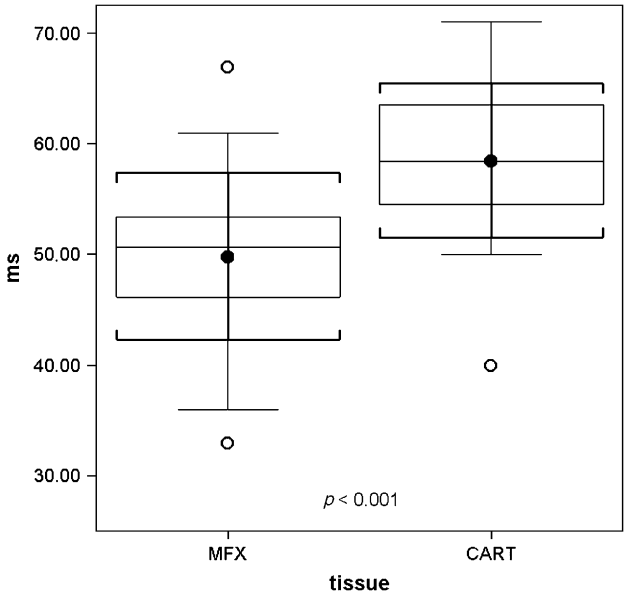


Fig. 2. T2 values of RT and articular cartilage: boxplot and mean ± 1 SD.

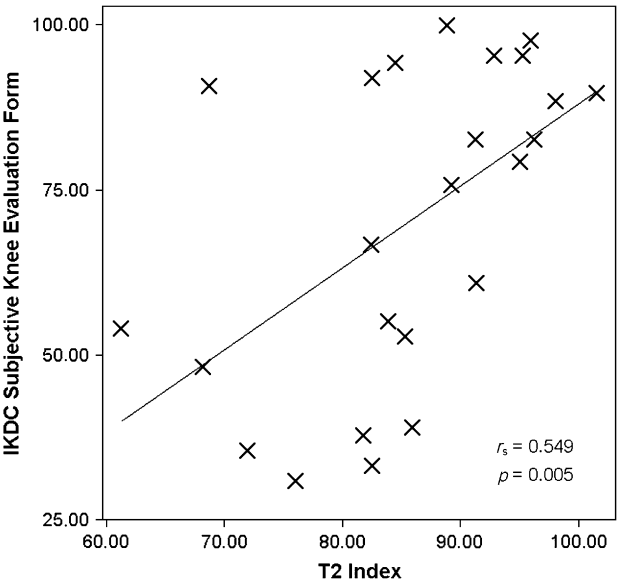


Fig. 4. Correlation of the T2 index and the subjective IKDC knee form.

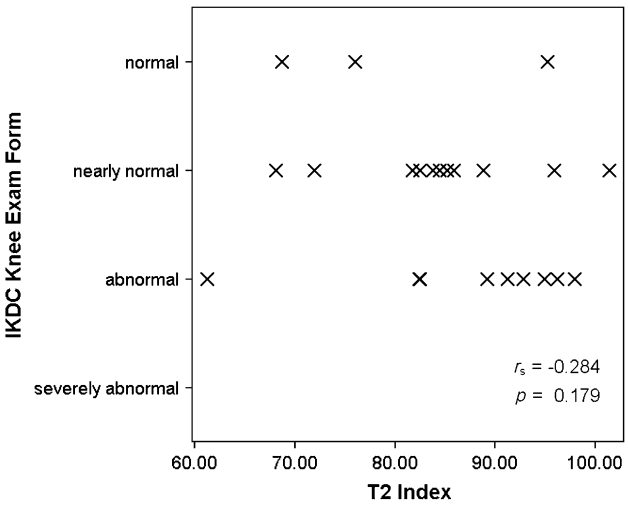


Fig. 5. Correlation of the T2 index and the IKDC form.

The T2 index ranged from 61.3 to 101.5 (mean 85.5, SD 10.3).

All patients reported improvement after surgery. The mean Lysholm score was 80.6 SD 18.5, mean outcome of the subjective IKDC form was 70.0 SD 23.8. In the IKDC rating, the knee status was normal in 41.7%, nearly normal in 45.8% and abnormal in 12.5%.

RT volume fill grade was above 75% in 66.7%. A range from 25 to 75% was found in 29.2%, in 4.1% filling grade was below 25% (see Table I). RT hypertrophy did not occur in this study.

We observed moderate subchondral edema in one patient.

We found the T2 index to correlate with outcome of the Lysholm score ($r_s = 0.641$, $P < 0.001$, see Fig. 3) and the IKDC subjective knee evaluation form ($r_s = 0.549$, $P = 0.005$, see Fig. 4).

Correlation of the T2 index and the IKDC knee form was demonstrated not to be significant ($r_s = -0.284$, $P = 0.179$, see Fig. 5).

Correlation of clinical outcome with volume fill, the BMI, lesion size, age and gender was not significant. Furthermore, there was no correlation of respective parameters with the T2 index (see Tables III and IV).

## Discussion

The overall results of clinical studies concerning MFX demonstrate improved knee function in 70–95% of patients[2–5]. The most substantial improvement apparently occurs 2 years after surgery[2–5], a finding which may be correlated to continuing remodeling and maturation of RT[3,21–24]. Although two recent studies of Kreuz *et al.* demonstrate a decline of knee function after 18 months[6,7], MFX can be considered a valid option for the first line of cartilage repair[1,25].

Different parameters related to successful cartilage repair with MFX were found in various studies. Several investigators found better clinical outcome in patients below 30 years[2,3]. Furthermore, better results were found in patients with a BMI below 30 kg/m$^2$. A size of defect below 4 cm$^2$ is generally deemed to be a parameter for better outcome. Mithoefer *et al.*[25] found evidence that the filling of the defect does play a role for clinical outcome. Still, deterioration in knee function did not solely occur in patients with poor filling of the defect.

In our study, a minimum follow up period of 12 months was chosen to ensure mature RT. BMI, defect size, age and gender did not correlate with clinical outcome. This may be due to the small number of patients examined. Defect filling did not correlate with clinical outcome either. However, we excluded patients without defect filling. These results thus may not be representative for the MFX technique. Except for one patient, bone marrow edema was not present and thus was not evaluated in correlation analysis.

MFX results in a predominantly fibrocartilaginous and less organized RT[2,21–24]. Studies of an equine model have demonstrated a filling of the defect of approximately two thirds, mostly consisting of fibrous like or fibrocartilaginous tissue[22,23]. White *et al.* performed direct comparison of histology and polarized light microscopy with quantitative T2 mapping and demonstrated the technique to be sensitive and specific for the assessment of fibrous RT[12].

In this study, we found T2 values of RT to be significantly lower than those of native cartilage. The magic angle effect is considered unlikely to account for regional differences[26], and was avoided since the reference ROIs were selected in weight bearing areas at an orientation approximately perpendicular to the magnetic field.

However, T2 values are known to be reflective of collagen organization and water content due to the interaction between water molecules and between water and surrounding macromolecules. T2 values increase with free water content[11], whereas lower water content leads to a decrease of T2, especially in the superficial zone of the weight bearing areas of the knee joint[27].

The mean follow up period in this study was 29 months; according to the findings of Kreuz *et al.*[6,7] RT can be expected to be fibrous at this time. Lower T2 values thus may be an indicator for fibrous RT composition and lower water content. Still, there remains a need for histologic biopsy analysis to permit a valid interpretation of these results. Furthermore, in studies concerning early osteoarthritis, increased T2 was found in degenerated cartilage, whereas other studies demonstrated no significant difference of T2, possibly due to collagenase activity and the creation of cleavage sites[14]. The exact interpretation of T2 remains a complex issue.

Table III
*Spearman's rho ($r_s$) and* P *values of clinical outcome and respective parameters*

| | Volume fill | | BMI | | Lesion size | | Age | | Gender | |
|---|---|---|---|---|---|---|---|---|---|---|
| | $r_s$ | $P$ | $r_s$ | $P$ | $r_s$ | $P$ | $r_s$ | $P$ | $r_s$ | $P$ |
| IKDC | −0.200 | 0.348 | 0.351 | 0.093 | −0.394 | 0.086 | 0.347 | 0.096 | 0.153 | 0.477 |
| Subjective IKDC | 0.238 | 0.262 | 0.127 | 0.554 | −0.241 | 0.306 | 0.037 | 0.865 | −0.351 | 0.093 |
| Lysholm score | 0.326 | 0.120 | −0.168 | 0.433 | 0.013 | 0.957 | −0.081 | 0.706 | −0.367 | 0.078 |

Table IV
*Spearman's rho ($r_s$) and* P *values of the T2 index and respective parameters*

| | Volume fill | | BMI | | Lesion size | | Age | | Gender | |
|---|---|---|---|---|---|---|---|---|---|---|
| | $r_s$ | *P* | $r_s$ | *P* | $r_s$ | *P* | $r_s$ | *P* | $r_s$ | *P* |
| T2 index | 0.328 | 0.118 | −0.256 | 0.228 | −0.310 | 0.184 | −0.135 | 0.530 | 0.126 | 0.558 |

Quantitative T2 mapping for assessment of cartilage repair comprises intact articular cartilage as a direct gold standard within the same joint. We therefore described the individual relative T2 values with a T2 index to take the large inter-individual variability of T2 values into account.

The Lysholm score has been demonstrated to assess functional impairment due to osteochondral defects[17]. The IKDC subjective knee evaluation form is sensitive for ligamentous and meniscal injuries, patellofemoral pain, and osteoarthritis[18,19]. Significant correlation of both scores with relative T2 may indicate that RT composition does influence clinical outcome. Conversely, criteria assessed with the IKDC knee examination form are not related to osteoarthritis or cartilage defects. Outcome of this form did not correlate with relative T2.

It is generally assumed that RT similar to hyaline articular cartilage does better[11]. Histology is the gold standard for the assessment of graft composition, but requires surgery and thus is not suited for routine monitoring. Furthermore a biopsy can merely assess a minimal area of a repair site which may be considered a substantial limitation. Quantitative T2 mapping allows the non-invasive assessment of the whole repair site. With the T2 index we could describe the grade of similarity between RT and normal, hyaline cartilage, and found better outcome in patients with a higher T2 index.

Limitations of this study predominantly concern the lack of histologic biopsy evaluation and the relatively small number of patients assessed. Furthermore, other cartilage repair techniques need to be assessed to evaluate if our findings are valid for the monitoring of cartilage repair in general or if these findings are limited to MFX. Naturally, clinical score outcome depends on other parameters aside chondral disorders. We tried to take this into account with the exclusion criteria of this study. Nevertheless, the significant correlation of Lysholm score and IKDC subjective knee form outcome with the T2 index indicates that RT collagen composition does influence RT function.

Quantitative T2 mapping is a promising tool for the monitoring of cartilage repair. Further investigation in larger numbers of patients and different repair techniques as well as longitudinal follow up will be required to define its exact role for clinical use.

## Conflict of interest

The authors have no conflict of interest.

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### References

1. Nehrer S, Minas T. Treatment of articular cartilage defects. Invest Radiol 2000 Oct;35(10):639–46.
2. Knutsen G, Engebretsen L, Ludvigsen TC, Drogset JO, Grøntvedt T, Solheim E, *et al.* Autologous chondrocyte implantation compared with microfracture in the knee. J Bone Joint Surg Am 2004;86-A(3):455–64.
3. Steadman JR, Briggs KK, Rodrigo JJ, Kocher MS, Gill TJ, Rodkey WG. Outcomes of microfracture for traumatic chondral defects of the knee: average 11-year follow up. Arthroscopy 2003;19:477–84.
4. Steadman JR, Rodkey WG, Singleton SB, Briggs KK. Microfracture technique for full-thickness chondral defects. Technique and clinical results. Oper Tech Orthop 1997;7:300–4.
5. Gobbi A, Nunag P, Malinowski K. Treatment of full thickness chondral lesions of the knee with microfracture in a group of athletes. Knee Surg Sports Traumatol Arthrosc 2005;13:213–21.
6. Kreuz PC, Steinwachs MR, Erggelet C, Krause SJ, Konrad G, Uhl M, *et al.* Results after microfracture of full-thickness chondral defects in different compartments in the knee. Osteoarthritis Cartilage 2006;14:1119–25.
7. Kreuz PC, Erggelet C, Steinwachs MR, Krause SJ, Lahm A, Niemeyer P, *et al.* Is microfracture of chondral defects in the knee associated with different results in patients aged 40 years or younger? Arthroscopy 2006;22:1180–6.
8. Steinwachs M, Kreuz PC. Autologous chondrocyte implantation in chondral defects of the knee with a type I/III collagen membrane: a prospective study with a 3-year follow-up. Arthroscopy 2007 Apr;23(4):381–7.
9. Bachmann G, Basad E, Lommel D, Steinmeyer J. MRI in the follow-up of matrix-supported autologous chondrocyte transplantation (MACI) and microfracture. Radiologe 2004 Aug;44(8):773–82.
10. Marlovits S, Singer P, Zeller P, Mandl I, Haller J, Trattnig S. Magnetic resonance observation of cartilage repair tissue (MOCART) for the evaluation of autologous chondrocyte transplantation: determination of interobserver variability and correlation to clinical outcome after 2 years. Eur J Radiol 2006 Jan;57(1):16–23.
11. Tins BJ, McCall IW, Takahashi T, Cassar-Pullicino V, Roberts S, Ashton B, *et al.* Autologous chondrocyte implantation in the knee joint: MR imaging and histologic features at 1-year follow-up. Radiology 2005 Feb;234(2):501–8 (Epub 2004 Dec 22).
12. White LM, Sussman MS, Hurtig M, Probyn L, Tomlinson G, Kandel R. Cartilage T2 assessment: differentiation of normal hyaline cartilage and reparative tissue after arthroscopic cartilage repair in equine subjects. Radiology 2006 Nov;241(2):407–14.
13. Trattnig S, Millington SA, Szomolanyi P, Marlovits S. MR imaging of osteochondral grafts and autologous chondrocyte implantation. Eur Radiol 2007;17:103–18.
14. Burstein D, Gray ML. Is MRI fulfilling its promise for molecular imaging of cartilage in arthritis? Osteoarthritis Cartilage 2006;14:1087–90.
15. Eckstein F, Hudelmaier M, Wirth W, Kiefer B, Jackson R, Yu J, *et al.* Double echo steady state magnetic resonance imaging of knee articular cartilage at 3 Tesla: a pilot study for the osteoarthritis initiative. Ann Rheum Dis 2006 Apr;65(4):433–41 (Epub 2005 Aug 26).
16. Trattnig S, Mamisch TC, Welsch GH, Glaser C, Szomolanyi P, Gebetsroither S, *et al.* Quantitative T2 mapping of matrix-associated autologous chondrocyte transplantation at 3 Tesla: an *in vivo* cross-sectional study. Invest Radiol 2007 Jun;42(6):442–8.
17. Kocher Mininder S, Richard Steadman J, Briggs Karen K, Sterett William I, Hawkins Richard J. Reliability, validity, and responsiveness of the Lysholm knee scale for various chondral disorders of the knee. J Bone Joint Surg Am 2004;86:1139–45.
18. Anderson Allen F, Irrgang James J, Kocher Mininder S, Mann Barton J, Harrast John J, Members of the International Knee Documentation Committee. The international knee documentation committee subjective knee evaluation form normative data. Am J Sports Med 2006;34:128 (Originally published online Oct 11, 2005).
19. Irrgang JJ, Anderson AF, Boland AL, Harner CD, Kurosaka M, Neyret P, *et al.* Development and validation of the international knee documentation committee subjective knee form. Am J Sports Med 2001;29:600–13.

20. Irrgang JJ, Anderson AF. Development and validation of health-related quality of life measures for the knee. Clin Orthop Relat Res 2002; 402:95–109.
21. Frisbie DD, Morisset S, Ho CP, Rodkey WG, Steadman JR, McIlwraith CW. Effects of calcified cartilage on healing of chondral defects treated with microfracture in horses. Am J Sports Med 2006 Nov;34(11):1824–31 (Epub 2006 Jul 10).
22. Frisbie DD, Oxford JT, Southwood L, Trotter GW, Rodkey WG, Steadman JR, *et al.* Early events in cartilage repair after subchondral bone microfracture. Clin Orthop Relat Res 2003 Feb;407: 215–27.
23. Frisbie DD, Trotter GW, Powers BE, Rodkey WG, Steadman JR, Howard RD, *et al.* Arthroscopic subchondral bone plate microfracture technique augments healing of large chondral defects in the radial carpal bone and medial femoral condyle of horses. Vet Surg 1999 Jul–Aug;28(4):242–55.
24. Dorotka R, Bindreiter U, Macfelda K, Windberger U, Nehrer S. Marrow stimulation and chondrocyte transplantation using a collagen matrix for cartilage repair. Osteoarthritis Cartilage 2005 Aug;13(8): 655–64.
25. Mithoefer Kai, Williams Riley J III, Warren Russell F, Potter Hollis G, Spock Christopher R, Jones Edward C, *et al.* The microfracture technique for the treatment of articular cartilage lesions in the knee. A prospective cohort study. J Bone Joint Surg Am 2005;87: 1911–2010.2106/JBJS.D.02846.
26. Mosher TJ, Smith H, Dardzinski BJ, Schmithorst VJ, Smith MB. MR imaging and T2 mapping of femoral cartilage: *in vivo* determination of the magic angle effect. AJR Am J Roentgenol Sept 2001;177
27. Smith HE, Mosher Timothy J, Dardzinski Bernard J, Collins Belinda G, Collins Christopher M, Yang Qing X, *et al.* Spatial variation in cartilage T2 of the knee. J Magn Reson Imaging 2001;14:50–5.