Biochemical T2* MR quantification of ankle arthrosis in pes cavovarus

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Abstract

Pes cavovarus affects the ankle biomechanics and may lead to ankle arthrosis. Quantitative T2 STAR (T2*) magnetic resonance (MR) mapping allows high resolution of thin cartilage layers and quantitative grading of cartilage degeneration. Detection of ankle arthrosis using T2* mapping in cavovarus feet was evaluated. Eleven cavovarus patients with symptomatic ankle arthrosis (13 feet, mean age 55.6 years, group 1), 10 cavovarus patients with no or asymptomatic, mild ankle arthrosis (12 feet, mean age 41.8 years, group 2), and 11 controls without foot deformity (18 feet, mean age 29.8 years, group 3) had quantitative T2* MR mapping. Additional assessment included plain radiographs and the American Orthopaedic Foot and Ankle Society (AOFAS) score (groups 1 and 2 only). Mean global T2* relaxation time was significantly different between groups 1 and 2 (p = 0.001) and groups 1 and 3 (p = 0.017), but there was no significance for decreased global T2* values in group 2 compared to group 3 (p = 0.345). Compared to the medial compartment T2* values of the lateral compartment were significantly (p = 0.025) higher within group 1. T2* values in the medial ankle joint compartment of group 2 were significantly lower than those of group 1 (p = 0.019). Ankle arthrosis on plain radiographs and the AOFAS score correlated significantly with T2* values in the medial compartment of group 1 (p = 0.04 and 0.039, respectively). Biochemical, quantitative T2* MR mapping is likely effective to evaluate ankle arthrosis in cavovarus feet but further studies are required.
Biochemical T2 STAR MR imaging of early active ankle arthrosis in pes cavovarus

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Running title: MRI for cavovarus ankle arthrosis
Biochemical T2 STAR MR imaging of early active ankle arthrosis in pes cavovarus

ABSTRACT

Pes cavovarus affects the ankle biomechanics and may lead to ankle arthrosis. T2 STAR (T2*) MRI allows high resolution of thin cartilage layers and quantitative grading of cartilage degeneration. Detection of early active anteromedial ankle arthrosis using T2* MRI in cavovarus feet was evaluated.

Eleven cavovarus patients with symptomatic ankle arthrosis (13 feet, mean age 55.6 years, group 1), ten cavovarus patients with no or asymptomatic, mild ankle arthrosis (12 feet, mean age 41.8 years, group 2), and 11 controls without foot deformity (18 feet, mean age 29.8 years, group 3) had T2* MRI. Additional assessment included plain radiographs and the AOFAS score (group 1 and 2 only).

In the medial ankle compartments significant differences of T2* relaxation time were detected between the three groups (p < 0.001) and between group 2 and 3 (p = 0.019). Significant correlations of ankle arthrosis on plain radiographs and the AOFAS score with T2* values in the medial compartment among the groups were found (p = 0.04 and p = 0.039).

Biochemical T2* MR imaging is effective to detect early active anteromedial ankle arthrosis in cavovarus feet. It may allow identifying patients at risk to develop anteromedial ankle arthrosis. 200/200

Key words: Pes cavovarus; Ankle arthrosis; MRI; T2 STAR
INTRODUCTION

Cavovarus is a complex deformity thought to occur mainly from muscular imbalance of idiopathic or neurological origin.\(^1,2\) Basically, the deformity consists of a plantarflexed medial forefoot, which contributes to hindfoot varus and dorsiflexion of the talus. Consequently, the biomechanics of the ankle are affected, resulting in instability and incongruity, and ultimately ankle arthrosis may occur.

Periarticular osteotomies are most effective in the early stages of arthrosis associated with deformity. In the cavovarus foot deformity biomechanical testing has shown anteromedial ankle joint pressure concentration and supramalleolar valgus osteotomy was found to be clinically successful.\(^3,4\)

Distinguishing active (i.e. progressive) focal cartilage degeneration from incidental anatomical variation and from total joint degeneration can be difficult but is crucial when an operative realignment of the deformity to unload the diseased area is to be planned.

Currently available methods of investigation have several disadvantages: poor detection of early arthritic changes on plain radiographs, radiation exposure and poor resolution in scintigraphy, low resolution and inability to quantify cartilage degeneration in standard MRI.

Modern ‘biochemical’ MRI techniques allow quantitative grading of cartilage degeneration but their availability is restricted to high Tesla-MRI units and either necessitate long scanning times in T2 mapping or require the administration of intra-articular contrast fluid in delayed Gadolinium enhanced MRI of cartilage (dGEMRIC). T2 STAR (T2\(^*\)) imaging is the advancement of T2 imaging in 1.5 Tesla units. It combines short scanning time with high resolution of thin cartilage layers e.g. of ankle joint and quantitative grading of cartilage.
degeneration. Therefore, T2* mapping is thought to be more suitable for a possible
implementation into a clinical MRI protocol than T2 mapping.\(^5\)

The purpose of this study was to assess the effectiveness of T2* MRI to detect early active
anteromedial ankle arthrosis in cavovarus feet.

**METHODS**

Written informed consent for this comparative study was obtained from all patients, and the
study was approved by the institutional review board.

A cavovarus foot deformity was defined by the talo-1\(^{st}\) metatarsal angle more than 5° on the
lateral (high medial arch or cavus component of the deformity, “Meary’s angle”) and
anteroposterior (forefoot adductus component) weightbearing radiographs of the foot and the
ankle.\(^6,7\) Ankle arthrosis was graded from 1 to 4 according to Takakura (Table 1).\(^8\) All
radiographic angles were measured digitally with threefold magnification (Sectra Medical
Systems, Linköping, Sweden).

**Patients**

Twenty-one patients with cavovarus foot deformity and 11 controls were included in the
study and divided in three groups. Patient’s data are summarized in table 2 (Table 2).

Inclusion criteria of group 1 (symptomatic patients) were a cavovarus foot deformity and
symptomatic anteromedial ankle arthrosis grade 2 to 4 (Fig. 1a-d). General complaints were
pain and discomfort at the ankle level mainly anterior and medial, and at the lateral border of
the foot, reduced walking capacity, and painfully decreased ankle dorsiflexion. In addition,
seven patients complained about lateral ankle instability, and one about claw toes.
Inclusion criteria of group 2 (asymptomatic patients) were a cavovarus foot deformity and asymptomatic anteromedial ankle arthrosis grade 1 or below. Patients presented with symptoms related to the deformity other than ankle arthrosis. Four patients had a lateral ligamentous hindfoot instability, three had a forefoot deformity (claw toes), and two had a fifth ray overload.

Group 3 were controls without a history of previous trauma or surgery of the foot and without any foot deformity or ankle arthrosis as confirmed by history, clinical examination, and MRI. For clinical assessment, the AOFAS Ankle Hindfoot score (American Orthopaedic Foot and Ankle Society) was taken at the time of MRI measurement (Table 3).

**MRI-Measurement**

MRI was performed on a 1.5-Tesla magnetic resonance (MR) scanner (Avanto®, Siemens Healthcare AG, Erlangen, Germany) using a dedicated 8 channel foot and ankle coil (INVIVO, Philips Healthcare, Netherlands). The patients were scanned in a supine position with the ankle at a plantigrade (90°) position. For assessment of T2* relaxation times a Gradient Recalled Echo (GRE) sequence with 6 echoes was used ( TE: 5.7 ms, 9.8 ms, 14 ms, 18.1 ms, 22.2 ms, and 26.4 ms; TR = 177 ms, flip angle 35°, two averages, bandwidth 260 Hz/pixel, 10 slices, slice thickness 3mm, 0.36 x 0.36 mm, total acquisition time 7:28 min).

T2* values were obtained using an in-line pixel-wise, mono-exponential, non-negative least squares fit analysis (MapIt®, Siemens Healthcare AG, Erlangen, Germany).

Starting medially, six sagittal T2* maps were analyzed in every ankle joint (Fig. 2 a, b). Three ROIs were drawn in the cartilage layer along the curvature of the talar dome and the tibial articular surface. For each ROI, mean T2* relaxation time values, as well as standard deviation (SD) and number of pixels were documented.
Clinically early to intermediate ankle arthrosis in cavovarus feet presents as a damaged anteromedial cartilage area which usually measures intraoperatively 8-12 mm in length and 3-5 mm in width. Consequently, the first two MRI slices were considered to represent this area ("medial ankle compartment") and were compared to the adjacent five or six lateral slices ("lateral ankle compartment") for calculation of statistical differences. Relaxation time values were calculated "global" (entire ankle dome) and separately for the "medial and lateral ankle compartment".

In ten randomized selected patients and ten randomized selected controls T2* measurements were done by an additional independent observer (TCM) and used for assessment of interobserver reliability. The main observers (FK, GK) re-analyzed these cases after one month in a randomized order to assess intraobserver reliability.

**Statistical analysis**

SPSS version 15.0 (SPSS Institute, Chicago, IL, USA) for Windows (Microsoft, Redmont, WA, USA) was used for statistical calculations, and a \( p \) value less than 0.05 was considered statistically significant. Significance of T2* values’ differences between the groups were calculated using three-way analysis of variance (ANOVA). Significance of T2* values’ differences between the medial and lateral ankle compartment within one group were calculated using the t-test for independent samples. Pearson correlation was performed for T2* values with the AOFAS score, for T2* values with the lateral-1st metatarsal (Meary’s) angles, and Spearman rank correlation for T2* values with the grade of ankle arthrosis. The
interobserver reliability and intraobserver reproducibility was assessed using intraclass correlation coefficient (ICC).

RESULTS

T2* measurements

Global, medial and lateral ankle compartment T2* relaxation time values are summarized in table 4 (Table 4). The mean global T2* relaxation time was 23.33 ms in the control group and 27.17 ms for patients (p = 0.113) (Fig. 3a - d). Between group 1 and 2 mean global T2* relaxation time was significantly different (p = 0.017). There was a trend for decreased T2* values of controls compared to the asymptomatic group (p = 0.345), and a highly significant difference between the controls and the symptomatic group (p = 0.001).

Compared to the medial compartment T2* values of the lateral compartment were significantly (p = 0.025) higher within group 1, while no significant differences in group 2 or in the control group were seen.

Significant differences of T2* values of the medial ankle joint were found among the groups for the medial (p = 0.013) and for the lateral (p < 0.0001) ankle joint compartment. T2* values in the medial ankle joint compartment of asymptomatic patients were significantly lower than those of controls (p = 0.019), while no significant differences of the lateral compartments were seen.

AOFAS Score, Meary’s Angle and arthrosis grading

The mean AOFAS score was 58.4 points in group 1 (range 40 to 68, SD 8.7), 79.2 points in group 2 (range 91 to 61, SD 8.5), and 100 points in group 3. Significant differences of the AOFAS scores were found between all groups (p < 0.0001). The mean arthrosis grading was
The mean lateral talo-1st metatarsal angle was 18.5 degree in group 1 (range 9 to 28, SD 5.2), 12.8 degree in group 2 (range 7 to 20, SD 4.3), and 1.6 degree in group 3 (range -4 to 3, SD 1.1).

Among the three groups correlation of the AOFAS scores and the T2* relaxation time in the medial ankle compartment was not significant (p = 0.44), while it was for the medial compartment and group 1 (p = 0.039). The correlation of ankle arthrosis grading on plain radiographs and T2* values in the medial compartment among the three groups was significant (p = 0.04). The correlation of talo-1st metatarsal angle and T2* values among the three groups in the medial compartment revealed a trend (p = 0.25).

**Inter- and intraobserver agreement**

Interobserver agreement (ICC) of T2* measurements was 0.90 for all values assessed, 0.88 for the medial compartment and 0.91 for the lateral compartment. Intraobserver agreement was 0.89 for all values, 0.92 for medial and 0.87 for lateral compartment.

**DISCUSSION**

The association between long-standing lateral ankle instability, cavovarus deformity and medial ankle arthrosis has already been studied.\cite{10,11} Next to clinical considerations there is recent evidence from biomechanical investigation that ankle joint incongruence alone increases the intraarticular contact stresses in cavovarus deformity potentially leading to anteromedial ankle arthrosis.\cite{3,12,13}
For patients with cavovarus foot deformity that are at risk to develop anteromedial ankle arthrosis, correction of the deformity may seem recommendable to prevent the onset of degeneration at all, which would likely lead to very good outcome.

However, the consequences of the complex cavovarus foot deformity with respect to onset or progression of the ankle arthrosis are poorly predictable despite thorough clinical assessment, plain radiographs, CT scan, or even standard MRI. Our previous review of weightbearing radiographs of 59 cavovarus feet for ankle arthrosis revealed that only the extent of the lateral talo-1st metatarsal angle (Meary’s angle) has a moderately strong correlation (r=0.65) to the severity of the ankle arthrosis, while the other radiological angles defining the cavovarus deformity (calcaneal pitch, anteroposterior talo-1st metatarsal angle and anteroposterior talocalcaneal overlap) showed a poor correlation.3

Once ankle arthrosis is obvious clinically and on plain radiographs, cartilage degeneration is already advanced, and a successful outcome after operative correction is less likely.

Consequently it would seem preferable to operate patients with a cavovarus foot deformity before the ankle arthrosis develops and becomes symptomatic. However, even patients with clinical and radiographic severe cavovarus foot deformity do not inevitably develop radiological ankle arthrosis, and not every patient with ankle arthrosis is symptomatic.

A diagnostic tool which detects early cartilage degeneration is therefore required to separate patients with cavovarus foot deformity who are at risk to develop anteromedial ankle arthrosis from those who are not.

New techniques in MRI of articular cartilage such as the biochemical T2* have shown promising results for assessment and monitoring of articular cartilage injury and degeneration in the knee and the ankle joint.14-15
T2* is the advancement of T2 imaging for clinically used 1.5 Tesla units. It combines short scanning times with high resolution cartilage imaging even in the thin cartilage layers of the ankle joint and quantitative grading of cartilage degeneration. Compared to standard T2 mapping the resolution of T2* is equivalent for detection of relevant changes of cartilage hydration but even more sensitive to proton density and micro-structural degenerative cartilage changes.

This study is the first to present a MRI comparison using T2* as a quantitative marker for cartilage status in cavovarus foot deformity with and without symptoms. Significant differences of T2* values of the medial ankle joint compartment were found between controls, asymptomatic patients, and patients with symptomatic anteromedial ankle arthrosis, while the differences of the lateral ankle joint were not significant between the asymptomatic patient group and controls. These findings correlate well to the hypothesis of cavovarus deformity inducing anteromedial ankle arthrosis. Interestingly, lower global and medial compartment T2* relaxation times were measured in the ankles of asymptomatic patients with pes cavovarus than for symptomatic patients and controls (Table 4). This finding has been reported previously for T2 MR imaging by Burstein et al.. Areas of low T2- weighted signal intensity were frequently observed in cartilage adjacent to subacute or chronic cartilage injuries that per se are usually associated with elevated T2 due to increased hydration. The finding was considered to be related to fragmentation of collagen fibrils exposing additional hydrophilic sites that could lead to more efficient T2 relaxation and greater magnetization transfer.

Finally, the generally lower T2* relaxation time in group 2 results in non-linear T2* relaxation time values across the groups, while the ankle arthrosis progression is expected to
be accompanied with a linear increase of arthrosis grade on plain radiographs, lateral talo-1st metatarsal angle (Meary’s angle) and a linear decrease of the AOFAS scores. Therefore, the correlation of T2* values and arthrosis grade on plain radiographs, Meary’s angle, and the AOFAS scores is weakened.

T2* relaxation time values in group 1 were higher for the lateral compartment than for the medial (Table 4). In contrast to the anteromedial ankle arthrosis that is seen clinically, intraoperatively, and on plain radiographs, these findings would indicate more severe arthrosis in the lateral ankle compartment in patients with symptomatic ankle arthrosis due to cavovarus foot deformity. This was interpreted as a measurement artifact. The anteromedial loss of cartilage causes a varus tilt of the talus and likely a distraction of the posterolateral ankle. Measuring not only the joint’s cartilage but also the synovial fluid inflow into this gap might have led to falsely high T2* values in the lateral compartment of group 1 ankles.

Morphologic T2 mapping and other new ‘biochemical’ MRI techniques allow quantitative grading of cartilage degeneration because they are highly sensitive to cartilage hydration and collagen structures.\(^\text{17}\) Delayed Gadolinium enhanced MRI of cartilage (dGEMRIC) MRI imaging has been reported to be potentially predictive of the development of radiographic arthrosis in knees that appeared normal on plain radiographs.\(^\text{18}\)

In this study T2* relaxation times were higher for patients with cavovarus foot deformity and symptomatic anteromedial ankle arthrosis than for asymptomatic patients or controls. Increasing T2* values in arthrosis compare well with established T2 mapping studies. As a quantitative marker for the cartilage status T2* may also be used to predict the probability of ankle arthrosis in cavovarus foot deformity. While low T2* values may represent the early phase of ankle cartilage degeneration, an increase of the T2* value exceeding the mean value
in asymptomatic patients may indicate a progression of the degeneration. However, given the low number of patients in this group and the lack of mid- or long-term radiographic follow-up, the predictive value of biochemical T2* MRI still needs to be established.

In our institution, asymptomatic patients with cavovarus feet and no or mild ankle arthrosis on plain radiographs are now monitored by repeat biochemical T2* imaging and radiographs. Appropriate statistical correlation of T2* relaxation times and progression of ankle arthrosis including more patients and long-term follow-up is required to evaluate whether T2* is potentially predictive of the development of radiographic arthrosis.

Strengths of the study are the evaluation of a new MRI technique and the availability of two patient groups, different in consideration of ankle arthrosis’ severity, and controls to compare the MRI results. Limitations of the study are the relatively small number of patients for comparison particularly in the patients groups and the lack of long-term follow-up and histological investigations of the cartilage to confirm considerations.

In conclusion, biochemical T2* MR imaging is effective to detect early active anteromedial ankle arthrosis in cavovarus feet that cannot be visualized with plain radiographs. It may allow identifying patients at risk to develop anteromedial ankle arthrosis but a larger number of patients and mid- to long-term follow-up is required.

T2* MR imaging methods for probing the macromolecular status of cartilage remain very promising in offering information that is not available with standard approaches. As such, this MR imaging has great potential to have a positive impact on the future development of disease-modifying strategies for arthrosis, not only in the ankle joint.

ACKNOWLEDGEMENTS
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REFERENCES


TABLES

Table 1: Ankle arthrosis grading according to Takakura.8
Grade 1 (mild)  
subchondral sclerosis, bony spurs, no joint space narrowing

Grade 2 (intermediate)  
medial joint space narrowing

Grade 3 (severe)  
direct contact of subchondral bone of medial tibia and talus

Grade 4 (complete)  
subchondral bone contact of the entire ankle joint

Table 2: Patients’ and controls’ data.

<table>
<thead>
<tr>
<th>Groups</th>
<th>No. patients/feet</th>
<th>Side left/right</th>
<th>Gender female/male</th>
<th>Mean age (years)</th>
<th>Etiology</th>
</tr>
</thead>
<tbody>
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<td>Symptomatic (1)</td>
<td>11/13</td>
<td>8/5</td>
<td>2/9</td>
<td>55.6 range 26 - 82</td>
<td>8 idiopathic 4 neurologic 1 posttraumatic</td>
</tr>
<tr>
<td>Asymptomatic (2)</td>
<td>10/12</td>
<td>6/6</td>
<td>2/8</td>
<td>41.8 range 18 - 63</td>
<td>6 idiopathic 5 neurologic 1 posttraumatic</td>
</tr>
<tr>
<td>Controls (3)</td>
<td>11/18</td>
<td>10/8</td>
<td>3/8</td>
<td>29.8 range 25 - 40</td>
<td>-</td>
</tr>
</tbody>
</table>

Table 3: The American Orthopaedic Foot & Ankle Society (AOFAS) Ankle Hindfoot score. 

<table>
<thead>
<tr>
<th>Assessment</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Pain</td>
<td>40</td>
</tr>
<tr>
<td>- Function</td>
<td>50</td>
</tr>
<tr>
<td>activity limitation, support requirement, maximal walking distances, walking problems on different surfaces, gait abnormality, ankle- and subtalar motion, and hindfoot stability</td>
<td></td>
</tr>
<tr>
<td>- Hindfoot alignment</td>
<td>10</td>
</tr>
<tr>
<td>total</td>
<td>100</td>
</tr>
</tbody>
</table>

Table 4: Summary of T2 * relaxation time values measured in the ankle joint in (1) patients with symptomatic ankle arthrosis due to cavovarus foot deformity, (2) patients with asymptomatic ankle arthrosis due to cavovarus foot deformity, and (3) controls.
TABLE

<table>
<thead>
<tr>
<th>Groups</th>
<th>T2* relaxation time (ms)</th>
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<tr>
<td></td>
<td>global</td>
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<tr>
<td>Symptomatic (1)</td>
<td>mean</td>
</tr>
<tr>
<td></td>
<td>SD, range</td>
</tr>
<tr>
<td>Asymptomatic (2)</td>
<td>mean</td>
</tr>
<tr>
<td></td>
<td>SD, range</td>
</tr>
<tr>
<td>Controls (3)</td>
<td>mean</td>
</tr>
<tr>
<td></td>
<td>SD, range</td>
</tr>
</tbody>
</table>

FIGURE LEGENDS

Figure 1a-d: Weightbearing anteroposterior (a) and lateral (b) radiographs of the foot and anteroposterior radiograph of the ankle (c) of a 54 years old male patient with symptomatic anteromedial ankle arthrosis grade 3 due to idiopathic cavovarus foot deformity. The relative dorsiflexion of the talus due to the plantarflexed medial rays and the varus tilt of the talus in the ankle mortise due to varus hindfoot alignment cause anteromedial load concentration in the ankle joint. Intraoperative view of advanced cartilage degeneration at the anteromedial talus through an anterior ankle arthrotomy (d).

Figure 2 a and b: Assessment of three ROI on a sagittal slice. ROI were selected at the original grey scale images (a) and T2* relaxation time values in ms were measured for same position at the map (b).

Figure 3 a-d: T2* grey scale images and maps of an asymptomatic patient with decreased T2* values (a,b) and a symptomatic patient with increased T2* values (c,d). Increased values (black arrow) in area of cartilage thinning and subchondral bone changes (white arrow).
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53x92mm (300 x 300 DPI)
Figure 1a-d: Weightbearing anteroposterior (a) and lateral (b) radiographs of the foot and anteroposterior radiograph of the ankle (c) of a 54 years old male patient with symptomatic anteromedial ankle arthrosis grade 3 due to idiopathic cavovarus foot deformity. The relative dorsiflexion of the talus due to the plantarflexed medial rays and the varus tilt of the talus in the ankle mortise due to varus hindfoot alignment cause anteromedial load concentration in the ankle joint. Intraoperative view of advanced cartilage degeneration at the anteromedial talus through an anterior ankle arthrotomy (d). 79x55mm (300 x 300 DPI)
Figure 1a-d: Weightbearing anteroposterior (a) and lateral (b) radiographs of the foot and anteroposterior radiograph of the ankle (c) of a 54 years old male patient with symptomatic anteromedial ankle arthrosis grade 3 due to idiopathic cavovarus foot deformity. The relative dorsiflexion of the talus due to the plantarflexed medial rays and the varus tilt of the talus in the ankle mortise due to varus hindfoot alignment cause anteromedial load concentration in the ankle joint. Intraoperative view of advanced cartilage degeneration at the anteromedial talus through an anterior ankle arthrotomy (d).

54x90mm (300 x 300 DPI)
Figure 1a-d: Weightbearing anteroposterior (a) and lateral (b) radiographs of the foot and anteroposterior radiograph of the ankle (c) of a 54 years old male patient with symptomatic anteromedial ankle arthrosis grade 3 due to idiopathic cavovarus foot deformity. The relative dorsiflexion of the talus due to the plantarflexed medial rays and the varus tilt of the talus in the ankle mortise due to varus hindfoot alignment cause anteromedial load concentration in the ankle joint. Intraoperative view of advanced cartilage degeneration at the anteromedial talus through an anterior ankle arthrotomy (d).

55x73mm (300 x 300 DPI)
Assessment of the three region of interest (ROI) on sagittal slices. ROI were selected at the original grey scale images (a) and T2* relaxation time values in ms were measured for same position at the map (b).

377x163mm (300 x 300 DPI)
T2* grey scale images and maps of an asymptomatic patient with decreased T2* values (a,b) and a symptomatic patient with increased T2* values (c,d). Increased values (black arrow) in area of cartilage thinning and subchondral bone changes (white arrow).

175x132mm (300 x 300 DPI)