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Relationship between meniscal integrity and risk factors for cartilage degeneration

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A B S T R A C T

Background: The purpose of this study was to use MRI to determine if a loss of meniscal intra-substance integrity, as determined by T2* relaxation time, is associated with an increase of Kellgren–Lawrence (KL) grade, and if this was correlated with risk factors for cartilage degeneration, namely meniscal extrusion, contact area and anterior–posterior (AP) displacement.

Methods: Eleven symptomatic knees with a KL 2 to 4 and 11 control knees with a KL 0 to 1 were studied. A 3 Tesla MRI scanner was used to scan all knees at 15° of flexion. With a 222 N compression applied, a 3D SPACE sequence was obtained, followed by a spin echo 3D T2* mapping sequence. Next, an internal tibial torque of 5 Nm was added and a second 3D SPACE sequence obtained. The MRI scans were post-processed to evaluate meniscal extrusion, contact area, AP displacement and T2* relaxation time.

Results: KL grade was correlated with T2* relaxation time for both the anterior medial meniscus (r = 0.79, p < 0.001) and the posterior lateral meniscus (r = 0.55, p = 0.009). In addition, T2* relaxation time was found to be correlated with risk factors for cartilage degeneration. The largest increases in meniscal extrusion and decreases in contact area were noted for those with meniscal tears (KL 3 to 4). All patients with KL 3 to 4 indicated evidence of meniscal tears.

Conclusions: This suggests that a loss of meniscal integrity, in the form of intra-substance degeneration, is correlated with risk factors for cartilage degeneration.

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1. Introduction

Previous studies have shown that the meniscus plays a primary role in distributing load and as a secondary stabilizer in the knee [1,2]. Given the important role of the meniscus, it is expected that should the meniscus lose its integrity, in the form of intra-substance degeneration, or if a meniscal tear is present it will no longer be able to fulfill these functions, and that osteoarthritic changes would result [3]. This notion was emphasized by the work of Gale et al. and Hunter et al., who have shown that meniscal extrusion is correlated with meniscal degeneration, as judged mainly by the presence of tears, and severity of osteoarthritis (OA) [4,5]. In addition, studies have shown that should the meniscus be torn, it is associated with a decrease in contact area and an increase in anterior–posterior (AP) displacement, both of which can lead to cartilage degeneration [6,7]. However, the impact of intra-substance meniscal degeneration on cartilage degeneration is not fully understood. Such intra-substance meniscal degeneration is expected to lead to a reduced radial stiffness of the meniscus and a reduction in mechanical function.

One method of assessing meniscal intra-substance integrity is through the use of the T2* relaxation time from MRI. Relaxation times have been extensively used for assessing cartilage properties but are only recently being evaluated for use with menisci [8,9]. As the T2* relaxation time increases, it indicates a disruption in the collagen network of the meniscus (the meniscus is composed of 98% type I collagen) and a decrease in water content, both indications of intra-substance meniscal degeneration. Zarins et al. [10] showed that relaxation times were associated with the Whole-Organ Magnetic Resonance Imaging Score (WORMS) and that they could be used to identify not only meniscal tears but intra-substance meniscal degeneration as well.

Therefore, the purpose of this study was to use MRI to evaluate the intra-substance integrity of the menisci of patients ranging in OA severity, as well as normal controls, using the T2* relaxation time, to determine if there is an association between a loss of meniscal intra-substance integrity and an increase in OA severity. The T2* relaxation

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time data would be compared with that obtained on the patient’s meniscal extrusion, contact area and AP displacement, to determine if there is a correlation between these risk factors for cartilage degeneration and meniscal intra-substance integrity. It is hypothesized that as severity of OA increases there will be an increase in intra-substance degeneration, which will be associated with an increase in meniscal extrusion, a decrease in contact area between the femur, meniscus and tibia and an increase in anterior–posterior (AP) displacements of the femur on the tibia.

2. Methods and materials

In accordance with Institutional Review Board approval and the Health Insurance Portability and Accountability Act (HIPAA) regulations, 11 patients (six males and five females, average age (mean ± standard deviation) 64 ± 11 years, average BMI 27.7 ± 3.8) were recruited to participate in this study from a non-therapeutic R01 NIH cohort (R01 AR052873) at our teaching hospital. In order to be included in this study, patients needed to have intact cruciate ligaments. In addition, control knees needed to have a Kellgren–Lawrence (KL) grade of 0 to 1 and symptomatic knees needed to have a KL grade of 2 to 4. All symptomatic knees had primary medial OA. The KL grade was assigned by a musculoskeletal radiologist who reviewed anteroposterior standing semiflexed radiographs of all knees [11]. Both knees of all 11 patients were analyzed for a total of 22 knees (11 control knees and 11 symptomatic knees).

All patients were placed supine in a plastic rig with the asymptomatic knee at 15° of flexion, representing the angle of flexion during heel strike in level walking and in descending stairs [12]. The subject’s foot was fastened in a surgical boot attached to a back plate on the rig. The back plate was positioned on two rails such that the distance from the receiving coil to the foot-rest could be adjusted based on the subject’s height. A rope was attached to the left and right panel of the back plate and pulled through the shoulder brace, where hooks were placed for the application of weights. A total compressive force of 222 N was applied along the tibial long axis and the first MRI scan completed (Fig. 1).

A Siemens MAGNETOM Verio 3 Tesla (3 T) MRI machine (Siemens, Malvern, PA) and Transmit/Receive 15 Channel Knee Coil with a 3D-Proton Density-nom-Fat Suppressed-SPACE (Sampling Perfection with Application optimized Contrasts using different flip angle Evolutions) sequence was used (flip angle = 120°; repetition time (TR) = 1000 ms; echo time (TE) = 46 ms; bandwidth = 460 Hz/pixel; Field of View (FOV) = 160 × 160 mm; matrix size = 320 × 300 pixels; voxel size = 0.5 × 0.5 × 0.5 mm³). This was followed by a 3D-T2* sequence with Gradient Echo (GRE) sequence (TR = 30 ms; TE = 10 echoes (2.01 ms to 25.50 ms); flip angle = 25°, bandwidth = 450 Hz/pixel; FOV = 220 mm × 84.4 mm; matrix size = 384 × 100; voxel size = 0.6 × 0.6 × 0.6 mm³).

Upon completion of this scan, an internal tibial torque of 5 Nm was applied at the surgical boot, in addition to the compression, and a second 3D SPACE scan was taken. This torque would act to anteriorly displace the medial femoral condyle on the tibia, and the opposite on the lateral side.

All three scans were then repeated for the symptomatic knee. A five minutes rest period was provided prior to scanning each knee. The T2* sequence allowed for determination of the T2* relaxation time as a measure of meniscal intra-substance integrity as well as meniscal tears, whereas the SPACE sequences allowed for analysis of meniscal extrusion, contact area and AP displacement. In addition, the SPACE sequence was used to evaluate meniscal tears by a musculoskeletal radiologist and confirmed with elevated T2* relaxation times. The torque scan was used to determine AP displacement under functional loads. However, contact area and meniscal extrusion were evaluated under compression only to represent the function of the meniscus under axial loading, similar to Gale et al. and Hunter et al. [4,5]. The loads used were based on data from instrumented knee studies which determined in vivo force data including compression, shear and torque [13,14].

Following testing, the scans were analyzed in 3DDoctor (Able Software Corp, Lexington, MA) using a previously established methodology [15–17]. The femur, tibia, femoral cartilage, tibial cartilage and menisci were manually segmented on each slice in the sagittal plane. Using this methodology, segmentations were previously shown to have an accuracy of 0.076 ± 0.011 mm and repeatability within − 0.056% error [17]. Both the repeatability and accuracy are well within the voxel size of this study. From these segmentations the software created 3D surface models which were exported into RapidForm XV (Inus Technology, Seoul, Korea) for analysis. The tibia from the compression-only and the compression-and-torque scans were superimposed using a least-squares algorithm, to act as a reference. The femur, femoral cartilage, tibial cartilage and menisci from the compression-and-torque scan were then transformed using the matrix from the tibial alignment. With the models properly aligned, the displacement of the femur relative to the tibia following the application of the torque was determined in RapidForm XV using the global coordinate system and represented by a color map.

The color map histogram from the medial anterior condyle and the lateral posterior condyle were used to determine the respective average AP displacements. A Student’s paired t-test or Wilcoxon Signed Rank test, depending on if the data followed a normal distribution, with significance of p < 0.05, was performed to determine if the displacements of the symptomatic knees were significantly different from the displacements of the control knees. A Spearman’s rank correlation with significance of p < 0.05 was performed to determine if there was a correlation between the displacements and the Kellgren–Lawrence grades.

The contact area was determined using a Rapidform algorithm which calculated where the perpendicular point-to-point distances between the articulating aspects of the femoral cartilage and menisci as well as femoral cartilage and tibial cartilage surface models of the compression-only model, were within 0.5 mm, based on the MRI voxel size. The contact area was highlighted on the menisci and tibial cartilage, and an axial image was captured. This image was then imported into ImageJ (National Institutes of Health, Bethesda, MD) where the contact area for the compartment was calculated as a percentage of the tibial cartilage and meniscus surface area (i.e., %Medial Contact Area = Medial Contact Area / Surface Area of the Medial Tibial Cartilage and Medial Meniscus, Fig. 2).

Fig. 1. All patients were placed supine in a plastic rig with the knee at 15° of flexion.
Next, axial images of the inferior view of the tibia and medial meniscus, tibia and lateral meniscus, medial meniscus only and lateral meniscus only were obtained and opened in a custom MATLAB (MathWorks, Inc., Natick, MA) script to determine the %Meniscal Extrusion. The images of the tibia and either the lateral or medial meniscus provided a view indicating the portion of the menisci that had extruded off the tibial plateau. The MATLAB script automatically segmented the extruded meniscus and calculated its area. The area of the whole medial or lateral meniscus was calculated from the axial image of the menisci only and the %Meniscal Extrusion determined (%Meniscal Extrusion = Area of Extruded Meniscus / Total Meniscus Area, Fig. 3). It is noted that the extrusion would be enhanced due to the axial loading of the knee during the taking of the MRI scans, compared to scans taken with the knee relaxed.

Lastly, to determine meniscal intra-substance integrity, the T2* mapping scans were processed offline using software (FireVoxel) developed at our teaching hospital [18]. The medial and lateral menisci were manually segmented on each sagittal slice of the scans and fitted using a least squares algorithm from 10 echoes. The T2* relaxation times were represented with color maps on the menisci. From the histogram, the average T2* values for the anterior medial meniscus and the lateral meniscus, to coincide with the femoral motion, were noted. A Student’s paired t-test or Wilcoxon Signed Rank test with significance of p < 0.05, was performed to determine if the T2* relaxation times of the symptomatic knees were significantly different from the T2* relaxation times of the control knees. In addition, a Spearman’s rank correlation with significance of p < 0.05, was used to determine if there was a correlation between the Kellgren–Lawrence grades and the T2* relaxation times. Spearman’s rank correlation was also conducted to determine if there was a correlation between the T2* relaxation times and %Meniscal Extrusion, %Contact Area and AP Displacement, respectively.

3. Results

Of the knees included in this study, seven had a KL grade of 0, four had a KL grade of 1, six had a KL grade of 2, four had a KL grade of 3 and one had a KL grade of 4. The MRI scans indicated that all knees with a grade of KL 3 or 4 had a tear of the medial meniscus (two complex tears, one radial tear and two oblique tears). One knee with a grade of KL of 2 and one knee with a grade of KL 1 had a complex tear of the menisci. A tear of the lateral meniscus was also present in one knee with a grade of KL 3 (horizontal cleavage lesion) and one knee with a grade of KL 4 (longitudinal tear). All tears were present in the posterior horn of the menisci. All knees had intact cruciate ligaments. The T2* relaxation times for the menisci of the symptomatic (anterior medial: 10.35 ± 1.52; posterior lateral: 11.33 ± 1.86) and control knees (anterior medial: 8.97 ± 0.83; posterior lateral: 10.08 ± 0.97) were found to be statistically different for both the anterior medial (p = 0.003) and the posterior lateral (p = 0.04) menisci. The T2* relaxation times were found to increase with KL grade, although, for KL 1 and KL 2 the T2* relaxation times were similar (Fig. 4). This correlation was found to be significant for both the anterior medial meniscus (r = 0.79, p < 0.001) and the posterior lateral meniscus (r = 0.55, p = 0.009).

Evaluating %Meniscal Extrusion, it was seen that less than 1% of the lateral meniscus extruded off the tibial plateau in all cases, regardless of the T2* relaxation time or the KL grade. In contrast, the medial extrusion was found to decrease slightly in cases with a KL grade of 1 or 2 and then sharply increase for cases with a KL grade 3 or 4, where a meniscal tear was present (Fig. 5). This was found to be correlated with the T2* relaxation time (r = 0.5, p = 0.03).

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similarly, no trend was found for lateral contact area with KL grade or T2* relaxation time ($r = 0.30, p = 0.18$). However, the medial contact area was found to slightly increase for cases with KL 1 or 2 and then sharply drop for cases with a KL 3 or 4, where a meniscal tear was present (Fig. 6). This was found to be correlated with the T2* relaxation time ($r = -0.43, p = 0.04$).

In the control knees, relative to the tibia, the femur underwent an external rotation, such that the medial condyle had a smaller anterior displacement and the lateral condyle had a larger posterior displacement (Fig. 7). In the symptomatic knees, a posterior translation occurred secondary to the external femoral rotation, with a decrease, although not statistically significant, in the average anterior medial displacement compared to the control knees ($p = 0.52$), and a statistically significant greater average lateral posterior displacement ($p = 0.04$). The lateral posterior displacement was correlated with KL grade ($r = 0.52, p = 0.01$), however no correlation was found between the anterior medial displacement and KL grade ($r = -0.15, p = 0.39$) (Fig. 8). There was also a significant correlation between the T2* relaxation times for the posterior horn of the lateral meniscus and the posterior lateral femoral displacement ($r = 0.58, p = 0.005$). No correlation was found between the medial anterior displacement and the T2* relaxation times for the anterior horn of the medial meniscus ($r = 0.05, p = 0.83$).

4. Discussion

It has been suggested that meniscal degeneration initiates with intra-substance degeneration, as opposed to cartilage surface degeneration, making it important to evaluate the role of meniscal degeneration on cartilage degeneration [19]. Previous studies, which looked at meniscal degeneration, have either focused on the presence of tears or have used a semi-quantitative grading method similar to the Whole-Organ Magnetic Resonance Imaging Score (WORMS) or the MRI Osteoarthritic Knee Score (MOAKS) [5,20–23]. However, these semi-quantitative scoring methods assess meniscal degeneration by measuring meniscal extrusion, evaluating signal intensity as well as by determining whether or not a tear is present and if so what kind of tear. However, in the absence of a tear neither of these techniques is sensitive to changes in intra-substance meniscal degeneration [21,23]. In contrast, the T2* relaxation time has been shown to be correlated to the organization of the collagen network and water content of the meniscus [10,24]. Due to this, it has been found to be sensitive to changes in intra-substance degeneration, thereby proving to be a useful tool for measuring meniscal intra-substance integrity [10,24].

The results of this study were consistent with others, indicating that the T2* relaxation time of both the medial and lateral menisci increased with KL grade. Rauscher et al. evaluated the relaxation time of the medial and lateral menisci of 60 patients with varying degrees of OA and found a statistically significant increase in relaxation time between groups [25]. Despite the small sample size of our study, similar trends were seen. A statistically significant correlation was found between the T2* relaxation time and the KL grade for both menisci, although the T2* relaxation time for knees with a KL grade of 1 or 2 was similar. In addition, it is important to note that in this study, there was one knee with a grade of KL 2 and one knee with a grade of KL 1 that had a tear of the medial meniscus. However, had the data from these two knees been removed from our cohort, there would have been no change to the results of this study. The high incidence of meniscal tears among those with severe OA (KL 3 to 4) in this study was also consistent with others, such as Zarins et al., who noted that 78% of the 18 patients studied with severe OA had a meniscal tear [10].

Meniscal tears have been found to be associated with an increase in meniscal extrusion [26]. This is consistent with our study where sharp increases in meniscal extrusion were noted in cases with meniscal tears (KL 3 and 4). However, in cases where no meniscal tears were present (KL 1 and KL 2), there was no major change in meniscal extrusion. In this study no association was found between meniscal intra-substance integrity and lateral meniscal extrusion. Previous studies have shown that joint space narrowing is one of the main predictors of meniscal extrusion [4]. As patients in this study had predominantly medial OA, and therefore predominantly medial joint space narrowing, this may account for the lack of association with lateral meniscal extrusion, even under load bearing.

Similarly, no association was found between lateral contact area and either KL grade or meniscal intra-substance integrity. However, medial contact area was correlated with meniscal intra-substance integrity. It would be expected that contact area and meniscal extrusion would be related, such that a decrease in contact area would result from an increase in meniscal extrusion [5,17]. This was clearly seen in the medial compartment in cases with meniscal tears (KL 3 and 4). In addition, cases without a meniscal tear (KL 1 and 2), which exhibited slight decreases in meniscal extrusion indicated slight increases in contact area.

However, medial meniscal intra-substance integrity had no association with medial anterior displacement. The reduction in medial anterior displacement, seen as KL grade increased, may be attributed to wear of the cartilage leading to further dishing of the tibial surface, and therefore greater conformity between the femur and tibia. In contrast, lateral posterior displacement was found to be correlated with both KL grade and meniscal intra-substance integrity. This is consistent with Scarvell et al. who suggested that OA severity had a greater effect on motion in the lateral compartment than the medial compartment [27]. They found that during a leg press activity, osteoarthritic knees exhibited a decrease in lateral mobility such that the knee achieved flexion through an increase in AP translation and a decrease in axial rotation [27]. This is consistent with our study, which indicated that in symptomatic knees, the femur exhibited an increase in posterior translation on the tibia secondary to the axial rotation.

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As mentioned throughout this paper, there are several limitations of this study that should be acknowledged. The small sample size of this study, particularly only one patient with a KL 4, can lead to type II (false negative) statistical error. However, this would suggest that the significant findings of our study are still valid, although greater significance may have been noted if more patients were included. In addition, all patients in this study had primary medial OA. Had patients with primary lateral OA been included, the location of meniscal degeneration may have varied thereby altering the conclusions for this group of patients. Lastly, there was a high incidence of meniscal tears particularly for those with severe OA, which may have impacted the results of this study.

In conclusion, T2* relaxation times, as a measure of meniscal intra-substance integrity, were found to increase as OA severity increased. In the lateral compartment, meniscal intra-substance integrity was correlated with AP displacement but not with meniscal extrusion or with contact area. In contrast, medial meniscus T2* relaxation time was correlated with increased meniscal extrusion and a decrease in contact area, although no correlation was found with AP displacement. Such a decrease in contact area can result in an increase in contact pressure which can lead to cartilage degeneration. However, these changes in medial meniscal extrusion and medial contact area were most noticeable in cases with meniscal tears (KL 3 and 4). In cases where no meniscal tears were present (KL 1 and 2), meniscal extrusion and contact area were not dramatically different than the KL 0 knees. This suggests that a loss of meniscal integrity, in the form of intra-substance degeneration, may not by itself influence risk factors for cartilage degeneration. Rather, intra-substance meniscal degeneration and cartilage degeneration may occur in parallel, whereas meniscal tears may be required for cartilage degeneration to reach a greater severity. However, further research is needed to verify this hypothesis.

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References


Fig. 7. The displacement of the femur relative to the tibia following the application of the torque was determined in Rapidform XOV using the global coordinate system and represented by a color map. In the control knees (right column), relative to the tibia, the femur underwent an external rotation, such that the medial condyle displaced anteriorly and the lateral condyle displaced posteriorly. In the symptomatic knees (left column) the femur typically achieved this external rotation with a greater lateral posterior displacement.

Fig. 8. Average displacement (mm) of the femur with respect to the tibia in the medial anterior and lateral posterior directions, per KL grade. Displacement measured in millimeters (mm). Error bars represent the standard deviation.