Relationship between alignment and cartilage thickness in patients with non-traumatic and post-traumatic knee osteoarthritis

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Running Head: Cartilage thickness between OA subtypes

Robbins SM, Abram F, Boily M, Pelletier JP, Martel-Pelletier J (2019). Relationship between alignment and cartilage thickness in patients with non-traumatic and post-traumatic knee osteoarthritis. Osteoarthritis and Cartilage, 27(4), 630-637. doi: 10.1016/j.joca.2019.01.002.

Abstract

Objective: To compare cartilage thickness between patients with non-traumatic and post-traumatic knee osteoarthritis (OA) and healthy controls and to determine if disease severity and alignment impact these differences. **Design:** Participants with non-traumatic (n=22) and post-traumatic (n=19) knee OA, and healthy controls (n=22) were recruited for this cross-sectional study. Participants underwent 3T magnetic resonance imaging (T1-weighted, 3D sagittal gradient echo sequence) and cartilage thickness was determined in four regions: medial and lateral condyle, and medial and lateral plateau. Lower extremity alignment (mechanical axis angle) and disease severity (Kellgren-Lawrence scores) were measured from full length radiographs. Statistical analysis included one-way analysis of variance and modified Bonferroni test adjusting for multiple pairwise comparisons. Linear regression analyses examined the relationship between cartilage thickness and knee OA group after controlling for disease severity, meniscal status, and alignment. **Results**: In participants with predominantly medial compartment knee OA, compared to healthy controls, those with non-traumatic knee OA had diminished cartilage thickness in the medial plateau ($p=0.035$) and those with post-traumatic knee OA had greater cartilage thickness in the lateral condyle ($p=0.044$). In the lateral condyle, data revealed that alignment accounted for the variance in cartilage thickness ($p=0.035$), in which a stronger relationship was found in the non-traumatic ($r=-0.61$) than the post-traumatic ($r=-0.12$) OA group. **Conclusions:** Emerging data demonstrated that participants with non-traumatic knee OA have a stronger relationship between alignment and cartilage thickness than those with post-traumatic knee OA. This indicates that factors involved in knee OA initiation and progression may differ between these OA subtypes. **Key Words:** knee osteoarthritis; magnetic resonance imaging; cartilage thickness; anterior cruciate ligament

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Introduction

Knee osteoarthritis (OA) can be classified as non-traumatic in patients having no history of knee trauma; or post-traumatic in patients who sustained a traumatic knee injury and subsequently developed knee OA. For instance, knee OA has been found in 41% of patients that sustained an anterior cruciate ligament (ACL) rupture 10 to 15 years after the initial trauma[1]. The factors that contribute to knee OA initiation might differ between these knee OA subtypes which could further impact disease progression. As evidence, radiographs indicate that OA changes (e.g. joint space narrowing) are more prevalent in the medial compartment in patients with non-traumatic knee OA, while these changes are more equally distributed between medial and lateral compartments in patients with post-traumatic knee OA[2].

Differences in OA related structural damage have been demonstrated on magnetic resonance imaging (MRI). Although results are not consistent, there is indication that the distribution of structural changes between medial and lateral compartments varies between non-traumatic and post-traumatic knee OA. Stein et al.[3] showed that normalized cartilage volume was not different in any knee region between patients with knee OA that had an intact or ruptured ACL. However, there were more frequent lateral compartment meniscal derangements and bone marrow lesions in patients with combined knee OA and ACL rupture. Johnson et al.[4] demonstrated a predisposition to medial tibiofemoral articular damage in patients with knee OA with either an intact or ruptured ACL; patients with an ACL rupture did demonstrate more frequent cartilage loss in some tibial (e.g. medial and lateral posterior) and femoral (e.g. medial posterior) regions. Finally, Amin et al.[5] showed that patients with knee OA and an ACL rupture

had increased risk of medial compartment cartilage loss over 30 months compared to patients with knee OA and an intact ACL, but not in the lateral compartment. However, statistical models were not significant once the presence of medial meniscal tears were accounted.

Potential differences in OA related structural damage in patients with post-traumatic knee OA might be due to damage sustained during the initial trauma. Following ACL disruption due to trauma, there are more frequent indicators of lateral, rather than medial, joint damage including bone marrow lesions, meniscal tears, and cortical depression fractures[6]. It is unclear if such changes will impact the distribution of structural damage once these patients develop OA. Other important factors, including disease severity and lower extremity alignment, might mediate the relationship between cartilage health and traumatic history. These factors have not been previously considered in comparisons of non-traumatic and post-traumatic knee OA. Also, the two studies[3,4] that compared cartilage morphology between OA subtypes using MRI analyzed existing databases and it was not clear if ACL ruptures occurred due to trauma or were a result of non-traumatic OA related degeneration.

The objective was to compare tibiofemoral cartilage thickness between patients with non-traumatic and post-traumatic knee OA and healthy controls, and to determine whether disease severity, meniscal status, and alignment impact these potential differences. We hypothesized that post-traumatic knee OA would be associated with diminished lateral compartment cartilage thickness and non-traumatic knee OA with diminished medial compartment cartilage thickness. Additionally, this relationship would be mediated by lower extremity alignment, meniscal status, and disease severity.

Methods

Participant Selection

Participants between 40 and 75 years of age diagnosed with knee OA according to the American College of Rheumatology clinical criteria[7] were recruited for this cross-sectional study. These clinical criteria include knee pain and at least 3 of 6 following criteria: age greater than 50 years, stiffness less than 30 minutes, crepitus, boney tenderness, body enlargement, and no palpable warmth[7]. They were recruited from hospitals and the community in Montreal, Quebec, Canada between May 2015 to January 2017. Exclusion criteria included previous joint replacement, scheduled for knee replacement, lower extremity trauma or surgery within one year, knee injection within three months, inflammatory arthritis, or contraindication to MRI (e.g. pacemaker, metal in or around the eye).

Participants that had no self-reported history of knee trauma were classified as non-traumatic knee OA. Seventy potential participants with non-traumatic knee OA were screened. After excluding participants that did not meet study criteria (n=48), 22 participants (16 women) remained in the non-traumatic OA group. Participants that self-reported a history of traumatic ACL rupture, which was confirmed by MRI, were classified as post-traumatic knee OA. Initially, 32 potential participants were recruited for the post-traumatic OA group and 13 participants did not meet the study criteria resulting in 19 participants (8 women) in this group. This included five participants with a partial ACL rupture, four participants with a complete ACL rupture, and

ten participants with an ACL reconstruction. Participants self-reported the time from initial ACL injury and the mean time was 24 years (standard deviation 12 years). For participants with bilateral knee OA, the most symptomatic knee was chosen based on the participant's self-assessment of the knee that had the greatest pain intensity over the last month.

In addition, a healthy group was recruited from the community in Montreal, Quebec, Canada to provide normative data. Additional exclusion criteria for the healthy group included history of lower extremity OA and knee trauma. Initially, 39 potential participants were recruited for the healthy group and 17 participants did not meet the study criteria resulting in 22 participants (16 women) in the healthy group. The study limb was randomly selected for healthy participants. All participants from an ongoing longitudinal study (unpublished) were enrolled in the present study. The sample size calculation was based on this longitudinal study. Thus, an a priori sample size calculation was not performed for the current analyses and all available participants from the longitudinal study were included in the present analyses.

The procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (Jewish General Hospital) and with the Helsinki Declaration of 1975, as revised in 2000. All participants provided written informed consent prior to study enrollment.

Radiographs

Participants in the non-traumatic and post-traumatic OA groups underwent bilateral, full length (hip to ankle) anterior-posterior radiographs to provide a measure of lower extremity alignment. Participants were required to stand barefoot, with the feet and toes facing forward, and patellae centered on the femoral condyles[8]. The mechanical axis angle (MAA) was determined as the angle between two lines: 1) line from the femoral head center to the knee center, and 2) line from the knee center to the ankle center. Femoral head center was identified from the center of a circle that was fit to the femoral head; knee center was the midpoint between the bases of the tibial spines; and ankle center was on the distal tibia at a point that bisects the talar dome[8]. Varus alignment was indicated by negative MAA values, valgus alignment by positive MAA values, and neutral alignment by a value of 0 degrees. Measurements were performed on ImageJ software (National Institutes of Health).

Kellgren-Lawrence (KL) radiographic disease severity scores were used to quantify the severity of radiographic changes and were measured from the anterior-posterior radiographs. The KL scoring system uses a five point scale (0=no OA, 1=doubtful, 2=mild, 3=moderate, 4=severe)[9]. Separate scores were provided for the medial and lateral knee compartments.

Magnetic Resonance Imaging

MRI was performed with a high-resolution, 3-dimensional, 3.0T MRI system (GE Discovery MR750) with an eight-channel knee coil, and the sequence acquisition was a T1-weighted, 3D sagittal gradient echo sequence with fat suppression (slice thickness 1.5 mm,

repetition time 42 ms, echo time 7 ms, flip angle 20 degrees)[10]. The approximate scan time for this sequence was 9 minutes and the field of view was 160 mm.

Cartilage thickness was determined using automatic knee cartilage segmentation (Figure 1) which has been previously described and validated[11]. Briefly, femur and tibia 3D images allowed the identification of the bone-cartilage interface and the cartilage-soft tissue interface[11]. Cartilage thickness was the Euclidean distance between bone-cartilage and cartilage-soft tissue interfaces at each sample[11,12]. Cartilage thickness was averaged over an entire region for four separate regions: 1) medial condyle, 2) lateral condyle, 3) medial plateau, and 4) lateral plateau. In addition, exploratory analyses examined sub-regions including the central and posterior aspects of the medial and lateral condyles, and the central and peripheral aspects of the medial and lateral plateaus. A previous study with a different sample demonstrated that this procedure has demonstrated low measurement error between repeated images (0.14 to 1.20%) and good agreement with semi-automated methods ($r \geq 0.76$; $p \leq 0.016$)[11].

The presence of an ACL rupture and/or reconstruction was confirmed on MRI by a fellowship trained, musculoskeletal radiologist with 8 years of MRI experience (MB); ensuring that participants in the post-traumatic OA group had evidence of an ACL rupture or a reconstructed ACL. The ACL rupture could be partial or a complete tear (i.e. no continuous fibers) and the ACL was considered as one bundle.

The status of the menisci were graded using the Whole-Organ Magnetic Resonance Imaging Score (WORMS)[13]. Three regions (anterior horn, body, posterior horn) were examined

and a cumulative grade (0 to 6, with higher scores indicating greater involvement) was determined for each meniscus as previously described[13].

<<<insert Figure 1>>>

Statistical Analysis

Participant characteristics and MAA were compared between groups using a one-way analysis of variance (ANOVA). WORMS meniscal scores were compared using a Kruskal-Wallis Test and pairwise comparisons were made between groups with Mann-Whitney U tests, adjusted using a modified Bonferroni's test. One-way ANOVA examined uncontrolled differences in cartilage thickness in knee regions and sub-regions between OA groups and healthy controls. Modified Bonferroni's test was used to adjust for multiple pairwise comparisons. Moreover, since we hypothesized that participants with medial versus lateral compartment knee OA would have differences in cartilage thickness between compartments, the ANOVA was repeated with only OA participants that had predominantly medial compartment knee OA and healthy controls. Medial compartment knee OA was defined as KL score in the medial compartment greater than or equal to KL score in the lateral compartment. This resulted in six participants with lateral compartment knee OA being excluded from the non-traumatic OA group, while no participants were excluded from the post-traumatic group for this analysis.

Hypothesis-driven, forward linear regression analyses examined the relationship between cartilage thickness and OA group (non-traumatic, post-traumatic) after controlling for disease

severity, meniscal status, and alignment for all participants with knee OA. The dependent variable was cartilage thickness for a region and separate models were conducted for each region. KL score, meniscal status, MAA, and OA group (0=non-traumatic OA group, 1=post-traumatic OA group) were entered into the analysis and potential interactions between MAA and OA group were entered in the final step. Interactions were only maintained in the final model if they significantly increased the explained variance. The highest KL score from the medial or lateral compartment was entered as KL score. Meniscal status was entered for the compartment of interest (e.g. medial meniscus for medial plateau) and the score was dichotomized (0=no tear, 1=tear). The unstandardized regression coefficients with 95% confidence intervals and associated significance levels from the t-statistic were examined. Explained variance and its significance from the F-ratio of the final models were also reported. Diagnostics statistics were examined to verify statistical assumptions including normality, linearity, homoscedasticity, and collinearity. Statistical analysis was performed using SPSS version 20.0 (IBM).

Results

Table 1 provides participant characteristics for each group. There were no significant differences in participant characteristics (e.g. age) between groups for the entire sample (Table 1). However, when only participants with predominantly medial compartment knee OA were considered, the non-traumatic OA group had significantly higher body mass index than the post-traumatic OA group ($p=0.030$; modified Bonferroni) (Table 2). There were significant differences in meniscal scores (Table 1) and both OA groups had higher mean rank medial and lateral meniscal scores than the healthy group ($p \leq 0.025$; modified Bonferroni). The post-

traumatic OA group also had significantly higher mean rank medial meniscal scores than the non-traumatic OA group (p=0.019; modified Bonferroni). The assumptions for all analyses were met and analyses were deemed appropriate.

<<<insert Table 1>>>

<<<insert Table 2>>>

Uncontrolled Analysis - One-way Analysis of Variance (ANOVA)

There were no significant differences in cartilage thickness between groups in any region (Table 1) or sub-region (Table 3). A post-hoc effect size analysis revealed nil to small effect sizes (f=0.01 to 0.09) for the ANOVA F-tests[14].

In participants with predominantly medial compartment knee OA (Table 2), a significant difference was found in the lateral condyle (p=0.044) and medial plateau (p=0.035) cartilage thickness. For the lateral condyle, participants with post-traumatic OA had significantly increased cartilage thickness compared to the healthy group (p=0.030; modified Bonferroni; mean difference=0.20 mm, 95% confidence interval=0.03, 0.36). For the medial plateau, participants with non-traumatic OA had significantly lower cartilage thickness than both healthy controls (p=0.030; modified Bonferroni; mean difference=0.17 mm, 95% confidence interval=0.03, 0.31) and participants with post-traumatic OA (p=0.036; modified Bonferroni; mean difference=0.17 mm, 95% confidence interval=0.02, 0.32). A post-hoc analysis revealed

small effect sizes for ANOVA F-tests for both the lateral condyle (f=0.12) and medial plateau (f=0.13) regions. Similar to the main knee regions, there were significant differences in cartilage thickness in some knee sub-regions (Table 4) in participants with predominantly medial compartment knee OA including the lateral condyle central sub-region (p=0.047) and medial plateau central sub-region (p=0.041). Participants with post-traumatic OA had significantly greater cartilage thickness in the lateral condyle central sub-region compared to the healthy group (p=0.029; modified Bonferroni). For the medial plateau central sub-region, participants with non-traumatic OA had significantly lower cartilage thickness than the healthy controls (p=0.024; modified Bonferroni).

<<<insert Table 3>>>

<<<insert Table 4>>>

Controlled Analysis – Regression (Table 5)

For medial condyle cartilage thickness, KL score (p=0.033) and MAA (p=0.002) significantly contributed to the model while OA group was not statistically significant. Lower KL scores and greater varus alignment (negative MAA values) were associated with lower medial condyle cartilage thickness. As the MAA-OA group interaction did not reach statistical significance, this interaction was not included in the final model. The final model accounted for 33% of the explained variance in medial condyle cartilage thickness (p=0.006).

For lateral condyle cartilage thickness, MAA (p=0.009) significantly contributed to the model while OA group was not statistically significant. However, in contrast to the medial condyle, the MAA-OA group interaction was statistically significant (p=0.035) and was retained in the final model. This interaction (Figure 2) indicated that higher MAA values (i.e. positive is valgus alignment, negative is varus alignment) was associated with decreased lateral condyle thickness in the non-traumatic OA group (r=-0.61) while there was no relationship between these variables in the post-traumatic OA group (r=0.12). The final model accounted for 29% of the explained variance in lateral condyle cartilage thickness (p=0.031).

In the medial plateau, only MAA (p=0.048) significantly contributed to the model while OA group was not statistically significant. Greater varus alignment (negative MAA) was associated with decreased medial plateau cartilage thickness. As with the medial condyle, the MAA-OA group interaction was not significant. The final model accounted for 12% of the explained variance in medial plateau cartilage thickness which was not statistically significant (p=0.282).

For lateral plateau cartilage thickness, only MAA (p=0.005) significantly contributed to the model. Greater valgus alignment (positive MAA) was associated with decreased lateral plateau cartilage thickness. The MAA-OA group interaction was also not significant. The final model accounted for 24% of the explained variance in lateral plateau cartilage thickness (p=0.041).

<<<insert Table 5>>>

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Discussion

Although the type of knee OA impacts the relationship between MAA and cartilage thickness, in contrast with our hypothesis, there were only a few differences in cartilage thickness between patients with non-traumatic and post-traumatic knee OA. In participants with predominantly medial compartment knee OA, differences in cartilage thickness in knee regions and sub-regions between OA groups and healthy controls were seen; although the observed effect sizes were small. When analyses were controlled, an interaction between alignment and knee OA group accounted for a significant amount of variance in lateral condyle cartilage thickness. Thus, the relationship between alignment and cartilage thickness varies between non-traumatic and post-traumatic knee OA, which could indicate that different factors are involved in disease initiation and progression between these OA subtypes.

Comparisons of cartilage thickness demonstrated differences only for participants with medial compartment knee OA. Removing participants with lateral knee OA decreased the heterogeneity within the non-traumatic OA group, and allowed the detection of between-group differences. Lower medial plateau cartilage thickness, especially in the central sub-region, in participants with non-traumatic OA compared to healthy controls was not surprising, and is supported by previous researh[15]. There was lower medial plateau cartilage thickness in participants with non-traumatic compared to post-traumatic knee OA. This finding was inconsistent with previous studies[3,4], although differences did not remain in controlled analyses.

The greater cartilage thickness in the lateral condyle, especially in the central sub-region, in participants with post-traumatic OA compared to healthy controls is likely due to the majority of participants in the post-traumatic OA group (17 out of 19) had none-to-mild OA severity scores in the lateral compartment. Cartilage swelling occurs in early knee OA, which potentially increases cartilage thickness[16]. Thus, the disease stage might account for this finding.

Comparisons between non-traumatic and post-traumatic OA groups that controlled for other disease factors demonstrated no significant differences in cartilage thickness. However, varus and valgus alignment were associated with decreased medial and lateral compartment cartilage thickness respectively. These findings agree with previous longitudinal studies[17,18]. Furthermore, current analyses accounted for 12 to 33% of the variance in cartilage thickness. There is a substantial amount of unexplained variance; although, these values are similar to another study (R^2=14 to 22%) that investigated the association of body mass index and knee alignment with cartilage thickness loss over 2 years in patients with knee OA[15]. In addition, the interaction between OA group and MAA significantly explained the variance in lateral condyle cartilage thickness. The relationship between MAA and lateral condyle cartilage thickness was stronger in the non-traumatic than the post-traumatic OA group. Thus, the impact of alignment on knee OA progression might play a lesser role in participants with knee OA that have a history of ACL rupture, although longitudinal research is required to test this hypothesis.

The study has limitations. Both participants with a ruptured ACL and those with a surgically reconstructed ACL were included to increase sample size. This is not truly a weakness as ACL reconstructive surgery does not decrease knee OA prevalence or fully restore normal

joint motion[19,20]. Additional factors could have been used as control variables. For instance, body mass index was different between OA groups when only participants with medial compartment knee OA were considered. However, considering the sample size, having additional variables would have decreased the statistical power. Although the sample size was limited, increasing the number of participants would unlikely substantially change ANOVA results given the nil to small effect sizes observed. Radiographs were not taken of the healthy controls in order to save costs since the study budget was limited. Patellofemoral cartilage thickness was not measured and should be investigated in future studies. Finally, OA participants generally had mild to moderate knee OA severity. Results are not generalizable to patients with severe knee OA or if different traumatic injuries are examined (e.g. meniscal tear in isolation).

In conclusion, of the participants with predominantly medial compartment knee OA, those with non-traumatic knee OA had diminished medial plateau cartilage thickness compared to participants with post-traumatic knee OA and healthy controls in uncontrolled analyses. Participant with post-traumatic knee OA had greater cartilage thickness in the lateral condyle than healthy controls. Although there were no differences in cartilage thickness between non-traumatic and post-traumatic OA groups in controlled analyses, the interaction between MAA and OA group explained the variance in lateral condyle cartilage thickness. Hence, the relationship between cartilage thickness in this region and MAA was stronger in the non-traumatic OA group. Thus, this study demonstrated no differences in cartilage thickness between non-traumatic and post-traumatic knee OA subtypes, although this classification can impact the relationship between alignment and cartilage thickness.

Acknowledgements

The authors would like to thank Larissa Fedorowich, Mohan Patel, and Antonys Melek for assistance with data collection. Drs. John Antoniou (Jewish General Hospital), Moreno Morelli (St. Mary's Hospital), and Paul Martineau (Montreal General Hospital) from Montreal, Canada assisted with participant recruitment.

Author Contributions

Shawn Robbins was responsible for obtaining funding, conception and design, data acquisition, data analysis and interpretation, and drafting the article. François Abram was responsible for setting the MRI sequences, data processing, and article revision. Mathieu Boily was responsible for interpreting MRI images and article revision. Jean-Pierre Pelletier was responsible for study design, data processing and interpretation, and article revision. Johanne Martel-Pelletier was responsible for study design, data processing and interpretation, and drafting the article. All authors approved the final version. Shawn Robbins (shawn.robbins@mcgill.ca) takes responsibility for the integrity of the work as a whole, from the inception to finished article.

Declaration and Role of the Funding Source

This work was supported by the Canadian Foundation for Innovation which provided funding for the infrastructure [Robbins, grant #31903], the Canadian Institutes of Health

Research [grant number ONM 137376], and the Arthritis Society [grant number YIO-14-096]. Shawn Robbins is supported by the Arthritis Society [grant number YIS-14-065] and the Fonds de recherche du Québec – Santé [grant number 33107]. The funding sources had no role in this research.

Competing Interest Statement

Jean-Pierre Pelletier and Johanne Martel-Pelletier are shareholders in ArthroLab Inc. François Abram is an employee of ArthroLab Inc. This company was responsible for processing the MRI images. Shawn Robbins and Mathieu Boily have no conflicts of interest to report.

Data Statement

Data are confidential and are not available through an online database.

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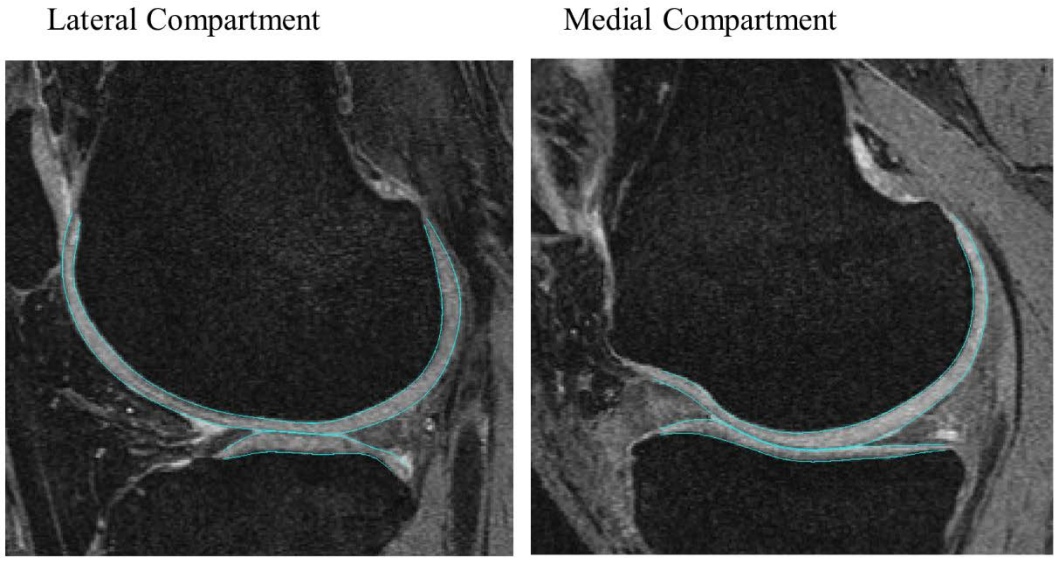

Figure 1. An example of cartilage segmentation for the lateral and medial knee compartment.

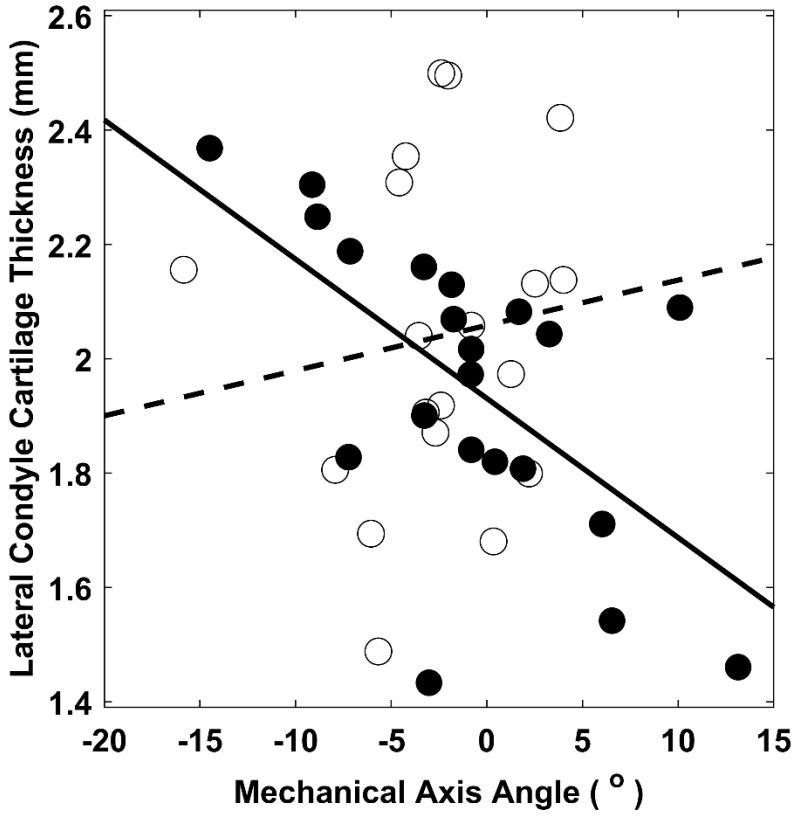

Figure 2. The relationship between lateral condyle cartilage thickness and mechanical axis angle for non-traumatic (filled dots) and post-traumatic (unfilled dots) knee osteoarthritis groups. The best fit lines are shown for the non-traumatic (solid line, r=-0.61) and post-traumatic (dashed line; r=0.12) knee osteoarthritis groups.

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Table 1: Participant characteristics and descriptive statistics for the study variables in the entire sample.

Variables		Healthy Controls (n=22)	Non-traumatic* OA (n=22)	Post-traumatic OA (n=19)	p value†
	Age, years	59 (7)	60 (7)	56 (9)	0.354
	Female, % (n)	73% (16)	73% (16)	42% (8)	-
	Body mass index, kg/m^2	27.0 (4.6)	29.63 (7.5)	26.0 (3.2)	0.093
	MAA*, degrees	-	-0.93 (6.59)	-2.48 (4.68)	0.398
WORMS	Medial Meniscus (/6)	1 (2)	2 (2)	4 (2)	<0.001
	Lateral Meniscus (/6)	0 (0)	2 (3)	2 (2)	<0.001
Cartilage Thickness Regions, mm	Medial Condyle	1.87 (0.17)	1.93 (0.31)	1.95 (0.23)	0.573
	Lateral Condyle	1.84 (0.24)	1.93 (0.27)	2.04 (0.29)	0.069
	Medial Plateau	1.90 (0.16)	1.85 (0.36)	1.90 (0.17)	0.760
	Lateral Plateau	2.34 (0.22)	2.25 (0.42)	2.39 (0.40)	0.462

			Compartment			
	Score		Medial	Lateral	Medial	Lateral
			Frequency			
KL score, frequency	0	-	0	9	0	7
	1	-	2	2	1	3
	2	-	12	4	11	7
	3	-	4	4	5	1
	4	-	3	2	2	1

Results are shown as mean (standard deviation) unless otherwise indicated.

Robbins SM, Abram F, Boily M, Pelletier JP, Martel-Pelletier J (2019). Relationship between alignment and cartilage thickness in patients with non-traumatic and post-traumatic knee osteoarthritis. Osteoarthritis and Cartilage, 27(4), 630-637. doi: 10.1016/j.joca.2019.01.002.

OA, osteoarthritis; n, number of patients; MAA, mechanical axis angle (varus alignment is negative); WORMS, Whole-Organ Magnetic Resonance Imaging Score; KL, Kellgren-Lawrence radiographic disease severity score.
*One participant from the non-traumatic OA group was missing MAA and KL scores.
†Statistical determination performed by analysis of variance.

Robbins SM, Abram F, Boily M, Pelletier JP, Martel-Pelletier J (2019). Relationship between alignment and cartilage thickness in patients with non-traumatic and post-traumatic knee osteoarthritis. Osteoarthritis and Cartilage, 27(4), 630-637. doi: 10.1016/j.joca.2019.01.002.

Table 2: Participant characteristics and descriptive statistics for the study variables in participants with predominantly medial compartment knee osteoarthritis and healthy controls.

Variables		Healthy Controls (n=22)	Non-traumatic* OA (n=16)	Post-traumatic OA (n=19)	p value†
	Age, years	59 (7)	59 (7)	56 (9)	0.511
	Female, % (n)	73% (16)	75% (12)	42% (8)	-
	Body mass index, kg/m^2	27.0 (4.6)	30.9 (8.0)	26.0 (3.2)	0.025
	MAA*, degrees	-	-3.66 (4.85)	-2.48 (4.68)	0.481
WORMS	Medial Meniscus (/6)	1 (2)	2 (2)	4 (2)	<0.001
	Lateral Meniscus (/6)	0 (0)	1 (1)	2 (2)	<0.001
Cartilage Thickness Regions, mm	Medial Condyle	1.87 (0.17)	1.82 (0.27)	1.95 (0.23)	0.218
	Lateral Condyle	1.84 (0.24)	2.00 (0.26)	2.04 (0.29)	0.044
	Medial Plateau	1.90 (0.16)	1.73 (0.31)	1.90 (0.17)	0.035
	Lateral Plateau	2.34 (0.22)	2.41 (0.24)	2.39 (0.40)	0.740

			Compartment			
	Score		Medial	Lateral	Medial	Lateral
			Frequency			
KL score, frequency	0	-	0	9	0	7
	1	-	2	2	1	3
	2	-	6	4	11	7
	3	-	4	0	5	1
	4	-	3	0	2	1

Results are shown as mean (standard deviation) unless otherwise indicated.

OA, osteoarthritis; n, number of patients; MAA, mechanical axis angle (varus alignment is negative); WORMS, Whole-Organ Magnetic Resonance Imaging Score; KL, Kellgren-Lawrence radiographic disease severity score.
*One participant from the non-traumatic OA group was missing MAA and KL scores.
†Statistical determination performed by analysis of variance.

Table 3: Cartilage thickness in the sub-regions for the entire sample.

Cartilage Thickness Sub-region (mm)	Healthy Controls (n=22)	Non-traumatic OA (n=22)	Post-traumatic OA (n=19)	p value*
Medial Condyle- Central	1.78 (0.19)	1.80 (0.29)	1.85 (0.23)	0.596
Medial Condyle- Posterior	2.03 (0.18)	2.12 (0.45)	2.12 (0.29)	0.575
Lateral Condyle- Central	1.78 (0.24)	1.88 (0.25)	1.98 (0.30)	0.059
Lateral Condyle- Posterior	1.94 (0.27)	2.03 (0.43)	2.15 (0.30)	0.146
Medial Plateau- Central	2.03 (0.22)	1.96 (0.37)	2.00 (0.17)	0.672
Medial Plateau- Peripheral	1.81 (0.16)	1.77 (0.36)	1.82 (0.22)	0.761
Lateral Plateau- Central	2.62 (0.27)	2.42 (0.49)	2.47 (0.53)	0.295
Lateral Plateau- Peripheral	2.13 (0.21)	2.13 (0.39)	2.33 (0.36)	0.102

Results are shown as mean (standard deviation).
OA, osteoarthritis; n, number of patients.
*Statistical determination performed by analysis of variance.

Robbins SM, Abram F, Boily M, Pelletier JP, Martel-Pelletier J (2019). Relationship between alignment and cartilage thickness in patients with non-traumatic and post-traumatic knee osteoarthritis. Osteoarthritis and Cartilage, 27(4), 630-637. doi: 10.1016/j.joca.2019.01.002.

Table 4: Cartilage thickness in the sub-regions in participants with predominantly medial compartment knee osteoarthritis and healthy controls.

Cartilage Thickness Sub-region (mm)	Healthy Controls (n=22)	Non-traumatic OA (n=16)	Post-traumatic OA (n=19)	p value*
Medial Condyle- Central	1.78 (0.19)	1.69 (0.26)	1.85 (0.23)	0.122
Medial Condyle- Posterior	2.03 (0.18)	1.99 (0.45)	2.12 (0.29)	0.413
Lateral Condyle- Central	1.78 (0.24)	1.93 (0.25)	1.98 (0.30)	0.047
Lateral Condyle- Posterior	1.94 (0.27)	2.12 (0.34)	2.15 (0.30)	0.056
Medial Plateau- Central	2.03 (0.22)	1.83 (0.33)	2.00 (0.17)	0.041
Medial Plateau- Peripheral	1.81 (0.16)	1.64 (0.32)	1.82 (0.22)	0.051
Lateral Plateau- Central	2.62 (0.27)	2.62 (0.28)	2.47 (0.53)	0.380
Lateral Plateau- Peripheral	2.13 (0.21)	2.26 (0.26)	2.33 (0.36)	0.084

Results are shown as mean (standard deviation).
OA, osteoarthritis; n, number of patients.
*Statistical determination performed by analysis of variance.

Robbins SM, Abram F, Boily M, Pelletier JP, Martel-Pelletier J (2019). Relationship between alignment and cartilage thickness in patients with non-traumatic and post-traumatic knee osteoarthritis. Osteoarthritis and Cartilage, 27(4), 630-637. doi: 10.1016/j.joca.2019.01.002.

Table 5. Coefficients for the regression analyses exploring the relationship between cartilage thickness and OA group while controlling for KL score, meniscal status, and MAA.

Cartilage Thickness Regions	KL score β (95% CI)	Meniscal Status* β (95% CI)	MAA β (95% CI)	OA Group* β (95% CI)	MAA-OA Group Interaction† β (95% CI)
Medial Condyle	0.12 (0.01, 0.23)	-0.03 (-0.27, 0.22)	0.02 (0.01, 0.04)	0.09 (-0.07, 0.24)	-
p value‡	*0.033*	*0.830*	*0.002*	*0.284*	-
Lateral Condyle	0.10 (-0.02, 0.21)	-0.01 (-0.21, 0.20)	-0.02 (-0.04, -0.01)	0.17 (-0.02, 0.35)	0.03 (0.00, 0.06)
p value‡	*0.094*	*0.954*	*0.009*	*0.074*	*0.035*
Medial Plateau	-0.03 (-0.17, 0.10)	0.08 (-0.21, 0.37)	0.02 (0.00, 0.03)	0.06 (-0.13, 0.24)	-
p value‡	*0.605*	*0.578*	*0.048*	*0.521*	-
Lateral Plateau	-0.08 (-0.25, 0.09)	0.01 (-0.30,0.32)	-0.03 (-0.06, -0.01)	0.04 (-0.21, 0.30)	-
p value‡	*0.356*	*0.955*	*0.005*	*0.729*	-

β, unstandardized regression coefficient; CI, confidence interval; OA, osteoarthritis; MAA, mechanical axis angle (varus alignment is negative); KL, Kellgren-Lawrence radiographic disease severity score.

*OA group was coded as 0=non-traumatic OA and 1=post-traumatic OA; meniscal status was coded as 0=no tear and 1=tear; one participant from the non-traumatic OA group was missing MAA and KL score.

†Interactions only remained in the final model if they were significant ($p<0.05$).

‡p values are from the t-statistic for the unstandardized regression coefficients.