Influence of High-Intensity Interval Running on Femoral Cartilage Deformation in Competitive Runners

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Abstract

Competitive compared with recreational runners have increased odds of having osteoarthritis and running-related injuries, which may be from engaging in different types of running. We compared femoral cartilage deformation in competitive runners following a continuous and high-intensity interval run and evaluated the association between running kinetics and cartilage deformation. Twenty-four competitive runners (11 females and 13 males) underwent ultrasound imaging of femoral cartilage before and after two running sessions that were one week apart in a counterbalanced order. Repeated measures 2 x 2 ANOVA revealed lateral femoral cartilage had greater deformation after interval compared to continuous running. Collapsed across conditions, medial femoral cartilage had similar deformation after running. Pearson correlation demonstrated no associations between cartilage deformation and vertical loading rate, peak ground reaction force, or impulse. Interval running may contribute to cartilage deformation through increased joint stress. Runners returning from patellofemoral pain should avoid high-intensity interval running to limit symptoms.

Keywords

Keywords: Running, Competitive Runners, Cartilage Thickness, Cartilage Deformation, Running Kinetics, Running Intensity, Interval Running, Patellofemoral Pain, Osteoarthritis, Joint Health

Summary for Lay Audience

Running is a popular form of exercise that may contribute to joint disease in competitive groups. Competitive runners train at fast speeds that can increase force placed on joints. A high amount of force and how fast that force acts on the limb may contribute to joint damage. Cartilage is part of the joint that covers the ends of bones to facilitate movement without restriction. Cartilage damage is present in osteoarthritis, which is a common degenerative joint disease. We examined the change in cartilage size after a fast interval run compared to a slow continuous run. We also examined if the change in cartilage size would relate to how fast force was applied to the body during running. Twenty-four competitive runners participated in this study. Participants had ultrasound images taken of the top of their knees from above the kneecap. These images happened before and after running on a treadmill. Participants were injury free and wore the same shoes for both visits a week apart. The fast interval running session was 10 x 400 meters with a 300-meter jog rest. The continuous running session was a continuous 7-kilometer run at a slower pace. After faster interval running, the outside part of knee cartilage was thinner than after the continuous slower run. The inside part of knee cartilage was similarly thinner after running between conditions. The middle section of knee cartilage was not different after running. No relationships were found between forces during running and the change in cartilage size. We concluded that fast interval running might increase stress to the outside of the joint and cause cartilage to briefly become thinner. This could be from participants bending their knees more which puts more stress on the outside of the knee and may happen in fast running. We recommend that runners who have pain on the front of their knee or behind their kneecap should avoid fast interval running to limit pain.

Co-Authorship Statement

A version of this Thesis is currently being prepared for publication in manuscript format. Ryan Evans is the lead author who assisted in developing the research question and protocol design along with leading the data collection and writing the report. Dr. Derek Pamukoff is the first co-author who led the research question development and protocol design. Dr. Pamukoff also assisted with data processing and revision of writing for the report. Harry Battersby is a co-author who assisted with data processing. Leah Williams is the final co-author who assisted with data collection sessions.

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Chapter 1

1 « Introduction »

Running is an accessible and popular form of physical activity.[1,2] Participation in running contributes to a lower risk of cardiovascular disease and more active lifestyle.[1,3] Despite numerous health benefits, 37 to 63% of runners suffer from a running related injury (RRI) annually.[4,5] The most common injury location is the knee joint which accounts for 24.3 to 42% of RRIs.[4,6] For example, the patellofemoral joint is commonly affected, and patellofemoral pain (PFP) may be associated with chronic degenerative diseases such as osteoarthritis (OA).[6,7] Osteoarthritis is a disease that contributes to physical disability in approximately 13% of Canadians over the age of 20.[8–11] The prevalence of knee OA in former athletes ranges from 16 to 95%, which may be partially attributed to previous injuries resulting from the high physical demands of sport participation.[12,13]

Running is also a competitive sport, which increases the cumulative amount of running and loading on the body, and may elevate the risk for RRIs and OA.[5,12,14–16] Most literature surrounding running and OA has focused on recreational runners, which has been described as running a minimum of 3 times per week totaling 16 kilometers or less.[17–19] However, this description does not provide an accurate representation of competitive runners who have a higher frequency/volume of running, engage in faster speeds, and are more likely to engage in different types of running (e.g. continuous and interval-based running).[14,15,20,21]

Biomechanical differences between competitive and recreational runners can influence knee joint loading and RRI history.[20] For instance, competitive runners run with less anterior pelvic tilt, greater knee flexion, and more perpendicular shank angles when striking the ground.[16,20] These biomechanical differences may also contribute to faster habitual running paces, which elevate joint stress. For instance, faster running contributes to a greater vertical loading rate (LR) and greater knee flexion, which are associated with greater patellofemoral contact force.[20,22–24] Furthermore, competitive runners have 3-7 times and 9.8% greater knee OA prevalence compared with non -athletes and recreational runners, respectively.[15,24]

Knee cartilage adaptations may be influenced by the biomechanical and behavioural characteristics of recreational and competitive runners. Competitive runners experience repetitive impacts and loading that differ depending on the type of running.[6,22,25–27] The majority of distance running occurs at lower intensities for prolonged periods of time and involves repetitive joint loading. However, a proportion of training may include running at high intensities for short durations but with higher levels of impact (i.e., interval running).[21,22,27]

The velocity of running influences the magnitude of joint loading and may contribute to RRIs and cartilage strain.[22,28] Strain rate refers to the deformation of cartilage over time in response to mechanical stress.[29,30] There is a positive linear relationship between faster running speed, patellofemoral joint stress (PFJS), and LRs among elite distance runners.[7,22,28,31,32] These applied loads contribute to an acute reduction in cartilage volume due to the porous and permeable extracellular matrix.[33–37] This allows water to exit and return to the tissue during periods of loading and unloading.[33–37] The influx of new fluids allows for nutrient exchange and facilitates cartilage maintenance.[33–37] However, more pressure is placed on cartilage following higher loading and strain rates, which may contribute to cell death, fissuring, and increased water content of the cartilage.[38] Additionally, repetitive high LRs during running are applied to the cartilage with little time to recover, which may induce acute damage to articular cartilage.[29,35,36,39,40]

High LR activities contribute to cartilage matrix damage in animal models due to their viscoelastic properties.[29,30] However, no studies to our knowledge have investigated the acute effect of high LR on cartilage in human models. Running at higher speeds and with faster LRs may contribute to greater acute cartilage deformation.[16,22,29,30,41]

Therefore, the purpose of this study was to investigate the influence of running type on acute femoral cartilage deformation in competitive runners. It was hypothesized that greater acute cartilage deformation would be present following high intensity interval running compared to continuous running. Finally, it was hypothesized that the magnitude of acute cartilage deformation would be associated with the vertical LR experienced during high intensity interval running.

Chapter 2

2 « Review of Literature »

There are health benefits from habitual running, but participation also increases risk for lower body musculoskeletal injuries that can limit participation.[1,2] Patellofemoral pain is common among runners and may contribute to OA.[6,7,25] This section provides an overview of running, different populations of runners, the relationship of running as a form of acute and chronic mechanical loading with cartilage remodeling, the unique role of LR, biomechanical factors that can contribute to PFP, and risk of OA.

2.1 « Running Prevalence and Running Related Injuries »

Running is a popular sport and physical activity that has high global participation.[1,42] In 2016, running was the 4th most popular sport amongst Canadians.[43] Running has few constraints to participation and is highly accessible compared with other forms of activity.[1,42] Furthermore, all age groups can participate in running at numerous ability levels from recreational joggers to elite athletes. Recently, participation in running has increased amongst adolescents and adults, which may be due to the Covid-19 pandemic.[44,45] Running contributes to a healthier lifestyle, weight management, and reduces risk of cardiovascular disease.[1] However, running has a high injury incidence rate and most runners have endured a RRI.[2,46] In a given year, between 19.4-79% of runners sustain a musculoskeletal injury from running.[46] These injuries may result in lost time from running, which may also contribute to decreased performance.[3,46,47] Anatomical, biomechanical, physiological, and behavioural characteristics vary across runners and may contribute to injury risk.[3,16,46,48] Injuries can be acute and chronic from a single action or repeated overuse, respectively. For example, overuse contributes to bone stress injuries and tendinopathies, which are common in runners due to repetitive loading.[3,49]

Additionally, 42% of RRIs encountered involve the knee joint and the most common injury cited is at the patellofemoral joint, known as PFP.[6] Patellofemoral pain is pain around or behind the area of the patella, and pain is elicited when the knee is flexed and in a weight-bearing position.[25] Patellofemoral pain is a common RRI that has detrimental effects on runners.[6,7] For instance, pain, altered mechanics, joint laxity, and muscular dysfunction contribute to an overall loss of joint function.[7] Moreover, PFP may contribute to future development of patellofemoral OA, which is a degenerative joint disease.[7]

2.2 « Knee Osteoarthritis in Athletic Populations and Runners »

Osteoarthritis is a disease that causes joint pain, inflammation, and stiffness.[10] Osteoarthritis contributes to physical disability and affected 13% of Canadians over the age of 20 between 2016 and 2017.[11] Osteoarthritis prevalence is increasing due to an aging population and rise in pre-disposing risk factors such as obesity.[8,50] It is estimated that ~303 million people in the world had OA in 2017.[9] Knee OA is the most common form of OA, and affects approximately 263 million people worldwide as of 2017.[9] Among Canadians, OA is the leading cause of long-term disability and is a financial burden on the healthcare system.[51,52] Predisposing factors like obesity, high impacts, and previous joint injury may contribute to knee OA.[8,10,12,13,29,53,54] For example, athletes undergo high amounts of chronic loading due to volume of training and type of physical activity.[12,24,55] Athletes also experience various joint injuries because of the high physical demands placed on their bodies over a competitive career, which may contribute to future diseases such as OA.[12,24,54,55] As a result, OA is more prevalent in athletic populations.[12] For instance, a 2012 study measured the prevalence of hip and knee OA in former elite Swedish male athletes compared to controls.[13] Former elite athletes were 2.5 times more likely to have had knee OA compared to the non-athlete controls.[13] Additionally, a systematic review found the prevalence of knee OA in former elite athletes across multiple sports ranged from 16% to 95%.[12] Conversely, occurrence rates of knee OA ranged from 10% to 20% in males over the age of 35 in the general population.[12]

Runners have been heavily investigated with regards to OA due to their consistent exposure to weight-bearing exercise. However, there is discrepancy in literature, and it is unclear if there is an association between running and OA. Running has large repetitive joint impacts and peak knee joint loads are three times higher than during walking.[56] However, most literature suggests that running has favourable effects on knee OA incidence and cartilage outcomes.[33,56] A recent survey conducted in 2017 reported high rates of uncertainty on running and the risk it plays in developing knee OA among the public and health care practitioners.[51] Many studies report that running is not associated with OA, and does not increase the risk of incidence or progression.[33,55,57,58] Some researchers suggest that running could be a treatment option to reduce severity of OA symptoms.[15,39,59] For example, a prospective study done by Chakravarty et al., found no signs of accelerated risk factors of OA from running over two decades in healthy older age long-distance runners radiograph imaging compared to healthy non-runners.[58] However, it is important to note that this study examined total amount of time spent on all vigorous forms of exercise and not exclusively from running.[58]

A systematic review of 43 studies by Khan et al., concluded that immediate changes to cartilage composition and morphology occurred following running but do not persist, and that repeated exposure results in biochemical adaptations that may protect cartilage from damage.[33] As such, a link to OA from running is not supported. However, the authors noted that most of the included studies focused on recreational runners and suggest that other runners may have different outcomes. For example, a study focusing on former elite female athletes including middle distance and long-distance runners reported that running had a detrimental effect on OA development due to its associations with radiological changes of osteophytes and joint space narrowing.[60]

A systematic review from Driban et al., 2017 reported that athletes including elite long distance runners have 3 to 7 times higher prevalence of knee OA than non-exposed counterparts, suggesting that former competitive runners could have a different risk than recreational runners.[24] Finally, a systematic review investigated the prevalence of hip and knee OA in recreational and competitive runners.[15] The authors found that recreational runners had lower prevalence (3.5%) of hip and/or knee OA compared with competitive (13.3%) runners and controls (10.23%).[15] It is possible that discrepancies in the literature on the association between running and OA could be due to the population and ability levels of the runners being investigated.

2.3 « Cartilage Biology and Osteoarthritis Disease Process »

Articular cartilage is a connective tissue that lines synovial joint surfaces of bones to provide low friction within the joint.[61,62] Cartilage is comprised of a solid matrix that is formed from collagen, proteoglycan molecules, and interstitial water.[62,63] The primary collagen of articular cartilage is type II collagen and provides tensile strength for the matrix.[61,62] Proteoglycans are proteins that provide compressive strength and maintain the fluid balance within the matrix.[61,62,64] Water comprises the majority of the cartilage matrix, which allows for deformation that is dependent on the applied load while also contributing to nutrition and lubrication.[61,63] Articular cartilage is avascular and does not receive nutrients through blood supply.[61,63,64] Chondrocytes, which produce the proteoglycans in the matrix, rely on diffusion of water through the matrix to receive nutrition.[61,64] Cartilage has a relatively small permeability but relies on normal physiological loading to receive its nutrients.[61,62,64] Low permeability of cartilage does not allow for interstitial water to escape easily during loading and causes the matrix to become optimally pressurized to the load applied, and act as a protective mechanism working against mechanical failure from excessive strain.[62] This viscoelastic property of cartilage allows it to respond differently to loading at various speeds. For example, cartilage stiffens in response to high LRs and but has an elastic response to slow LRs.[62,65]

Osteoarthritis is a disease that affects all joint structures and negatively influences functional ability.[66] Damage to ligaments and meniscus are common in OA from vascularisation and increased nerve densities.[66] Furthermore, bone undergoes remodeling beginning in areas that experience repetitive stress, resulting in thickening of the subchondral bone plate.[66,67] Synovitis occurs in early stages of OA and increases with disease progression from macrophage infiltration to the synovium.[66,68] Degradation to articular cartilage is also present and increases with progressive OA.[66]

A hallmark feature of OA is disruption and degeneration to the cartilage matrix from an interaction of mechanical, cellular, and biochemical factors.[61,62,66,67] This disruption contributes to chemical changes in the matrix, and an increase in enzymatic activity breaks down collagen and proteoglycans.[10,67] There is a resulting increase in matrix permeability that allows greater water accumulation and a reduction in the elastic properties of the cartilage.[61,67,69] Progression of cartilage degeneration is comprised of three stages: (1) breakdown of cartilage matrix, (2) fibrillation and erosion of the cartilage surface where the biproducts are released into the synovial fluid, and (3) synovial inflammation that occurs once the synovial cells ingest the breakdown products from the second stage through phagocytosis and production of proteases and proinflammatory cytokines occurs.[67] In early OA, cartilage swells from an upregulation of fluid in the joint to repair the damaged collagen network. This increase in synthetic activity causes chondrocytes to form in clusters.[50,67,70,71] These chondrocytes are unable to respond to growth factors and cannot maintain the cartilage matrix leading to more degeneration.[50,71] Inflammatory mediators such as proteinases, cytokines, matrix metalloproteinases, and aggrecanase continue to release after initial damage and accelerate degeneration.[50,71] Erosion, fibrillation, and cracking of the most superficial cartilage layer begins, which contributes to additional joint-space narrowing.[10,67]

2.4 « Risk Factors for OA »

There is no known direct cause of OA. However, there are factors that contribute to risk of OA development. For example, older age is a predictor of OA,[8,50] and OA incidence increases with age.[8,50,72] The Framingham group demonstrated a trend of increasing OA prevalence where 27% of those aged 65-69 years had radiographic evidence of OA which rose to 51% in those over 85 years.[72] Etiology of increasing incidence with age could be attributed to other age-related changes.[73] For example, sarcopenia contributes to decreased strength and joint function.[8,50,72,73] Increased bone turnover and subchondral stiffness also occur with age and influence OA disease state.[50,66,69,72,73] Finally, decreased responsiveness of chondrocyte growth limits the response to mechanical stimuli.[50,73]

Sex also influences OA risk.[50,72,74] Hormonal differences, particularly after menopause, reduces estrogen content which has been linked to OA in females.[50,69,73] Joint alignment and laxity in females compared with males affects load distribution through varus and valgus knee alignment and influence load distribution.[8,50,69] Additional differences in strength and bone density may also elevate risk of OA in females.[50,74] These differences may contribute to a 34.4% prevalence of OA in women compared to 30.9% of men.[72]

Obesity increases OA risk via metabolic and mechanical mechanisms.[50,74,75] Higher body mass places additional excess loading and stress to the joints.[50,53,67,74,75] A recent meta-analysis reported that a 5 unit increase in body mass index (BMI) is associated with a 35% increased risk of knee OA.[75] Furthermore, for every 1 pound increase in body weight, the knee experiences 2 to 3 pounds more force.[69] The increase in body mass likely overloads the joints over time and contributes to cartilage breakdown.[69]

The level / type of physical activity, and occupation contributes to the amount and type of mechanical stress the joint experiences and OA risk.[50,74,76] Activities and occupations that demand repetitive joint use could be a contributing factor through chronic overload and fatiguing of muscles that protect the joints.[8,50,53,73,74] For example, a systematic review reported that high physically demanding occupations are associated with knee OA, such as farming, floor laying, and brick laying required repetitive squatting, kneeling, carrying, and crawling.[77]

Joint injury history also increases the likelihood of OA.[50,70] For example, knees with a history of anterior cruciate ligament (ACL) injury have a 4.2 times higher odds of developing knee OA in the injured compared to contralateral knee.[78] Similarly, a history of meniscal injury contribute to a 6.3 times greater odds of having OA compared to no injury.[78] Joint dysplasia, fractures of articular surfaces, and ligament tears also contribute to joint instability and greater contact stress, which may precede OA.[50,69] Therefore, injury prevention is important for reducing OA risk.

Running is a repetitive activity that contributes to overuse injuries.[49] Runners have high likelihood of suffering a RRI.[46] Patellofemoral pain is common in runners and can be attributed to overuse.[46] Among ultra marathon runners, PFP prevalence ranged from 7.4 to 15.6%.[3] Additionally, high weekly training volume and a history previous injuries increase the risk for further injury.[46] Since previous injury is a risk factor for OA, it is possible that previous injuries sustained from competitive running could increase risk of disease. Furthermore, there is a possible link between RRIs and OA. Since PFP is a commonly occurring RRI, it has also been proposed that PFP may contribute to patellofemoral OA.[7]

2.5 « Gait Biomechanics of Cartilage Morphology and Osteoarthritis »

There are a variety of mechanical factors that contribute to knee OA. External joint moments are determined by external forces (e.g., ground reaction force) that are applied to the body, kinematics of a joint (e.g., acceleration), and the distance of the force vector to the center of mass and moments of inertia around the center of mass. The external knee adduction moment occurs in the frontal plane and is a surrogate of medial compartment knee load.[79] A higher knee adduction moment during walking is associated with knee OA progression.[79] For every 1% increase in knee adduction moment, knee OA progression increased 6.46 times.[79] A larger external knee adduction moment places disproportionate load on the medial tibiofemoral compartment.[80] A larger knee adduction moment can also be influenced by greater varus thrust, which is also associated with patellofemoral OA.[81,82] In human walking, varus thrust presents worsening or immediate varus alignment.[81] This is an anatomical malalignment that can affect load distribution, and has been associated with higher odds of patellofemoral OA in patients with medial knee OA.[53,81] However, the association between the knee adduction moment and knee cartilage outcomes and knee OA is mainly found during walking.[17,83] In a group of collegiate and recreational runners, no associations were found with the knee adduction moment and cartilage features (thickness and echo intensity).[17]

The knee flexion moment is an external moment that acts in the sagittal plane to flex the knee joint and predicts overall compressive force within the knee. The knee flexion moment is also associated with knee OA.[84] The relative contribution of the knee flexion moment to the total joint moment in patients with medial knee OA decreased from baseline to a 5-year follow up as disease progressed.[84] It is possible that changes were related to adaptations from pain to reduce medial compartment load.[84] Patients with knee OA who have greater pain have lower knee flexion moments, while patients with no change in pain also showed no change in the knee flexion moment.[85] Therefore, a high knee flexion moment may increase medial joint loading and pain in OA patients. An increased knee flexion moment is also associated with greater peak knee flexion, which may increase loading on the patellofemoral joint.[86,87] Furthermore, the internal knee extensor moment, which is equal and opposite to the external knee flexion moment, and has been associated with greater medial femoral cartilage thickness in healthy groups.[88] Schmitz et al., reported that thicker medial femoral cartilage was associated with a larger internal knee extensor moment in healthy participants during gait.[88] Moreover, the knee flexion moment in recreational runners has been associated with lower medial femoral cartilage echo intensity, which suggests a positive adaptation against OA.[17]

The magnitude of the GRF and lever arm determine knee joint moments.[89] In patients with ACL reconstruction who were 6 months post-surgery, a higher knee flexion moment, knee adduction moment, and vertical GRF were associated with increases in T_{1p} and T_2 relaxation times in the medial tibial and femoral cartilage 1 and 2 years after surgery.[90] In patients with OA, a greater peak knee flexion, and knee flexion excursion have been associated with higher peak vertical GRF.[87] As such, reducing the GRF could reduce knee moments and knee loading. In running, more extended knee contact angles increase forces on the body.[41] Therefore, altering the knee contact angle in running could reduce the GRF and resulting knee moments that influence joint loading.

Findings on mechanical factors that contribute to cartilage changes and OA progression are commonly reported in walking. However, there is a gap in the literature surrounding how mechanical factors contribute to OA in running. The joint health of runners may be influenced by mechanical factors and should be further investigated.

2.6 « Acute and Chronic Cartilage Responses to Mechanical Loading and Running »

Mechanical loading acutely causes compression and deformation of cartilage that takes up to 90 minutes of unloading to recover.[65] Habitual loading is needed for cartilage to maintain homeostatic function and provide nutrient diffusion.[62] Cartilage responds differently to applied loads and physical activities.[62,64] These responses can be both mechanical and biochemical.[65] Certain forms of physical activities have higher prevalence of OA.[24] Therefore, various activities that include walking, jumping, and running may have different effects on cartilage.

A previous study utilized a repeated measures design with uninjured participants between the ages of 18-35 years who reported physical activity participation for at least 30 minutes, 3 times weekly.[91] Researchers compared the acute femoral cartilage response and recovery to walking and landing using ultrasound imaging.[91] Walking at self-selected speeds for 5000 steps caused more medial cartilage deformation compared to a non-weight bearing control condition.[91] Moreover, participants had greater deformation of medial cartilage after 120 drop landings compared to the control condition.[91] When comparing walking and drop landing, the drop landing task contributed to greater medial cartilage deformation, and took longer to recover to baseline.[91] This difference was attributed to greater knee flexion and higher-magnitude joint loading.[91]

Similarly, Eckstein et al., investigated cartilage deformation after exercise in various knee regions of 12 healthy volunteers with no history of surgery or knee trauma.[92] They found that patellar cartilage deformation was higher following activities with greater range of motion like squatting, running, and knee bends.[92] Moreover, high impact loading from jumping caused the greatest amount of deformation in tibial cartilage.[92] These findings suggest that loading with higher magnitude and greater joint range of motion may have detrimental effects on acute cartilage thickness and recovery time.

Cartilage biochemistry is influenced by acute loading.[93] In a sample of healthy subjects completing single and double leg jumping, higher joint loads were significantly related to the composition of the cartilage.[93] A greater knee flexion moment during hopping was associated with lower T_{1p} and T_2 values.[93] The authors concluded that cartilage composition was associated with higher knee loading.[93]

Activities of daily living result in a loss of interstitial water in cartilage that can take hours for recovery.[94] Coleman et al., had ten healthy participants undergo magnetic resonance imaging (MRI) of their right knee at 8am and later that day at 4pm. Cartilage thickness decreased during the day due to fluid loss from continuous compression but recovered overnight as fluid re-entered cartilage during rest.[94] Continuous compression from other activities including running could provide similar findings that also require recovery time.

Running involves cyclical mechanical loading for long durations that have knee contact forces that may exceed 12 times body weight.[33,95] Furthermore, cartilage size is acutely reduced after a single bout of running.[33–37] Boocock et al., recruited 20 healthy participants who ran recreationally 2.5 times per week. All participants ran 5000 steps at a self-selected speed and cartilage volume was compared prior to and following running.[34] There was significant deformation after running in the medial (5.3%) and lateral (4.0%) femoral, and lateral tibial (5.7%) cartilage volumes.[34] A significant correlation was also found between greater lateral knee compressive stress and a greater reduction in lateral femoral cartilage volume.[34]

Kessler et al., investigated volume changes in patellar cartilage, tibial cartilage, and lateral meniscus after a 20km run in 20 male recreational runners with marathon experience.[35] When comparing pre- and post- imaging, patellar cartilage had decreased by 7%, tibial by 5.1%, and lateral meniscus by 8.2% following running.[35] After a one-hour recovery period, cartilage deformation was reduced to 2.1% in the patellar cartilage, 1.2% in the tibial cartilage, and 5.9% in the lateral meniscus compared with pre-running measurements.[35] Therefore, cartilage was able to exhibit some recovery within an hour of loading, which may be due to its high water content and permeability.[35]

Heckelman et al., found that patellar cartilage thickness decreased immediately following a 10- and 3- mile run in 8 healthy males who typically run at least 5 miles each week.[96] After 24 hours of recovery, cartilage thickness was not different from the original baseline measurements.[96] Interestingly, patellar cartilage underwent larger mean compressive strains following the 10-mile run compared to the 3-mile run.[96] These findings suggest a dose-response relationship between the magnitude of joint loading and cartilage deformation.

Conversely, some studies have found no change in cartilage structure following running.[97–99] A study evaluating 8 non-professional male marathon runners compared MRI’s before and after their race and discovered no changes in cartilage thickness, or new/worsening lesions to the cartilage surface.[100] Similarly, Qiu et al., found no new or worsening changes to the cartilage surfaces at various regions of the knee when comparing pre- to post- running imaging 2 and 14 days afterward.[99] The lack of changes in cartilage morphology following running in these studies could be due to the timing of the post run imaging as cartilage may have recovered.

Moreover, Karanfil et al. evaluated MRIs of 32 physically active healthy males and reported that the right limb lateral femoral cartilage thickness decreased after 30 minutes of running, but right limb medial tibial plateau cartilage increased.[97] There were also biochemical changes seen as T_2 signal intensity decreased in all compartments except the lateral patella in both limbs of the participants.[97]

Biochemical activity has also been evaluated acutely following running.[36,37,99,101–103] Serum cartilage oligomeric matrix protein (COMP) is a glycoprotein that interacts with proteins of the cartilage extracellular matrix of cartilage and relates to cartilage damage.[36,37] One report claimed that COMP increased following running,[37] while another report found that greater COMP was correlated with lower cartilage volume after running.[36]

T_{1p} corresponds to proteoglycan content and T_2 corresponds to integrity of the collagen matrix. Both outcomes are affected by running but findings are conflicting.[97,99,101–103] For example, some reports have found that T_{1p} and T_2 are reduced after running,[97,102,103] and others have found an increase after running.[99,101] T_2 relaxation time has an inverse relationship with collagen organisation and direct relationship with water content.[104] Conversely, T_{1p} relaxation time is sensitive to changes in the extracellular matrix. Therefore, when cartilage is compromised, T_2 and T_{1p} relaxation times are prolonged due to water freely moving within the cartilage.[104] These findings suggest that running may increase fluid outflow following joint loading.[97,102,104]

It is important to note that runners do not partake in a singular bout of running within their lifetime. Repeated exposure provides a better representation of what could be anticipated when evaluating runners' joint health, but data are contradicting.[33] There is clear evidence that running in moderate amounts does not contribute to knee OA.[33] However, the type running activity may moderate this relationship.[33]

The site of knee cartilage evaluation can influence findings as well.[59] Horga et al., examined if marathon running could improve knee damage in novice runners who were middle-aged adults.[59] Their sample of 82 volunteers underwent baseline MRIs of their knees before adopting a 4-month training program leading to a marathon race with additional MRIs 2 months after completion.[59] Damage to the lateral patella cartilage and bone was found.[59] A total of 21 cartilage lesions were seen in the patellofemoral joint, 12 of which were to the lateral patellar facet while the subchondral bone of the patellofemoral joint had the highest number of new/worsened lesions in the knee.[59] Conversely, there was improvement in the tibial and femoral condyles subchondral bone marrow with 10 lesions improved in the medial tibia and 9 in the medial femur.[59] Therefore, some knee areas may show benefits from adopting a running program with prolonged repeated exposure while others may see negative effects.[59]

A sample of 10 novice marathon runners underwent a 6-month training program that ended with a marathon race.[105] Over the 6 months, training distance per week increased on average of 10.5-34.5km per week and MRI's of participants knees were taken at baseline and 1 day post race.[105] There was a significant 1.7% decrease between baseline and follow up for cartilage thickness of the lateral femur, while no significant differences in thickness were seen in medial tibial, medial femoral, lateral tibial, and patellar regions.[105] The authors from this study concluded that 6 months of intensive running results in significant but small cartilage loss.[105] However, it should be noted that the follow-up measurement occurred the day after running a marathon. Therefore, the change in cartilage thickness could be an acute result of the marathon run and not representative of the 6 months of training. A 10-year longitudinal study evaluating magnetic resonance tomography in the knee joints of 10 marathon runners found no new major internal damages in the knee joints.[100] However, it was noted that one participant quit running and deterioration to the intra-articular surface was found in that participant.[100]

Miller et al., suggests it is doubtful that knee cartilage has the ability to handle a lifetime cumulation of running without the presence of a positive physiological adaptation.[38] A musculoskeletal model predicted failure of the joint cartilage without an adaptation response as running amasses large amounts of damage.[38] The authors suggest that cartilage adaptations occur when triggered by the high mechanical stress from running.[38] However, the amount of loading required for cartilage to fail without other influences such as injury, likely would not be reached by typical runners.[38]

A recent review by Khan et al. examined the influence of running on lower-limb cartilage and suggested that acute changes to lower limb cartilage after running are not long lasting.[33] Authors believe that cartilage recovers quickly from a single bout and adapts to repeated exposure because of its porous and permeable matrix that allow for water diffusion and nutrient exchange.[33] Therefore, positive cartilage adaptations are possible from repeated exposure.[33] However, the authors did not consider variables such as the distance and duration of runs.[33] Furthermore, they examined studies that only investigated young and healthy recreational runners, which may not be generalizable to competitive or previously injured runners.[33]

Van Ginckel et al., investigated 9 female participants in a 10-week start-to-run program and underwent delayed Gadolinium Enhanced Magnetic Resonance Imaging of Cartilage imaging (dGEMRIC).[39] Their findings indicated that a positive adaptation by the higher dGEMRIC index values was present after the intervention in the runners compared to controls.[39] The change in dGEMRIC is an estimate for glycosaminoglycan (GAG) content, which is a component of the extracellular matrix of cartilage that regulates osmotic pressure to prevent cell damage.[39,106]

Conversely, unloading cartilage for prolonged periods could contribute to negative effects, and cartilage may atrophy when not exposed to loading.[107] For example, knee cartilage size is decreased in patients with spinal cord injury who unloaded their lower limbs for prolonged periods of time.[107] After 6 months of unloading, cartilage thickness decreased by 10% in the patella, and 16% in the medial tibia. Moreover, the decreases in cartilage thickness after 2 years rose to 23% and 25% for the patella and tibia, respectively.[107] Atrophy can be attributed to the absence of nutrient influx to the cartilage that is brought on from joint loading.[62,107] Therefore, habitual loading from activities of daily living and exercise is necessary for cartilage maintenance.

2.7 « Different Populations of Runners»

There are biomechanical and behavioural differences between runners of different abilities and competition levels that may influence knee joint loading, cartilage development, and knee OA risk.[20,21] Recreational running is widely investigated, completed at lower intensities, and can be quantified as running a minimum of 3 times per week totaling 16 kilometers.[17–19] Conversely, competitive runners could run up to 7 days per week for up to 130 – 220 kilometres depending on the event discipline.[21] One report claimed that world-leading marathon and track runners could train anywhere from 450-700 hours per year.[21] Competitive runners also utilize diverse training methods that manipulate the magnitude and duration of joint loading. For example, training includes long runs, tempo runs, fartleks, progressive runs, and interval training.[21] However, recreational running is more prominent among the general population. As such, most research concerning running and knee OA/cartilage has focused recreational running.[15,33] A recent review supported this notion claiming the risk of OA was higher amongst competitive compared with recreational runners.[15] This finding was attributed to the likelihood of higher mileage and intensity exposure in competitive runners.[15]

Mitchell et al., found no difference in femoral cartilage thickness or quality between recreational and collegiate runners, suggesting that moderate amounts of running does not adversely affect femoral cartilage.[17] However, a greater knee flexion moment was associated with lower medial cartilage echo intensity in recreational runners, and greater running amount was associated with higher medial and lateral femoral cartilage echo intensity in collegiate level runners.[17]

Running speed may also differ between populations along with the different types of training mentioned earlier.[14,17,20,21] A study comparing running biomechanics between recreational and collegiate runners recorded different average running speeds of recreational runners at 3.47±0.45 m/s and collegiate at 4.14 ± 0.34 m/s during collection.[17] Clermont et al., also recorded different running speeds in their research within their sample of male and female competitive and recreational runners.[14] Recreational males and females ran with an average speed of 2.68 ± 0.23 m/s and 2.47 ± 0.22 m/s respectively, while competitive male and females ran at 3.08 ± 0.23 m/s and

2.84 ± 0.3 m/s respectively.[14] Race time differences have also been recorded between competitive and recreational groups.[20] Recreational runners presented times of 63.25 ± 5.44 minutes, 120.13 ± 14.56 minutes and 263.99 ± 18.53 minutes while competitive runners were 35.01 ± 3.71 minutes, 98.91 ± 17.01 minutes, and 184.59 ± 37.36 minutes in the 10 kilometer, half marathon, and marathon races respectively.[20] Reports on training characteristics of world class athletes state that easy runs can range from 3:45-4:30 minutes per kilometer for men and 4:15-5:00 minutes per kilometer for women.[21] These easy run paces in training that can last for 40-70 minutes and equates to a 37.73-44.76 minute 10 kilometer run for men and 42.55-50.0 minute 10 kilometer for women.[21]

Behavioural characteristics may also be associated with biomechanical differences that influence knee joint loading. For instance, competitive runners have less anterior pelvic tilt throughout the gait cycle, greater knee flexion during stance, and a less inverted ankle in late stance phase compared with recreational runners.[20] The biomechanical differences between competitive and recreational level runners contribute to different joint stress and injury risk.[20] These are key differences because greater knee flexion in competitive runners attenuate impact and can decrease shock to the tibia.[20,108] A more flexed knee decreases the vertical spring stiffness of the body.[108] Greater foot eversion in recreational runners may contribute to greater forces experienced at the knee and tibia.[20] Competitive running and faster running speed is also characterised by landing positions where the feet contact the ground closer to the runners center of mass position, and shank angles more perpendicular to the ground compared to lower level runners including recreational.[41,109,110] Furthermore, competitive runners experience larger ground reaction forces (GRF) and higher LRs, which is likely due to faster running speeds.[2,27,109,110] Higher LRs may contribute to additional cartilage deformation due to the viscoelastic properties and matrix permeability of cartilage. Therefore, higher intensity running in competitive runners could have adverse effects on cartilage.

2.8 « Patellofemoral Pain and Loading »

Patellofemoral pain is also referred to as anterior knee pain, and/or runners' knee, and can be defined by pain behind or around the patella from patellofemoral joint loading.[7,25] Patellofemoral pain is prevalent in runners and may contribute to patellofemoral OA later in life.[6,7,25] The patellofemoral joint is often the first articulation of the knee affected by OA, and excessive running may exacerbate cartilage degeneration.[7,32] A variety of factors contribute to PFP such as malalignment, muscular imbalance, and overactivity,[25,111] which all influence cumulative joint stress that can be exacerbated by faster running speeds. Joint stress is quantified by the compressive force acting per unit of area.[111] Therefore, factors that manipulate force or joint contact area may contribute to greater joint contact stress and cartilage responses to running.

Running speed has a profound influence on patellofemoral loading, and various running intensities coincide with biomechanical differences that alter joint stress, particularly to the patellofemoral joint. In 12 runners (7 with PFP and 5 without PFP), peak PFJS was greater at faster compared with slower speed regardless of participants' PFP status.[112] Therefore, faster running contributes to greater loading on the patellofemoral joint. Another study found greater hip and knee internal rotation when running at faster (13 km/h) compared with slower speeds (9 km/h) in runners with PFP.[113] The effects of speed on the patellofemoral joint were also investigated in a sample of 20 high performance distance runners.[22] Patellofemoral joint stress increased from slower to faster running speeds, but no difference was found between faster running speeds when running along a 40-meter runway at four different speeds (3.3, 3.9, 4.8, & 5.6 m/s).[22] Faster speed also contributed to an increase in vertical GRF and LRs.[22] Moreover, greater step length and step frequency are observed with faster speed.[22] Runners in this study employed both techniques and increased step length by 43% and step rate by 14.7% across all speeds.[22] For these reasons, faster running may contribute to greater cartilage deformation and may contribute to the difference in knee OA prevalence across different types of runners.

Faster running speed also elevates muscular demands during running, which may exacerbate lateral patellofemoral contact stress in runners with PFP. Muscle activation and coordination influence the distribution of patellofemoral contact stress.[32,111,114–116] The vastus medialis (VM) and vastus lateralis (VL) activation ratio and VM function is altered in those with PFP.[32,114,115] In a cadaveric study, increasing force from the vastus medialis obliquus (VMO) was associated with decreasing maximum lateral patellofemoral cartilage pressure and increasing maximum medial pressure at 40, 60, and

80 degrees of knee flexion.[114] With no force applied to patellofemoral joint, intact cartilage pressure was up to 18% greater than with the force from the VMO.[114] With lateral cartilage lesions, up to 27% greater pressure was applied to the lateral cartilage with no force from VMO than with force from the VMO.[114] This suggests that lower VMO function may contribute to disproportionate loading of the lateral joint cartilage.[114]

Similarly, one report comparing controls and PFP subjects found a correlation between the VL : VM activation ratio and lateral mal-tracking PFP participants.[115] A correlation was also present between the VL : VM activation ratio and the VM activation delay in mal-tracking PFP patients.[115] This suggests that the delay in VM activation could contribute to patellar mal-tracking.[115] Another report found that the VMO and VM longus of PFP patients with malalignment contributed less to total knee extension torque than controls.[117] Moreover, the VL of PFP patients contributed more to knee extension torque than the VMO and VM longus muscles combined, whereas controls contributed equivalent amounts to knee extension torque from their quadriceps muscles.[117] Furthermore, individuals without PFP have synchronous onset of the VMO and VL while those with PFP had the onset of the VL precede the VMO during concentric and eccentric tasks.[118] Therefore, timing delays and torque distribution may contribute to patellar mal-tracking, and contribute to additional lateral knee joint stress during running.

Differences in muscle forces have been found between individuals with and without PFP during walking and running.[116] Besier et al., recruited 27 people with PFP and 16 controls to walk and run at self-selected speeds to collect EMG and kinematic data.[116] During running, those with PFP produce 13% less internal knee extension moment compared to controls without PFP. However, the only difference in muscle force was a 30% greater peak gastrocnemius force in PFP patients, which may elevate knee loading.[116] Quadriceps muscle forces increased in running compared to walking by 5% in the VM and decreased 6% in theVL.[116] Additionally, greater co-contraction between the quadriceps and hamstrings was seen during running compared to walking in those PFP, which also increases cumulative knee loading.[116] Therefore, running at faster speeds may further exacerbate muscle contributions to internal joint loading.

Collectively, those with PFP have elevated stress on the lateral portion of the joint given the disparity in lateral to medial quadriceps muscle force and activity. Faster running speeds may exacerbate the imbalance and contribute to additional lateral cartilage compression from higher joint contact stress.

Running kinematics may also influence the magnitude of patellofemoral contact stress that are exacerbated by faster speeds. A systematic review reported altered biomechanics in runners with PFP compared to those without based on the 28 studies.[31] Significant associations were found between PFP and peak hip internal rotation, contralateral pelvic drop, and reduction in peak hip flexion.[31] The authors also suggests kinematic risk factors for PFP in runners included greater peak hip adduction, greater peak force under the second and third metatarsals, and shorter time to peak force under the lateral heel.[31] These kinematic alterations may be exaggerated with faster running speed and increase peak PFJS by manipulating the joint contact area and net joint muscle moments.[119]

Santos et al. evaluated the effect of foot strike pattern, cadence, and trunk position on PFJS in recreational runners.[120] Findings indicated that a forefoot strike lowered peak PFJS by 27.09%, with reduction to the PFJS integral per step and per kilometer, and lower peak knee flexion angle compared to rearfoot strike pattern.[120] As running speed increases, runners may transition to a more anterior foot strike pattern.[27] This suggests thar faster running may reduce PFJS if the runner adopts a forefoot strike pattern. Similarly, the 10% increase in step rate resulted in an 11.78% lower peak PFJS, lower peak PFJS integral per step and kilometer, and lower peak knee flexion angle.[120] Step length during running is associated with PFJS.[121] A sample of 20 participants who engage in running at least twice a week for a minimum of 16km ran with a self selected step length to determine how a 10% increase and reduction to that step length would affect patellofemoral joint kinetics.[121] A 10% reduction in step length contributes to a 17% decrease in the peak patellofemoral joint reaction force and 15% reduction to peak PFJS, potentially due to reductions in knee flexion.[121] A 10% increase in step length significantly increased peak patellofemoral joint reaction force by 16% and PFJS by 11%.[121] Importantly, patellofemoral joint loading may influence cartilage features during running.[96] However, the effect of faster interval running on cartilage deformation is unclear given the complex interaction(s) between biomechanical features when running at different speeds.

Running kinetics may also influence PFP because runners with PFP have greater instantaneous and average LRs compared to controls without PFP, which likely contribute to higher patellofemoral contact stress.[122] Cheung et al., investigated how pain scores and kinetics of 3 female runners from a local running club would be affected by 8 non-rearfoot landing pattern training sessions.[123] At a 3-month follow-up, the trained non-rearfoot running pattern was maintained along with a 10.9% to 35.1% reduction in vertical impact peak, instantaneous vertical LR, and average vertical LR.[123] Improvements to PFP scores for reduced pain were also reported which suggests reduction to LRs in running may have beneficial outcomes on PFP.[123]

Esculier et al., evaluated a rehabilitation program in 21 recreational runners with PFP.[124] Participants underwent an 8 week training program that consisted running and an exercise program.[124] The running intervention consisted of reducing patellofemoral joint loads through increasing step frequency, and/or modifying foot strike pattern to midfoot or forefoot, increasing training frequency but decrease daily volume, avoid fast and downhill running, and maintain PFP level at 2/10. The exercise program consisted of 4 phases targeted to improve strength, endurance, control, flexibility, and lower limb alignment, specifically through better recruitment of gluteal, quadriceps, and hip muscles.[124] After the intervention, decreases of 13.5% and 17.8% was seen in the instantaneous vertical LR and average vertical LR respectively.[124] Therefore, running with higher/lower LR during high-intensity interval or continuous running may influence PFP-related outcomes such as patellofemoral contact stress and cartilage deformation.

It is possible that relationships exist between running characteristics during high-intensity interval running such as higher LRs contribute to greater joint stress and cartilage deformation.[22,28,112,113] Moreover, competitive runners are likely to engage in faster running that induces more cumulative PFJS. Therefore, greater cartilage strain from high intensity running throughout a competitive running career may contribute to PFP and to the discrepancy in OA prevalence between competitive and recreational runners.

2.9 « Strain Rate on Cartilage »

Strain rate is the change in deformation of cartilage over time, which may contribute to cartilage damage and vary across exercise intensity.[29] Blunt impacts have high LRs and contribute to cartilage matrix damage.[29,30] Research using explants found greater matrix damage and cell death in those that experienced high LRs to those who experienced low rates of loading.[29] Greater damage from high strain rates may be due to viscoelastic properties where greater amounts of load are put on the fluid phase at a faster rate which increases the tissues' fluid pressure.[29] The fluid phase refers to the combined functions of the extracellular matrix and interstitial water. The increase in fluid pressure in the tissue creates larger tensile stresses, ultimately resulting in fissures of the articular cartilage.[29]

Ewers et al., investigated blunt impacts in rabbit patellae.[30] They found similar results that the high LR group had more surface fissuring of the cartilage compared to low LR.[30] The authors discovered more thickening of bone beneath the joint cartilage in the high LR but similar degrees of cartilage softening between groups.[30] They concluded that chronic injury mechanisms may be dependent on the rate of impact loading due to viscoelastic properties.[30] With short relaxation time and magnitude of the forces, bone stiffness increases in higher speed loading that causes higher stress levels distributed to the cartilage.[30] However, they believed that the solid phase of the model would carry a larger portion of the load also resulting in higher stresses placed on the cartilage.[30]

Li et al., found that the fluid drives the stiffening of the matrix and causes pressure within the cartilage under high LRs.[125] Therefore, there may be load-sharing between the solid and fluid phases depending on the strain rate.[125] A higher strain rate may include a greater contribution from the solid phase while load is absorbed by the collagen fibers, but more load is absorbed by interstitial fluid flow with a lower strain rate.[125] Consequently, strain rate should be considered as an important contributor to injury and a mechanism for cartilage damage.[126–128] Running includes repetitive impacts that exceed 3X body weight with high LR. Therefore, running at higher intensities compared to lower intensities may increase the strain rate. Additionally, higher level runners who are more likely to engage in faster running may also be prone to exposure of higher strain rates that could be damaging to cartilage.[15]

2.10 « Summary »

Running is a popular activity and findings are mixed with regards to running and OA risk. Much of the available data focuses on recreational runners. Recreational running does not influence OA, but the data in competitive runners are sparse and may suggest a higher risk for OA. Biomechanical and behavioral differences between recreational and competitive runners may influence cartilage outcomes that have implications for joint health. Therefore, more research including competitive runners is needed to clarify the mechanisms that may contribute to injury and OA among competitive runners.

Increased running speed is associated with greater vertical GRF and LR, and increased LRs in animal models contribute to matrix damage by increasing cartilage strain. Therefore, different intensities of running including fast running may simulate higher LRs in human cartilage. This difference in LR and cartilage strain may consequently be observed during high-intensity interval compared to continuous slower running.

Therefore, the purpose of this study was to investigate the influence of continuous and high-intensity interval running on acute cartilage deformation in competitive runners and to determine any association between LR and acute cartilage deformation. Findings of this study provide insight to how different intensities of running and high LRs affect human cartilage, and why OA risk may differ between competitive and recreational runners.

Chapter 3

3 « Methods »

This experiment used a within subjects' crossover design (Figure 1). Participants completed two separate running sessions (continuous and interval) with ultrasound imaging taking place before and after running. The order of sessions was counterbalanced. Each visit consisted of 30 minutes of joint unloading, initial ultrasound imaging, a warmup, either running condition, second round of ultrasound imaging, and a cool down. The total accumulated distance of the running condition totalled to 12 km during each visit. All participants were instructed to not exercise on the day of collection and wore the same self-selected footwear for both sessions. A washout period of 2-7 days was used between visits. The participants' trial order was counterbalanced between participants.

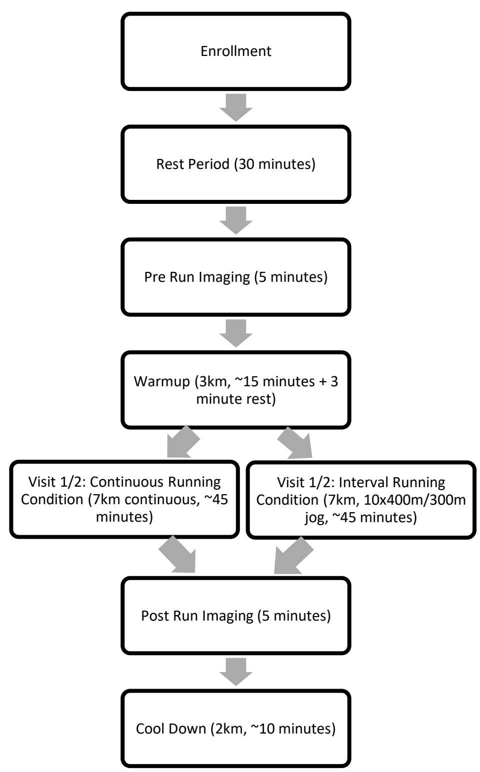

Figure 1: Flow Diagram of Study Procedures

3.1 « Participants »

Twenty-four competitive distance and middle-distance runners were recruited for this study. This sample size was selected based on an ability to detect a moderate effect size (d=0.33) and decrease of 6 to 8% in femoral cartilage thickness which has been seen in jumping and landing studies with similar ultrasound methodology and study design (α=0.05, β=0.2).[91,129] A competitive distance and middle-distance runner was defined as anyone currently running and competing on an intercollegiate team, or at a provincial/national championship in the events ranging from the 800m to the 10,000m within the preceding 12 months.[17] All participants were recruited through local university teams, track and field clubs, and running groups between 18 to 35 years of age.[17] Running ability was characterized by point totals from the World Athletics Scoring Tables of Athletics 2022 Revised Edition and the World Athletics Scoring Tables of Indoor Athletics 2022 Revised Edition and used as a descriptive statistic.[130,131] Additionally, participants were free from any RRI that contributed to a loss of one full week of training for 6 months prior to the study.[132] Participants were excluded for any history of knee surgeries or intra articular injections.

All participants provided informed written consent prior to participation, and all methods and procedures were approved by the Western University Health Sciences Research Board (HSREB). Each participant also provided a negative Covid-19 rapid antigen test outside of the laboratory before participating in each session.

3.2 « Ultrasound Imaging »

On the day of collection, the participants were asked to refrain from any physical activity prior to the test. Upon arrival, participants laid supine with full lower limb extension on a physio table for 30 minutes to unload any immediate weight-bearing effects on cartilage. Participants' knees were positioned in 140º of flexion using a goniometer for imaging to obtain a clear view of the distal anterior femur.[17] The ultrasound probe was positioned in between the medial and lateral condyles of the femur and superior to the patella to obtain 3 images of the femoral cartilage. Image procedures took place on both limbs of the participant. To ensure for imaging accuracy and consistency from pre to post running measurements, the placement of the goniometer was marked with a marker on the participant's skin (Figure 2). The center of the goniometer was marked on the lateral femoral epicondyle with a circle and the slope of the angle was also marked to maintain alignment with the greater trochanter of the femur and the lateral malleolus. The probe position was also outlined with a marker and the deepest point of the trochlea was centered on the ultrasound screen.

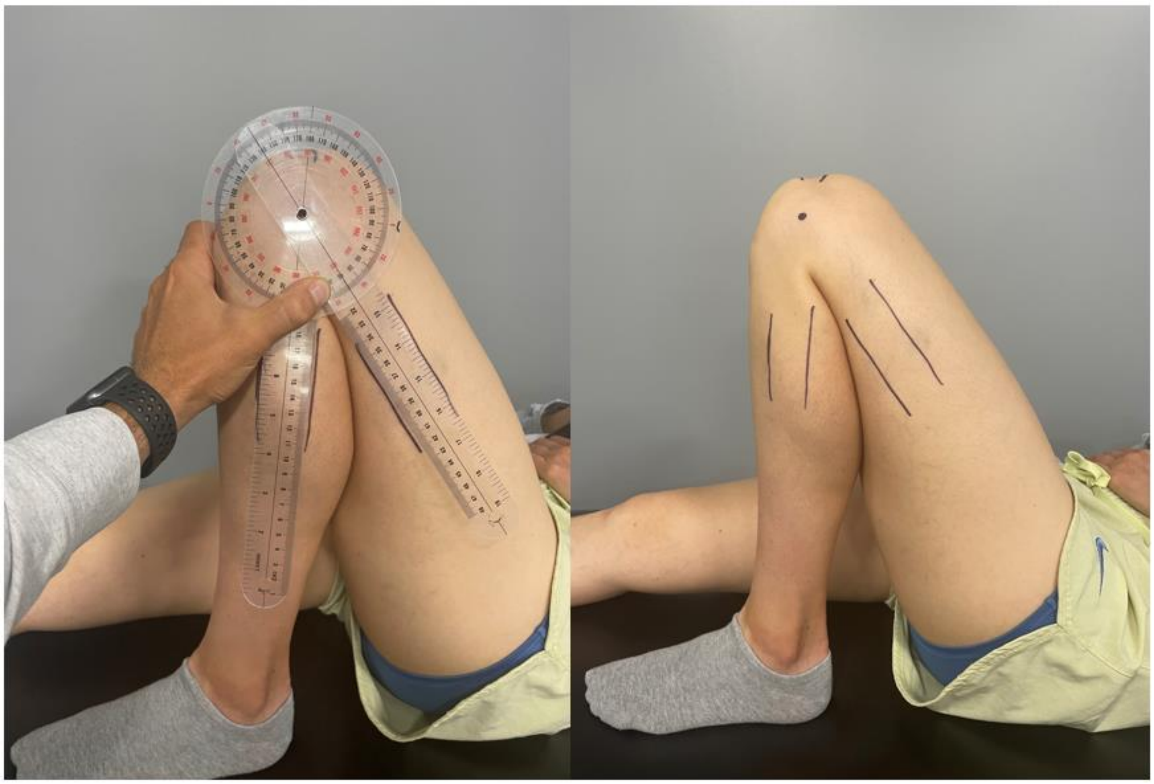

Figure 2: Images Showing Goniometer Placement and Alignment Markings; The center of the goniometer is on the lateral femoral epicondyle, the slopes of the angle are in line with the lateral malleolus and the greater trochanter of the femur, and the probe position are outlined with a marker with the knee in 140° of flexion.

3.3 « Kinetic Data »

Participants running shoes were outfitted with the Loadsol pro pressure sensing insole (Figure 3; Novel Electronics, Inc, Saint Paul, MN). The Loadsol's allowed for collection of in shoe normal plantar GRF data. Loadsols are valid to measure peak vertical GRF and linear LR against force plates during running.[133] The insole is equipped with a thin leather strap connected to an electronics box that clips onto the shoe's laces on the dorsum of the foot as to not interfere with participant's motion. This strap was taped to the participants shoes for their running trials to ensure it did not detach during data collection (Figure 3). Data were streamed via Bluetooth (Figure 4) to an Apple iPad (Apple Inc, Los Altos, CA), and exported for analysis.[133]

Figure 3: Image of Loadsols; The Left image is the Loadsols outside of the shoes to see the insole, strap, and electronics box. The right image is of the Loadsols in the participants shoe, replacing the insoles, strapped to the shoelaces, and the strap taped around the shoe to ensure it did not detach.

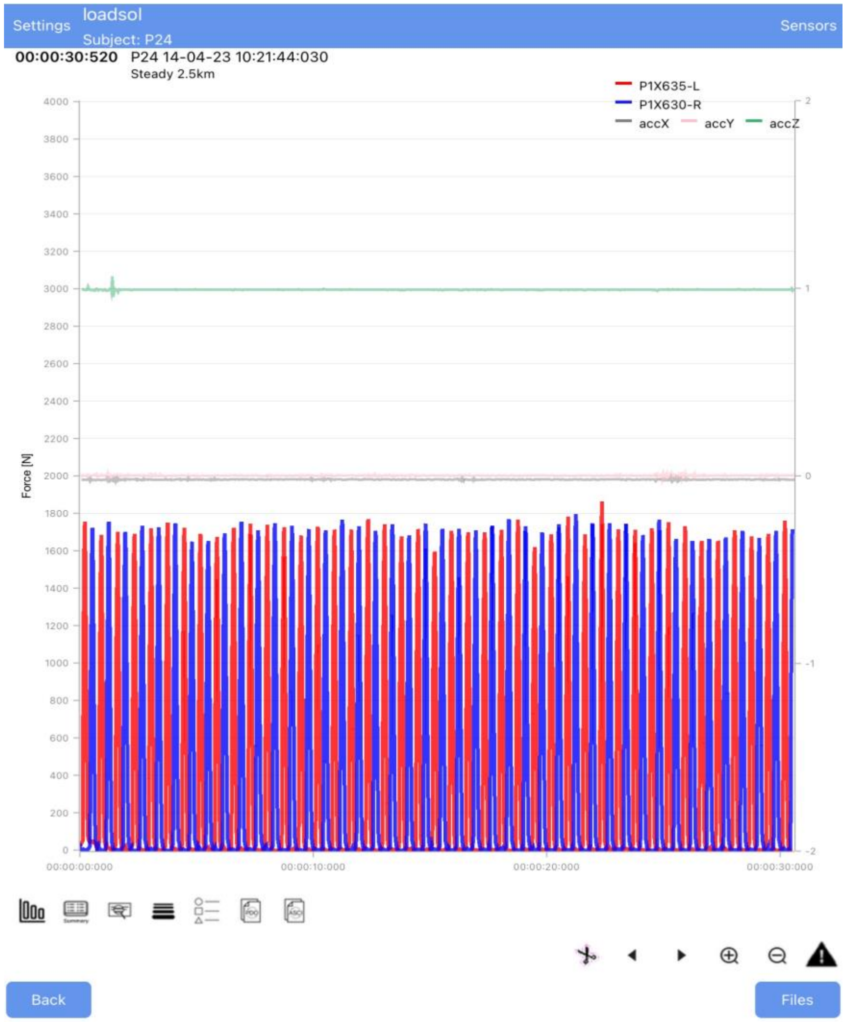

Figure 4: Screenshot of Loadsol Kinetic Data Bluetooth Stream to Apple iPad During Collection; The y axis is force in newtons and the x axis is time in seconds. The lines represent the force reading for each contact (red = left, blue = right).

3.4 « Warmup and Cooldown Protocol »

Participants ran at a self-selected running speed with the Loadsol placed in their shoes on a commercially available single belt LifeFitness 95T treadmill (Franklin Park, IL). Warmup distance totaled 3 kilometers of running for all participants and sessions. The warmup also served as a familiarization for the participants to adjust to running on the treadmill and served as the pace for the rest intervals during the interval condition. Three minutes of rest was then taken before beginning one of two of the running conditions.

The cooldown took place at the end of the running trial at the same self-selected running speed as the warmup. The cooldown distance was 2km for all participants and sessions.

3.5 « Continuous Running Trial »

The continuous running condition was performed on the same standard treadmill with the Loadsols. The trial was performed at the participants self-selected ‘usual’ “easy run” pace. This was defined as a pace that the participant was able to maintain for the duration of the trial. This pace has reported to be typically between 3:45 and 4:30 minutes per kilometer for males and 4:15 and 5:00 minutes per kilometer for females, lasting between 40 to 70 minutes.[21] Each trial concluded when the participant completed 7 kilometers.

3.6 « Interval Running Trial »

The interval running condition was intended to mimic a typical interval training session for a 1500m to 5000m runner. Upon completing the warmup protocol, the participants completed 10 x 400m with 300m recovery jog between the reps at a predetermined pace.[21] The predetermined pace was 85 to 90 percent of their most recent 1500m personal best pace per 400m. The interval session reflected what has been described as “Lactate Tolerance Training” among world class runners with running pace around 800m-1500m times, near maximal perceived exertion (18-20 RPE), and in zone 6 of 7 on a recently developed intensity model.[21] Therefore, the 85-90 percent of 1500m personal best was selected to reflect this running pace with the primary goal of creating two running sessions that presented significantly distinguishable kinetic outcomes. During the recovery period, the participants had their running pace reduced to the selected recovery pace for an entire 200m before increasing the pace once again for the next repetition. The selected recovery pace was determined to be the same self-selected warmup pace for their interval session. The additional 100m of recovery distance was to account for treadmill deceleration from the interval to the recovery pace and acceleration from the rest to the interval pace again. The accumulated distance totals to 7 kilometers of running.

3.7 « Data Reduction »

A custom MATLAB program was used to analyze the ultrasound images taken during collection. The 3 images from each timepoint and limb had the thickness averaged. Each image was assigned 300 evenly spaced data points between the cartilage bone interface and the synovial space cartilage interface with three average thicknesses between points 1-100, 101-200, and 201-300 to represent the medial, central, and lateral, regions of the cartilage which gives the Euclidian distance (Figure 5). Cartilage image analysis was completed by a researcher that was blinded to running condition and participant demographics during manual image segmentation. Intra- and Inter- rater reliability of image acquisition and segmentation were established prior to the start of the study during preliminary testing from 5 participants.

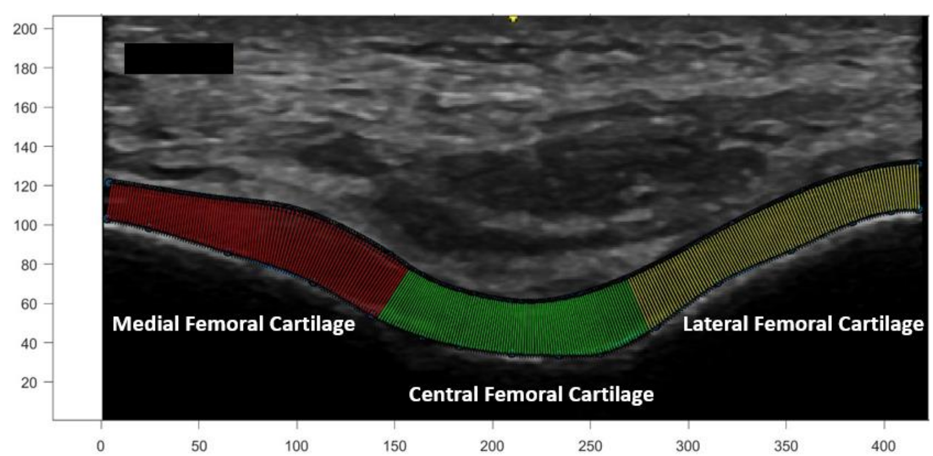

Figure 5: Image of MATLAB Cartilage Thickness Analysis; The coloured area shows the Euclidian distance between the 300 evenly spaced data points from the cartilage bone interface to the synovial space cartilage interface for the medial (red, points 1-100), central (green, points 101-200), and lateral (yellow, points 201-300). The scale on the left and bottom of the image is in pixels, where one pixel is 11mm.

LoadSol data were sampled at 100Hz and analyzed in LabView (Figure 6; National Instruments, Austin TX).[133,134] Collection occurred in the middle 15 seconds of each repetition for the interval running trial (at 200m mark of the 400m rep) with the first 12-foot strikes extracted, excluding the first and last to obtain 10-foot strikes averaged from each repetition and then each repetition averaged overall (Total of 100 foot strikes per participant). The middle kilometers of the continuous run, kilometers 2, 3, 4, 5, and 6 were sampled at the 500m mark of each kilometer for 30s to obtain at least 10-foot contacts per recording (Total of 50-foot strikes per participant). All GRFs and LRs were normalized to time and body weight and calculated during the stance phase of running. The stance phase of running was defined by the point of initial contact with the treadmill (GRF >50N) to when there was no longer contact (GRF <50N).[135] Loading rate was calculated as the linear slope of the GRF curve from 3% to 12% of stance,[133,136] and the vertical impulse was extracted using trapezoidal integration. All GRF characteristics were normalized to body weight (N) for further analyses. Ground reaction force waveforms were time normalized to 101 data points, and the ensemble average and 95% confidence interval across participants for each condition was plotted for visualization purposes.

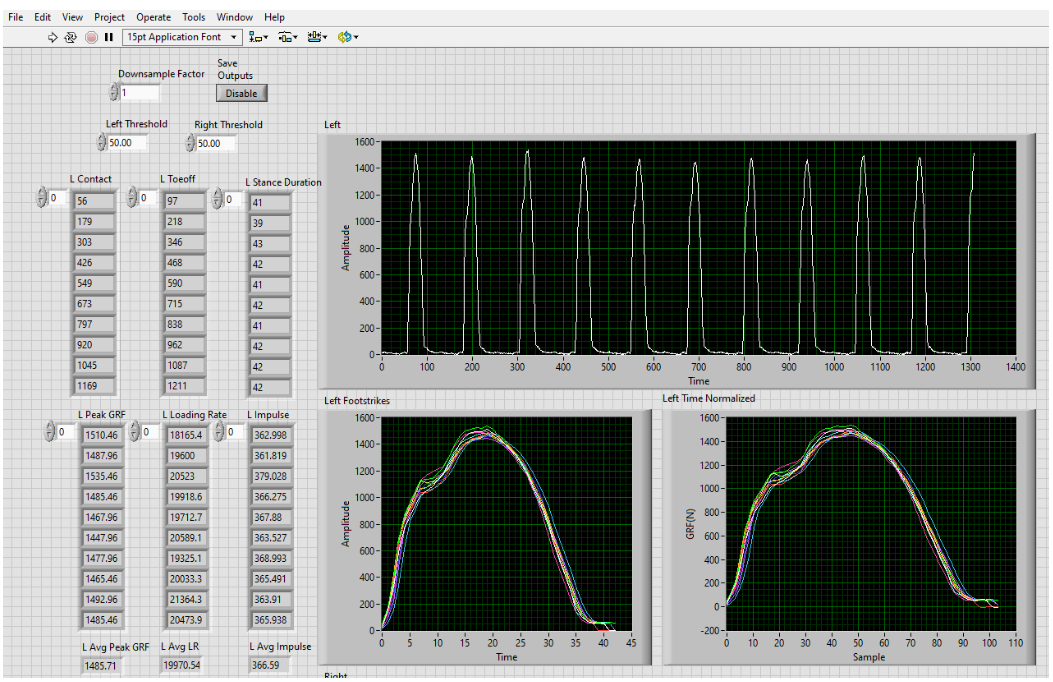

Figure 6: Image of LabView GRF Analysis; The graphs show the 10-foot contacts being analyzed and time normalized waveforms. The columns show the frame of each foot contact, toe off, and the total frames for the stance phase with each corresponding peak GRF, LR, and Impulse (Newtons). The peak GRF was extracted as the maximum value from the waveform, the LR was the linear slope between 3 and 12% of stance, and impulse was extracted using trapezoidal integration for area under the curve.

3.8 « Statistical Analysis »

SPSS Version 25 (IBM, Armonk, NY) was used to complete all statistical analyses. Descriptive statistics were calculated for all outcomes and the Shapiro-Wilk test assessed for normality and screened for outliers. Intraclass correlation was used to establish intra-rater ($ICC_{2,1}$) and interrater reliability ($ICC_{2,k}$) from preliminary data collection (n=5; 3 images per rater). Cartilage thickness was compared between running conditions with a 2 (condition) x 2 (time) ANOVA with repeated measures, and post hoc comparisons were made using a Bonferroni correction (Family-wise α=0.05). Pearson correlation assessed the association between kinetic outcomes and the change in cartilage thickness in each condition (α=0.05). While not an aim of the study, GRF characteristics were compared between sessions using paired samples t-tests to confirm a difference in loading magnitude.

Chapter 4

4 « Results »

4.1 « Demographic Information »

All data were normally distributed, and no outliers were identified. Descriptive statistics of demographic information can be found in Table 1. Self reported personal bests in primary events ranged from the 800m to the 10,000m. Warmup and recovery interval pace for the interval trial averaged 4:57 minutes per kilometer (12.12 ± 0.50KPH, 3.37 ± 0.14m/s) for males and 5:18 minutes per kilometer (11.28 ± 0.69KPH, 3.13 ± 0.19m/s) for females. Average interval running paces ranged from 2:45 to 3:13 minutes per kilometer (21.70KPH, 6.03m/s to 18.60KPH, 5.17m/s) for men and 3:11 to 3:46 minutes per kilometer (18.80KPH, 5.22m/s to 15.88KPH, 4.41m/s) for women. Self-selected continuous running pace ranged from 4:20 to 4:45 minutes per kilometer (13.80KPH, 3.83m/s to 12.60KPH, 3.50m/s) for males and 4:30 to 5:00 minutes per kilometers (13.30KPH, 3.69m/s to 12.00KPH, 3.33m/s) for females. Baseline cartilage measurements were thinner in females compared with males (Appendix D), which was expected. However, sex did not uniquely influence the response to interventions (Appendix D), and we proceeded with intended analyses to preserve statistical power.

Table 1: Demographic Information (Mean ± Standard Deviation)

	Male (n=13)	Female (n=11)
Age (years)	20.62 ± 1.82	22.91 ± 3.42
Height (cm)	178.35 ± 4.99	166.75 ± 5.48
Mass (kg)	71.14 ± 5.98	56.47 ± 5.80
Weekly Running Amount (Km)	83.46 ± 17.14	72.45 ± 16.16
1500m PB (WA scoring tables points)	878.69 ± 93.42	924.18 ± 106.95
1500m PB (sec)	239.27 ± 7.82	278.14 ± 16.70
Average Continuous Run Pace (KPH)	13.20 ± 0.30	12.44 ± 0.48
Average Continuous Run Pace (m/s)	3.67 ± 0.08	3.46 ± 0.13
Average Interval Run Pace (KPH)	19.93 ± 0.88	17.28 ± 0.95
Average Interval Run Pace (m/s)	5.54 ± 0.24	4.80 ± 0.26

WA: World Athletics

Table 2: Intra- and inter- rater reliability and 95% confidence interval analyses from preliminary data (n=5 participants; 3 images per participant).

	Intra rater ($ICC_{2,1}$)	Inter rater ($ICC_{2,k}$)
Medial thickness (mm)	0.858 (0.481, 0.983)	0.920 (0.235, 0.992)
Central thickness (mm)	0.952 (0.786, 0.995)	0.940 (0.425, 0.994)
Lateral thickness (mm)	0.947 (0.766, 0.994)	0.971 (0.724, 0.997)

4.2 « Cartilage Outcomes »

Baseline cartilage thickness did not differ between sessions for any region of measurement, and preliminary data suggested excellent intra- and inter- rater reliability (Table 2). The condition by time interaction effect was not significant for medial cartilage thickness ($F_{1,23}$=0.556, p=0.463). There was a significant main effect of time ($F_{1,23}$=14.029, p=0.001). Collapsed across condition, cartilage was thinner after running compared with baseline (1.92 (1.82, 2.02) vs. 1.83 (1.73, 1.93) mm; Mean Difference=-0.094 (-0.147, -0.042) mm, p=0.001, partial η^2=0.379).

The condition by time interaction effect was significant for lateral cartilage thickness ($F_{1,23}$=10.839, p=0.003, partial η^2=0.320). Post hoc comparisons demonstrated a significant difference between conditions in post running cartilage measurements (Mean difference=0.062 (0.014, 0.042) mm, p=0.014, d=0.545) where the interval condition showed smaller post-run cartilage than after continuous running, and significant reduction in thickness from pre to post run in the interval condition (Mean difference=0.057 (0.012, 0.103) mm, p=0.015, d=0.535) (Table 3).

There was no significant condition by time interaction ($F_{1,23}$=0.864, p=0.362), main effect of time ($F_{1,23}$=3.475, p=0.075), or main effect of condition ($F_{1,23}$=0.005, p=0.942) for central cartilage thickness.

Table 3: Descriptive Statistics of Cartilage Thickness Pre and Post Interval and Continuous Running Trials (Mean ± Standard Deviation)

	Interval Running		Continuous Running		P value		
	Pre	Post	Pre	Post	Condition x time	Condition (main effect)	Time (main effect)
Medial (mm)	1.92 ±0.25	1.84 ±0.26	1.92 ±0.24	1.81 ±0.23	0.463	0.431	0.001
Central (mm)	2.28 ±0.29	2.33 ±0.34	2.29 ±0.29	2.31 ±0.29	0.362	0.942	0.075
Lateral (mm)	2.02 ±0.32	1.96 ±0.30	2.00 ±0.32	2.02 ±0.31	0.003	0.125	0.234

4.3 « Kinetic Variables »

All kinetic variables differed between the interval and continuous running conditions (Table 4, Figure 7). Paired sample T-Tests revealed that peak GRF ($p=0.011$) and LR ($p<0.001$) were significantly higher in the interval running compared with the continuous condition. The impulse ($p<0.001$) was significantly higher in the continuous compared with interval running condition.

Table 4: Paired Sample T-Test Statistics (Mean ± Standard Deviation)

	Interval	Continuous	Mean Difference	p	d
Peak GRF (BW)	2.96 ± 0.38	2.89 ± 0.35	0.068 ± 0.120	0.011	0.564
Loading Rate (BW/S)	59.86 ± 13.91	51.92 ± 9.05	7.940 ± 8.665	<0.001	0.916
Impulse (BW·S)	0.34 ± 0.03	0.38 ± 0.03	0.012 ± 0.01	<0.001	1.355

GRF: Ground Reaction Force, BW: Body Weight

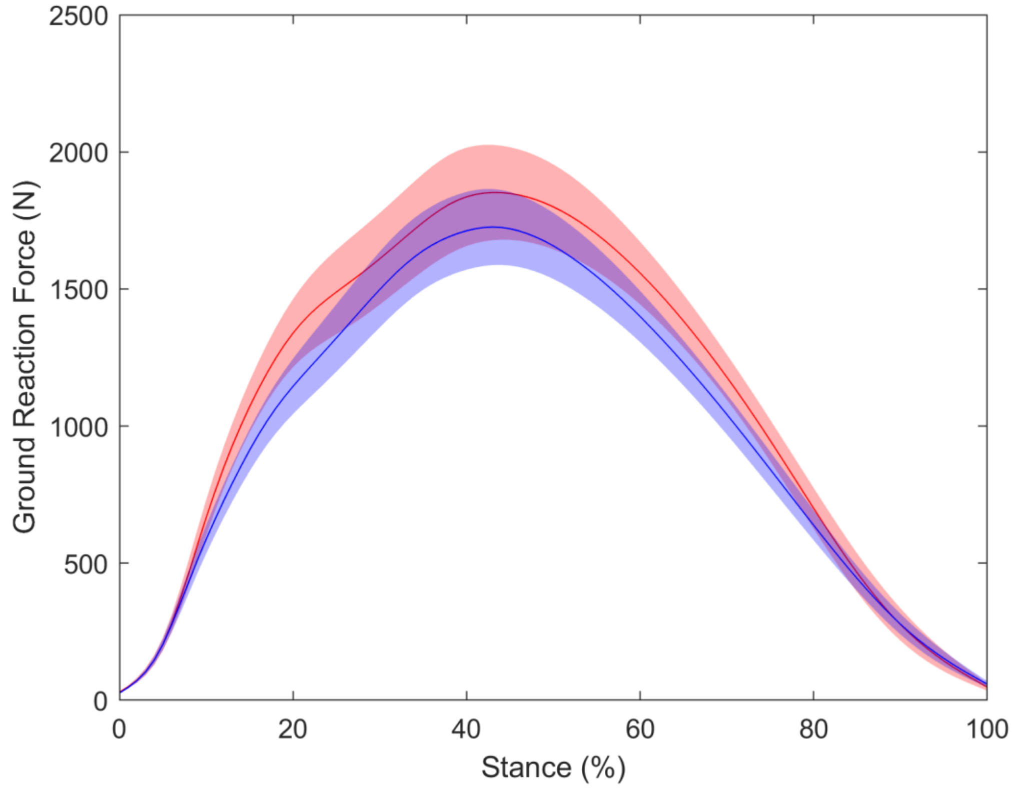

Figure 7: Ensemble Ground Reaction Force Waveform Average and 95% Confidence Interval; Red is the interval session and blue is the continuous session.

4.4 « Correlations »

No associations were found between peak GRF, LR, and Impulse and changes in central medial and lateral cartilage thickness values for both continuous and interval running conditions (all p>0.05, Table 5).

Table 5: Correlation and P-values for Kinetics Variables and Change in Cartilage Compartment Thickness for Continuous and Interval Running Sessions

	Medial Thickness		**Central Thickness**		**Lateral Thickness**	
	Continuous	Interval	Continuous	Interval	Continuous	Interval
Peak GRF	0.199 (p=0.351)	0.019 (p=0.931)	0.312 (p=0.146)	-0.004 (p=0.984)	0.008 (p=0.970)	-0.097 (p=0.653)
Loading Rate	0.017 (p=0.936)	-0.105 (p=0.624)	0.255 (p=0.229)	-0.051 (p=0.814)	0.060 (p=0.779)	-0.167 (p=0.436)
Impulse	0.206 (p=0.334)	-0.093 (p=0.665)	0.213 (p=0.318)	0.293 (p=0.165)	0.003 (p=0.990)	0.038 (p=0.858)

GRF: Ground Reaction Force

Chapter 5

5 « Discussion »

The purpose of this study was to investigate the influence of running type on acute femoral cartilage deformation in competitive runners. Our first hypothesis was that there would be greater acute cartilage deformation following a high-intensity interval running session compared to a continuous running session. This hypothesis was partially supported as there was greater acute deformation of the lateral cartilage following the interval running condition, but no effect was observed during the continuous running condition. A significant main effect of time was present when collapsed across conditions in the medial cartilage compartment demonstrating thinner cartilage after running regardless of condition.

Our second hypothesis was that the magnitude of acute cartilage deformation would be associated with the LR experienced with high intensity interval running, which was not supported. The peak GRF and vertical LR were significantly higher in the interval running condition while impulse was significantly higher in the continuous running condition. Despite a difference between conditions, there were no significant associations found between running kinetics and acute cartilage deformation for the interval or continuous running conditions.

High-intensity interval running is common among competitive runners, and most research in this area has examined recreational running activities. However, this is the first study, to our knowledge, to examine the influence of high-intensity interval running on cartilage deformation in a group of highly trained middle- and long-distance runners.

5.1 « Cartilage Deformation After Running »

Our main finding was that lateral femoral cartilage deformation was greater after the high-intensity interval running session compared to the continuous running session, which supported our hypotheses. As such, high-intensity interval running with faster running speeds may have contributed to greater lateral joint stress compared with continuous running.[29,30] Previous studies have observed acute cartilage deformation following running of up to 5.7% in some regions of knee joint cartilage.[34,96,137] High LRs during interval running may contribute to cartilage matrix damage from the increase in strain it exerts on the matrix.[29,30] Similarly, faster running speed also contributes to greater PFJS and patellofemoral LR.[22,112] The interval running session was faster than the continuous running condition, and resulted in more acute lateral cartilage deformation, possibly from greater patellofemoral joint stress that increased tissue strain. This increased acute cartilage deformation occurs from interstitial fluid leaving the matrix temporarily after loading.[29,30,96,138] Therefore, the deformation is transient as fluid re-enters the matrix immediately following loading.[34,96,137,138] Repeated exposure to interval running without adequate recovery time could contribute to insufficient time for fluid to re-enter the matrix. More research is needed on the effects of tissue recovery and repeated exposure to interval running.

There was a similar acute reduction in medial cartilage thickness following both running conditions. Joint kinematics during interval running may have contributed to the disparity in findings between the medial and lateral regions. For example, faster running speed is associated with greater knee flexion,[20,119] which may contribute to additional PFJS and force.[22,139,140] As the knee flexes, the distal end of the patella contacts the lateral aspect of the femur.[111] This may create an uneven distribution of load and increase stress to the lateral aspect of the patellofemoral joint,[111,114] and could contribute to an explanation for our findings. Additionally, the VL muscle provides a lateral pull to the patellae that may increase the lateral joint contact force during running at faster speeds.[111] When the VL is activated during running, the lateral pull and resulting lateral PFJS may increase. Previous research found that greater lateral compressive stress was associated with greater lateral femoral cartilage deformation when measured with MRI after a 5000-step run in recreational runners.[34] As such, the interval running in our study may have required greater contribution from the quadriceps, which would increase the amount of lateral PFJS and lateral femoral trochlear cartilage deformation with no additional stress placed on the medial region.[32,34] Collectively, high amount of knee flexion combined with pull from the VL during faster running in the interval session could have redistributed the patellofemoral joint stress laterally. This may have increased the focal stress and explain the greater amount of acute lateral femoral trochlear cartilage deformation following faster interval compared with slower continuous running.

Finally, there was no significant acute change in the central region of cartilage after running in either condition. It is possible that the anatomy of the joint allows for reduced contact to the central region. The depth of the trochlear grove and greater gap between the femoral condyles may allow for reduced contact stress on this region during running.[32] The points of contact between the patella and femur may be primarily on the medial and lateral edges of the femoral condyles, which elevates loading to these regions.[32,34]

Mechanical loading is necessary for maintenance of cartilage health.[62] The acute cartilage deformation following running in this study could be beneficial by facilitating nutrient diffusion through the permeable matrix.[62] Therefore, positive cartilage adaptations could occur from habitual running with sufficient recovery time,[33,65] which may contribute to healthier cartilage and reduce the risk of knee OA.[33,57,58] For instance, consistent loading is associated with greater proteoglycan content and integrity of the collagen matrix that may improve compressive and tensile resistance, respectively.[97,102,103] However, cartilage damage could occur without adequate recovery or under higher levels of joint stress.[29,34,38,126–128] A previous report indicates that the medial knee cartilage would be unlikely to withstand a lifetimes worth of mechanical loading from running without positive adaptations from mechanosensitive cells that can extend the fatigue life of cartilage.[38] Positive cartilage adaptations may not occur if the intensity and frequency of the stress placed on the joints exceeds its tolerance.[29,30,62] Interval running could provide an intensity where repeated exposure in competitive runners may exceed joint tolerance if adequate rest is not provided. As such, faster and high-intensity interval running may contribute to the discrepancy in OA prevalence in elite compared with recreational runners/athletes.[24,33,60] Therefore, mechanical stress from consistent slower continuous running may be beneficial, but high joint stress from interval and faster-pace running without adequate recovery may be detrimental to joint health.

5.2 « Implications for Patellofemoral Pain and Osteoarthritis »

High PFJS and impact loading has been reported in runners with PFP compared to those without.[122,141] Similarly, our findings demonstrated that faster interval running caused greater acute deformation to the lateral patellofemoral joint. Interval running may exacerbate symptoms in runners with PFP who have biomechanical and anatomical differences than those without PFP. [7,25,111] This indicates a connection between our findings after fast interval running and previous PFP reports. For example, those with PFP present characteristics such as malalignment, altered patella shapes, [7,25,111] varying muscle forces,[116,117] and muscle activation ratios,[32,115,118] muscle onset timing, and muscle contributions that all may contribute to laterally directed increase in PFJS. Moreover, faster running speed is a contributing factor to PFP in runners due to high stress placed on the joint.[22,28] Our finding that high-intensity interval running compared to slower continuous running caused more acute lateral femoral cartilage deformation suggests that interval running should be avoided in runners with PFP.

It is also possible that engaging in interval running may contribute to the onset of PFP symptoms from increased stress on the lateral patellofemoral joint compartment. Previous reports indicate higher joint stress and impact loading in runners with PFP than those without,[141] and running speed could be a contributing factor.[22] Increases in step length occur with increased running speed,[119,142] and contribute to higher patellofemoral joint kinetics.[121] The thinner lateral cartilage after interval running suggests that the lateral portion of the patellofemoral joint received additional loading. As such, interval running in our study can be linked to previous research in runners with PFP and could contribute to the onset of PFP. Patellofemoral pain may also contribute to future patellofemoral OA.[7] Therefore, repeated exposure to interval running without adequate recovery time for cartilage may contribute to lateral patellofemoral joint cartilage matrix damage and contribute to knee OA progression. This signifies the need for information on how repeated exposure to faster running over time contributes to cartilage health.

5.3 « Running Kinetics and Cartilage »

Our secondary hypothesis was that the magnitude of acute cartilage deformation would be associated with the vertical LR during high intensity interval running. We based this hypothesis on results from previous studies that noted cartilage deformation was affected by LR in animal models,[29,30] and attempted to apply these theories to human models. As expected, the vertical LR and peak GRF were higher in the interval running, likely due to faster running speed.[22,27] However, there were no associations with acute cartilage deformation and GRF variables in this study despite a significant difference between running conditions for the peak GRF, LR, and impulse.

The lack of association between running kinetics and cartilage outcomes could be attributed to lack of specificity in kinetic outcomes. Force data were collected at the foot using pressure-sensing insoles that measured normal plantar force data to provide surrogates of GRFs applied to the entire body. Therefore, these outcomes may not reflect forces exerted to the knee where cartilage measurements were obtained.[31,41,119] Distal to proximal dissipation of force occurs throughout the leg through tissues like muscles and tendons, and through joint motions (e.g., plantar flexion) before reaching the knee.[119] Foot strike pattern could have changed between session for some participants from a rearfoot to more forefoot when increasing running speed.[27] A more anterior foot strike compared to rearfoot strike reduces the vertical LR and for some, may have contributed reduced patellofemoral joint stress.[27] For this reason, our hypothesis of patellofemoral joint contact stress contributing to cartilage deformation may not be best evaluated by force measurements at the foot.[31,41,119] The normal plantar force measured by the Loadsols were placed in the shoe for measurement rather than a force plate measuring from the outside of the shoe. This differs from previous literature which typically has measured GRFs rather than normal force from a force plate outside of the shoe.

Secondly, the sampling frequency used in data collection may influence measurement precision of kinetic outcomes. The Loadsol is valid and reliable for measuring GRF data in running.[133,134] However, our data were sampled at a frequency of 100Hz, which exceeds the natural frequency of the vertical GRF and has exceptional agreement when extracting the peak value.[133–135] However, sampling at 100Hz may influence the precision of the LR, due to its sensitivity from quickly occurring peak forces.[135] The LR occurs immediately after impact and a lower sampling frequency may fail to record important data points related to the initial rise in GRF (e.g., impact peak). Nonetheless, we still observed a consistently higher LR in the interval compared with continuous condition, but LRs may be better captured if recorded at higher sampling frequencies.[133–135]

It is also possible that the lack of associations could be due to the methodology of protocol design and timing of the GRF sampling. The continuous running protocol consisted of one continuous run, while the interval running condition had periods of rest (decrease in speed) between intense running bouts. The GRF samples for the interval running sessions occurred during the intense running bouts. It may be that the rest periods utilized after each interval allowed the cartilage to recover briefly and reduce the magnitude of observed deformation. Previous reports indicated that combinations of slow and fast running compared to running at one pace, contribute to higher estimates of cumulative vertical average LR.[143] Therefore, it is possible that the interval running session contributed to more cumulative loading despite including rest intervals compared to the continuous condition.[143]

5.4 « Strengths and Limitations »

Study strengths included a sample of competitive distance and middle distance runners that may be at higher risk of OA compared with recreational runners.[15,24] Competitive runners typically engage in variations of continuous running and high-intensity interval running throughout their training and our interval running session was meant to replicate a track workout they would typically complete.[21] Additionally, we were able to control a variety of confounding factors such as footwear, running surface, and running environment (e.g., air temperature) by conducting research in a laboratory setting to maintain high internal control. The within subjects' study design negated between subject differences such as height, weight, sex, and running ability level. The order of interventions was counterbalanced for participants to remove order effects. Furthermore, image segmentation for cartilage outcomes was completed by an investigator that was blinded to intervention order and measurement point (pre or post) to mitigate bias during analysis.

There are also limitations to consider when evaluating the findings of this study. The use of a 3-dimensional motion capture system with a force instrumented treadmill could have provided precise kinetic measurements that could differ between running conditions (e.g., patellofemoral contact force).[135] Secondly, we did not monitor changes in foot strike pattern between sessions which could have influenced our kinetic outcomes,[27] and contributed to the lack of association between kinetics and cartilage deformation. Furthermore, ultrasound imaging of cartilage is limited by the view of the probe and position of the knee. This imaging method cannot be applied to all articulations of the knee including the tibiofemoral articulation and patellar cartilage. Magnetic resonance imaging could have provided the most accurate measurement of each compartment's cartilage at the knee joint along with information on cartilage composition, water content, and T_{1p} and T_2 relaxation times.

We controlled for some variables to increase the internal validity of our study that may not reflect habitual training. For instance, participants wore the same pair of shoes for both running sessions. Competitive runners often use different footwear such as standard running shoes, racing flats, and spiked footwear.[144] Footwear may influence running biomechanics and alter joint loading.[144,145] The prescription of running paces were all relative to participants' personal best time and self-selected typical running paces rather than physiologically determined pace for both sessions. This was done so that each participant underwent the same relative effort as they would in habitual workouts and was successful in differentiating GRF characteristics. Finally, participants ran on a treadmill for both sessions, which may alter running mechanics compared to running outdoors or on a track.

5.5 « Conclusion »

Findings demonstrate that high-intensity interval running compared to slower continuous running resulted in an acute deformation of the lateral femoral trochlear cartilage. Moreover, there was a similar acute medial femoral trochlear cartilage deformation between running conditions. High-intensity interval running also had greater vertical LRs and peak GRFs than slower continuous running, but kinetic outcomes were not associated with acute femoral cartilage deformation. Runners with or recovering from PFP symptoms should avoid interval running sessions that contribute to greater cartilage deformation and may exacerbate symptoms.

Longitudinal data are needed to determine if repeated exposure to interval running contributes to long-term damage to the joint. This may elucidate the mechanisms by which competitive runners are at greater risk for knee OA. Furthermore, determining the adequate recovery time needed for cartilage to return to baseline measures after different running intensities would be beneficial. These data would facilitate training and competition schedules that optimize tissue recovery, joint health and running performance.

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Appendices

Appendix A: Data Collection Form

Running intensity and cartilage thickness in competitive runners

Data Collection Sheet

Date:

Database ID:

Assessors Staff ID:

Age: Sex: Height: Mass: Primary Event:

Weekly Running Amount:

Personal Bests:

Dominant Limb:

Trial order (circle first completed):

Steady State Run / Interval Running Trial

Steady State-Run Visit

Pre-run Imaging (check completed) (140 degrees, 12 MHz, Gain: 50, Depth 4cm)

Cartilage	Image 1	Image 2	Image 3
Left			
Right			

Steady State Run

Self-Selected 3km warmup running pace:

Predetermined 7km steady state running pace:

2km cooldown running pace:

Post-run Imaging (check completed) (140 degrees, 12 MHz, Gain: 50, Depth 4cm)

Cartilage	Image 1	Image 2	Image 3
Left			
Right			

Notes:

Steady State Pace (Km/h): **Km/min:**

Distance	Stay/Sample	Check	Sample Number
0.0 to 2.5 km	Stay		
2.5 km	Sample 30s		1
2.5 to 3.5 km	Stay		
3.5 km	Sample 30s		2
3.5 to 4.5km	Stay		
4.5 km	Sample 30s		3
4.5 to 5.5 km	Stay		
5.5 km	Sample 30s		4
5.5 to 6.5 km	Stay		
6.5 km	Sample 30s		5
6.5 to 7km	Stay		

Interval Running Trial

Pre-run Imaging (check completed) (140 degrees, 12 MHz, Gain: 50, Depth 4cm)

Cartilage	Image 1	Image 2	Image 3
Left			
Right			

Interval Running

Self-Selected 3km warmup running pace:

Predetermined 10x400m repetition running pace:

Predetermined 200m recovery running pace:

2km cooldown running pace:

Interval Repetition Pace Checklist

400m Repetition	1	2	3	4	5	6	7	8	9	10
Pace (km/h)										

Recovery Repetition Pace Checklist

300m Repetition	1	2	3	4	5	6	7	8	9	10
Pace (km/h)										

Post-run Imaging (check completed) (140 degrees, 12 MHz, Gain: 50, Depth 4cm)

Cartilage	Image 1	Image 2	Image 3
Left			
Right			

Notes:

Interval Pace (Km/h): **Km/min:**

Recovery Pace (Km/h): **Km/min:**

Distance	Sample/Speed Change	Check	Int Number
0.0 to 0.05km	Increase to first Int speed		
0.25km	**Sample 15s**		
0.45km	Speed Change Down		1
0.7km	Speed Change Up		
0.95km	**Sample 15s**		
1.15km	Speed Change Down		2
1.4km	Speed Change up		
1.65km	**Sample 15s**		
1.85km	Speed Change Down		3
2.1km	Speed Change Up		
2.35km	**Sample 15s**		
2.55km	Speed Change Down		4
2.8km	Speed Change Up		
3.05km	**Sample 15s**		
3.25km	Speed Change Down		5
3.5km	Change Speed Up		
3.75km	**Sample 15s**		
3.95km	Change Speed Down		6
4.2km	Change Speed Up		
4.45km	**Sample 15s**		
4.65km	Change Speed Down		7
4.9km	Change Speed Up		
5.15km	**Sample 15s**		
5.35km	Change Speed Down		8
5.6km	Change Speed Up		
5.85km	**Sample 15s**		
6.05km	Change Speed Down		9
6.3km	Change Speed up		
6.55km	**Sample 15s**		
6.75km	Change Speed Down		10
7.0km	Final Rest Interval		
7.0km	End Protocol (50m to decrease speed)		

Appendix B: Letter of Information and Consent Form

1

Running intensity and cartilage thickness in competitive runners

Principle Investigator:

Derek Pamukoff, Ph.D

[redacted]

Co-Investigator

Ryan Evans, Graduate Student

[redacted]

Funding Source:

Conflict of Interest: There are no conflicts of interest to declare related to this study

Introduction:

- You are being invited to participate in this student research study about the influence of running intensity on cartilage thickness using ultrasound imaging
- You are being invited as a possible participant because you are between the ages of 18-35 years, a distance or middle-distance runner competing in the 800m to the 10 000m within the last 12 months
- It is asked that you read this form in its entirety to ask any possible questions before agreeing to participate in the study.

Purpose of Study:

- The purpose of this study is to investigate the influence of running type on knee cartilage strain in competitive runners.
- Participants in the study are from local track and field clubs, running groups, and the Western University track and field team.
- We expect up to 24 participants to take part in this study expected to take 2 weeks to complete.

Description of the Study Procedures

If you agree to participate, you will be asked to visit the biomechanics testing laboratory for two sessions in Thames Hall at Western University. Each session will last for approximately 90-120 minutes and there will be one week between each visit. The two visits will consist of a steady state easy run, and a high intensity interval running workout on a standard treadmill with pressure sensing insoles in your shoes. Each running trial visit will also have additional ultrasound imaging to obtain measures of knee cartilage.

The following experimental procedures will be carried out.

Ultrasound imaging: On the day of collection, you will be asked to refrain from any physical activity prior to the test. Upon arrival, you will lay down on your back with full lower limb extension on a physio table for 30 minutes to unload any weight bearing effects on the cartilage. Your knees will then be positioned in 140 degrees of flexion by the investigator for imaging to obtain a clear view of the knee joint. A goniometer will be placed at the center of the knee joint to make the 140-degree angle between the ankle and the side of the hip. The ultrasound probe will be positioned in between the on the top of the knee and above the kneecap to obtain 3 images of the knee cartilage. Image procedures will be repeated for both legs. Imaging will take place each session, once prior to each session upon arrival, directly after both the steady state and interval running trials, and again after the protocol for each trial.

Warm up and Cooldown Protocol: Using a standard single belt LifeFitness treadmill with pressure sensing insoles in your shoes (Loadsols), you will run at a self-selected running speed. Warmup distance will be controlled for and total 3 kilometers of running. You will then have three minutes of rest before beginning the running trials. This same warmup protocol will follow before the steady state, and interval running conditions. The cooldown will take place at the end of each running trial at the same self selected running speed as the warmup. Distance will again be controlled for at a total of 2 kilometers.

Steady State Running Trial: The steady state running condition will be performed on the same treadmill with the pressure sensing insoles, loadsols. The trials will be performed at your self selected typical easy run pace. The trial will conclude when you have completed a total of 7 continuous kilometers.

Interval Running Trial: The interval running trial is intended to mimic a typical workout for a 1600m to 2000m runner. Upon completing the warmup protocol, you will then complete 10 x 400m with 300m recovery jog between the reps. The 400m repetitions are to be completed at 85 to 90% of your personal best 1500m pace per 400m, while the recovery runs are to be done at the same self-selected pace as your warmup runs, to allow for proper recovery. During the recovery period, you will have the running pace reduced to the recovery pace before increasing the pace once again for the next repetition. The first and last 50 meters of the recovery interval are to allow for the treadmill to adjust speeds so that an entire 200 meters of the recovery will be at the proper pace. The total accumulated distance of running is 7km. The trial will conclude when you complete the final 400m repetition and 300m jog recovery.

Timeline for Testing Procedures and Protocol

Activity	Expected Time (minutes)
Consent	30
Ultrasound imaging	35
Running trials	45
Ultrasound imaging	5
Total Time	115

Risks/Discomforts of being in the Study:

- There are no known risks associated with diagnostic ultrasound imaging.
- The running trials offer no additional risk to the participants that they would experience outside of their own training and daily life encounters.
- Participation is entirely voluntary, and you may withdraw at any time.
- There may be additional risks to this study that are presently unknown.

Benefits of Being in the Study:

- You will be contributing to the understanding of how knee cartilage reacts to different running intensities in competitive level distance and middle-distance runners.

Voluntary Participation/Withdrawal:

- Participation in this study is completely voluntary. You can choose to either not be in this study entirely, or to be in the study now and then change your decision at a later time. You have the right to leave the study at any time with no affect on your relations with study team personnel or the University presently or in the future.
- Participants have the right to withdraw their study data and any and will not lose compensation for doing so however, a record of participation (i.e. signed consent form and names on master list) will remain.
- Choosing to not participate in the study will in no way affect your standing on the track and field team nor grade in any class.

Dismissal From the Study:

- Your participation in the study may end at any time for any of the following reasons: (1) it is in your best interest or, (2) failure to complete or attend each of the three visits (i.e. you have not met the research requirements).

Rights of Study Participants:

- You may withdraw from the study at any time.
- The investigators will do everything they can to help you in any event that may result in any harm experienced.

Costs and Compensation to Participate:

- There are no costs for you associated with your participation in this study.
- For your participation you will receive $20 for each visit.

Contacts and Questions:

- Derek Pamukoff is the primary investigator on this study and the student co investigator is Ryan Evans. If there are any questions or additional information needed regarding this study, you can contact Derek Pamukoff at [redacted] or Ryan Evans at [redacted]
- If you feel you have suffered an injury related to the research, contact Derek Pamukoff at [redacted] for further instructions.

- For information regarding your rights as a participant or the study, you can contact The Office of Human Research Ethics [redacted] email: [redacted] The REB oversees the ethics of research studies and the HSREB is not included as part of the study team.

Confidentiality and Privacy

- Collected data will include demographic information such as age, sex, height, mass, primary track event, weekly running amount, and personal bests. Further information regarding the running paces of the trials, images of knee cartilage and 3D motion capture video will also be collected.
- All data will be stored electronically via Western Universities institutional drive and OneDrive, non electronic data will be stored in the office of the PI (TH 4178).
- Identifiable data will only be able to be accessed by Derek Pamukoff (PI), Ryan Evans (Research Assistant), and the Western University Health Sciences Research Ethics Board
- Identifiable data includes name, email address, sex, age, height, mass, primary track event, personal bests, cartilage images, and 3D motion capture video.
- All identifiable data will be retained for 7 years as per Western University policy after which all hard copies of consent forms will be shredded. Electronic data will be erased using FileShredder using a standard DoD (5220-22.M 3 pass) method of erasing data.

Copy of Consent Form:

You will be given a copy of this form to keep for your records and future reference.

Informed Consent to Participate in the Research Study:
Influence of running intensity on cartilage thickness using ultrasound imaging

Principle Investigator:
Derek Pamukoff, Ph.D
[redacted]

Co-Investigator:
Ryan Evans, Graduate Student
[redacted]

CONTACT FOR FUTURE STUDIES:

Please check the appropriate box below and initial:

___ I agree to be contacted for future research studies

___ I do NOT agree to be contacted for future research studies

I have read the Informed Consent to participate in the study described above, have had the nature of the study explained to me and I agree to participate. All questions have been answered to my satisfaction. I know that I may leave the study at any time. I agree to take part in this study.

Print Name of Person	Signature	Date (DD-MM-YYYY)

My signature means that I have explained the study to the participant named above. I have answered all questions.

Print Name of Person Obtaining Consent	Signature	Date (DD-MM-YYYY)

Appendix C: Ethics Approval Letter

Western Research

Date: 21 November 2022

To: Dr Derek Pamukoff

Project ID: 121330

Review Reference: 2022-121330-73323

Study Title: The influence of running intensity on cartilage thickness in competitive runners

Application Type: HSREB Amendment Form

Review Type: Delegated

Full Board Reporting Date: 13/Dec/2022

Date Approval Issued: 21/Nov/2022 15:21

REB Approval Expiry Date: 18/Oct/2023

Dear Dr Derek Pamukoff ,

The Western University Health Sciences Research Ethics Board (HSREB) has reviewed and approved the WREM application form for the amendment, as of the date noted above.

Documents Approved:

Document Name	Document Type	Document Date
Ryan Evans - Research Protocol, Amendment	Protocol	13/Nov/2022
Ryan Evans - Consent Form, Amendment	Consent Form	13/Nov/2022
Ryan Evans - Data Collection Sheet, Amendment	Other Data Collection Instruments	13/Nov/2022
Recruitment poster, Ryan Evans, Amendment	Recruitment Materials	13/Nov/2022
Recruitment email, Ryan Evans, Amendment	Recruitment Materials	13/Nov/2022

REB members involved in the research project do not participate in the review, discussion or decision.

The Western University HSREB operates in compliance with, and is constituted in accordance with, the requirements of the TriCouncil Policy Statement: Ethical Conduct for Research Involving Humans (TCPS 2); the International Conference on Harmonisation Good Clinical Practice Consolidated Guideline (ICH GCP); Part C, Division 5 of the Food and Drug Regulations; Part 4 of the Natural Health Products Regulations; Part 3 of the Medical Devices Regulations and the provisions of the Ontario Personal Health Information Protection Act (PHIPA 2004) and its applicable regulations. The HSREB is registered with the U.S. Department of Health & Human Services under the IRB registration number IRB 00000940.

Please do not hesitate to contact us if you have any questions.

Electronically signed by:

Karen Gopaul , Ethics Officer on behalf of Dr. Roberta Berard, HSREB Vice-Chair, 21/Nov/2022 15:21

Reason: I am approving this document.

Note: This correspondence includes an electronic signature (validation and approval via an online system that is compliant with all regulations).

Appendix D: Sex-Included Model for Cartilage Characteristics

Effect of interval versus continuous running on cartilage deformation with sex included as co-variate in model. Analyses suggest no interaction between sex and condition, or sex and time, or a 3-way interaction between condition sex and time. Main effects of sex were observed and expected indicating smaller central and lateral cartilage in females compared with males at all measurement points.

	Interval Running		**Continuous Running**		**P value**						
					Interaction Effects				**Main effects**		
	Pre	Post	Pre	Post	Condition x time x sex	Condition x time	Condition x sex	Time x sex	Condition	Time	Sex
Medial (mm)	1.92 ±0.25	1.84 ±0.26	1.92 ±0.24	1.81 ±0.23	0.126	0.115	0.576	0.115	0.345	0.004	0.064
Central (mm)	2.28 ±0.29	2.33 ±0.34	2.30 ±0.29	2.31 ±0.29	0.407	0.224	0.608	0.837	0.767	0.152	0.035
Lateral (mm)	2.02 ±0.32	1.96 ±0.30	2.00 ±0.32	2.02 ±0.31	0.377	0.006	0.575	0.886	0.138	0.443	<0.001

Curriculum Vitae

Academic History

Western University, Master of Integrative Biosciences in Kinesiology (Biomechanics), 2021-2023

Thesis – Influence of High Intensity Interval Running on Knee Cartilage Deformation in Competitive Runners

Western University, Bachelor of Science, Honours Specialization in Kinesiology, 2017-2021

Academic Accomplishments/Research Contributions

Publications:

- **Evans RJ**, Mitchell PK, Moffit TJ, Pamukoff DN. *Biomechanical Differences Between Recreational and Collegiate Runners.* In Preparation (Draft Available). Target Journal: Sports Biomechanics

- Battersby HS, **Evans RJ**, Eghobamien IJ, Pamukoff DN. *Measurement Position Influences Sex Comparisons of Distal Femoral Cartilage Thickness with Ultrasound Imaging.* In Preparation (Draft Available). Target Journal: Ultrasound of Biology and Medicine

- **Evans RJ**, Battersby HS, Williams L, Pamukoff DN. *Influence of High-Intensity Interval Running on Femoral Cartilage Deformation in Competitive Runners.* In Preparation (Draft Available). Target Journal: Journal of Sports Sciences

Presentations:

- **Evans RJ,** Mitchel PK, Moffit TJ, Pamukoff DN. Biomechanical Differences Between Recreational and Collegiate Runners. *American Society of Biomechanics.* Knoxville TN. August 10th, 2023. Poster Presentation.

- **Evans RJ**, Mitchell PK, Moffit TJ, Pamukoff DN. Biomechanical Differences Between Recreational and Collegiate Runners. *Western University Undergraduate Student Research Internship Research Output Conference.* London, ON. August 2021. Poster Presentation.

Experience

- **Teaching Assistantship:** KINESIOL 2241 Biomechanics, Western University Sept 2021-May 2023
    - Once to twice a month took up assignments in class to provide feedback and information to an introductory in biomechanics course. Also assisted with proctoring and marking assignments/ exams along with hosting office hours to provide individual feedback.

- **Teaching Assistantship:** KINESIOL 2222 Anatomy, Western University, Jan 2023-May 2023
    - Led two laboratory teaching sessions each week assisting students in learning basic introduction to anatomy. Also assisted with marking weekly lab quizzes and proctoring exams.

- **Research Assistantship:** Wolf Orthopedic Biomechanics Laboratory, Western University, June 2021-Present
    - Assist with data collection for ongoing biomechanics research.
    - Experienced gained using: Cortex motion capture software, Biodex Dynamometer, and Logiq E – Ultrasound.

- **Undergraduate Student Research Internship (USRI):** Western University, The Biomechanical Differences Between Recreational and Collegiate Runners, Poster, May 2021-Sept 2021

Funding and Support

- **Kinesiology Graduate Student Conference Travel Award:** Western University, $500 2023, Travel for American Society of Biomechanics Conference

Scholarships and Awards

- **Four Year Continuing Admissions Scholarship:** Western University, $2 500 2017, 2018, 2019, & 2020

- **Gordon Risk Award:** Western University, $1 000 2017, $700 2018, $ 1 000 2019 & 2020

- **James G Farmer Award:** Western University, $1 300 2018 & 2019

- **Returning Athletic Financial Awards:** Western University, $2 000 2020, 2021 & 2022

- **Undergraduate Student Research Internship:** Western University, $7 500 2021

- **UWO Admissions Bursary:** Western University, $1 300 2017

- **UWO Bursaries Kinesiology:** Western University, $1 000 2018, $1 500 2019

Other Academic Accolades

- **Dean's Honour List:** Western University, 2018, 2019, 2020, 2021 & 2022 (fall/winter)
- **Graduated with Distinction:** Western University, 2021
- **USports Academic All-Canadian:** Western University**,** 2018/19, 2019/20, 2020/21 & 2021/22
- **OUA All-Academic:** Western University**,** 2018/19, 2019/20, 2020/21 & 2021/22

Professional Society Memberships

American Society of Biomechanics: 2023-Present