The Effects of Lower Body Positive Pressure Treadmill Running on Acute Femoral Cartilage Deformation in Healthy Males and Females

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The Effects of Lower Body Positive Pressure Treadmill Running
on Acute Femoral Cartilage Deformation
in Healthy Males and Females

A Thesis
Presented to the Faculty of the
Department of Sports Medicine
West Chester University
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the Degree of
Master of Science

By
Megan Graff, LAT, ATC

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Abstract

The Effects of Lower Body Positive Pressure Treadmill Running on Acute Femoral Cartilage Deformation in Healthy Males and Females

By: Megan Graff, LAT, ATC

Chairperson: Nicole M. Cattano, PhD, LAT, ATC

Context: Lower body positive pressure treadmills (LBPPT) have been integrated into athletic performance and rehabilitation, but the physiologic and biomechanical effects of LBPPT unloading are not well known. As LBPPT use increases, it is imperative to know its effects on local joint cartilage. Assessing femoral cartilage deformation through ultrasonography after running on a LBPPT may provide a better understanding of effects on knee cartilage. Objective: Compare the effects of running at 100% and 80% body weight (BW) on a LBPPT on femoral articular cartilage and gait biomechanics between sexes and limbs in healthy, physically active participants. Design: Two group crossover. Setting: Division II University. Participants: 10 males and 10 females. Interventions: Independent variables included sex and running condition. Main Outcome Measures: Dependent variables were femoral cartilage deformation, vertical ground reaction force, and patient reported outcomes (PROs). Possible covariates included foot strike, mass, and height. Results: Data was analyzed using Pearson’s correlations, independent, and dependent T-tests. Femoral cartilage width significantly reduced after running at 100% BW. No significant reduction in femoral cartilage width in the majority of compartments after running at 80% BW. 100% BW had significantly greater reduction in cartilage width unilaterally compared to 80% BW. All biomechanical measures were significantly different between body weight trials. Females had significantly greater reductions in cartilage width unilaterally compared to males. PROs were negatively correlated with right cartilage percent change at both
conditions. **Conclusion:** Running at 80% BW on a LBPPT lead to reduced cartilage deformation and altered biomechanics compared to 100% BW.

**Key Words:** Alter-G, ultrasound, vertical ground reaction force, knee
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REVIEW OF LITERATURE

Osteoarthritis

Osteoarthritis (OA) is a degenerative condition of articular joints, most frequently affecting weight-bearing joints such as the knees and hips.\textsuperscript{1} The joint surfaces begin to degenerate over time, triggering a regenerative response in early OA.\textsuperscript{1} This attempt at regeneration results in bony outgrowths that compromise the typically smooth articular surface.\textsuperscript{1} This cycle leads to the eventual complete destruction of the cartilage and exposes the subchondral bone.\textsuperscript{1} OA is most frequently seen in the elderly population, therefore as life expectancies rise, the size of the elderly population grows, and the amount of people diagnosed with OA rises as well.\textsuperscript{2} OA is also the most predominant form of arthritis seen in the active population.\textsuperscript{1}

Knee OA is one of the most common sites for OA.\textsuperscript{1,3} Knee OA affects nearly 251 million people worldwide and is considered one of the top 15 causes of disability.\textsuperscript{4} Knee OA is associated with generalized joint stiffness, decreased range of motion and strength, contributing to decreased function.\textsuperscript{1} One of the largest risk factors outside of age is a major knee injury.\textsuperscript{1,3,5-7} Over 30\% of patients with anterior cruciate ligament (ACL) or meniscal injuries present with symptoms of knee OA within 5 years of their injury.\textsuperscript{8} This number increases to over 50\% in individuals 10 to 20 years post ACL or meniscal injury.\textsuperscript{9} Knee OA signs and symptoms include painful range of motion, crepitation with range of motion, joint effusion, lateral instability, valgus or varus deformity, and the presence of a Baker’s cyst.\textsuperscript{3}

The primary changes are the loss of articular cartilage, bony remodeling, and osteophyte formation in early OA, while synovial, capsular, ligamentous, and muscular changes are secondary.\textsuperscript{10} Initially the cartilage becomes softened and edema forms due to decreased capacity
of the matrix to bind or exclude water, this causes the matrix to expand, making it more susceptible to further damage.\(^2\) The softening of the cartilage leads to increased transmission of force to subchondral bone, resulting in increased stiffness and greater load being transmitted to the now compromised cartilage. OA progression is accelerated by the failure of the individual’s repair response.\(^2\) Irreversible damage will decrease repair capacity, ultimately contributing to further depletion and progressive structural damage.\(^2\)

Diagnosis. OA is diagnosed primarily using weight bearing radiographs and physical exam. The physical exam is specifically looking for local warmth, swelling, tenderness along the medial joint line, crepitus, and checking range of motion.\(^11\) Radiographs are used to grade the severity of OA, monitor it’s progression, as well as to rule out other possible pathologies.\(^2,3\) Clinicians will assess joint space width when looking at the radiographs, the joint space width should be noted, as well as any osteophyte formation, subchondral sclerosis, and cyst formation.\(^2,11\) The joint space width for the knee has been defined as the minimum distance between the femur and tibia in the medial femoral tibial compartment.\(^11\) Radiographic images are used to determine if the joint space has undergone narrowing, which would correlate to increased severity and further progression of the disease.\(^11\) There is some evidence that shows joint space width being a flawed method in the early stages of knee and hip OA because the joint space will only narrow once the disease has reached the erosive stage.\(^2\)

Earlier diagnosis is critical for possible intervention and management of OA. Specific magnetic resonance imaging (MRI) techniques may be used to examine the biochemistry of the extracellular matrix and assess and diagnose the early, predominantly biochemical stages of OA.\(^2\) However, this can be very costly. Some believe a computed topography (CT) arthrogram is more sensitive for detecting the early stages of OA, and that it is even superior to plain MRI for this.\(^12\)
High frequency ultrasound has also been thought of a tool for cartilage assessment, using wavelet magnitude and echo duration of the ultrasound to evaluate cartilage quality.²

Biomarkers have been identified as another way to potentially diagnose or check severity of OA or assess the effectiveness of a treatment or intervention. Biomarker has been defined by Lohmander and Eyre¹³ as “a structural or physical measure of cellular, molecular, or genetic change in a biologic process that can be identified and monitored, with resulting diagnostic or prognostic utility.”¹³ In other words, biomarkers are substances that can be measured to provide information about a change that has occurred within the body. Patient biomarkers can be assessed through such means as blood/serum, urine, or synovial fluid. Measuring biomarkers in OA patients would give insight into whether a specific treatment is working or not, this would be especially useful in the early stages of OA when most changes are biochemical prior to structural changes occurring.²

Biomarkers may be most beneficial in studying early OA. Markers of interest include C-telopeptide fragments of type II collagen, hyaluronan, collagen-II propeptides, and COMP. Markers of aggrecan turnover have shown great relevance diagnostically.¹⁴ C-telopeptide fragments of type II collagen (CTX-II) is a biomarker that has been comprehensively studied and has shown elevated levels in OA patients compared to healthy controls.¹⁴-²⁰ These elevated levels are consistent with clinical and radiological markers, making it a reliable tool in grading the severity and progression of hip and knee OA.¹⁴-²⁰ Hyaluronan correlates with OA and rheumatoid arthritis, and can be combined with CTX-II to be a measure for knee and hip progression.¹⁵,¹⁹,²¹,²²

There are multiple biomarkers that have been studied and shown to be elevated in OA, but due to their non-specificity must be interpreted cautiously. Systemic biomarkers, such as
from urine or serum, may not be isolated to what is occurring at a local joint. Collagen-II propeptides have been used to measure collagen-II synthesis and in studies have exhibited decreased levels in knee OA patients, however due to their serum source they are non-specific and could be exhibiting low levels due to decreased collagen-II synthesis in other joints and not the knee.\textsuperscript{2} C-reactive protein is an inflammation biomarker shown to be elevated in OA patients, but is not specific to the knee joint and it therefore not a reliable tool in assessing inflammation.\textsuperscript{2} Cartilage oligometric matrix protein (COMP) has been studied extensively and shown to have elevated serum levels in knee OA.\textsuperscript{2} Elevated baseline levels of COMP are associated with reduced cartilage volume and disease progression; however, COMP is not exclusive to cartilage and therefore is not specific and must be interpreted cautiously.\textsuperscript{18,23,24}

Confounding variables (e.g. age, gender, ethnicity, body mass, comorbidity) affect the reliability of biomarkers and make it difficult to validate them, especially when concentrations can be influenced by renal and liver function, food intake, diurnal variations, drug interactions, and other sites of inflammation in the body.\textsuperscript{2} Therefore, it has been suggested that longitudinal monitoring of multiple biomarkers is a more valid way to assess disease progression.\textsuperscript{25}

Risk factors. There are multiple factors that increase a person’s risk to developing OA, including age,\textsuperscript{1,3,26,27} sex,\textsuperscript{1,3,7,26} other genetic factors,\textsuperscript{2,3} body mass index,\textsuperscript{1,3,28,29} and previous injury and previous surgery.\textsuperscript{1,3,5-7} It is well known that age increases risk of OA, but the reason is not well known. It could be hypothesized that as people age there is increased microtrauma to the joints from activities of daily living, which increases the risk of OA. Body mass index is positively associated with both knee OA and severe OA.\textsuperscript{28} Obese men and women (body mass index $\geq 30$ kg/m$^2$) had increased relative risk for knee OA compared to normal weight persons (body mass index 18.5 to 24.9 kg.m$^2$).\textsuperscript{28} There was a statistically significant increase in the
relative risk for knee OA and severe OA per unit increase in body mass index for both men and women.\textsuperscript{28} A meta-analysis conducted by Zhou, Liu, Chen, & Liu\textsuperscript{29} found knee OA risk increased as body mass increased, attributing this increase in risk to excessive body weight increasing the load on the knee.\textsuperscript{29}

Previous injury to the knee joint significantly increases the chance of developing OA.\textsuperscript{1,3,5,7,26} A meta-analysis conducted by Muthuri, McWilliams, Doherty, & Zhang\textsuperscript{7} concluded that a history of knee injury increases the risk for knee OA fourfold.\textsuperscript{7} An acute knee injury is most commonly caused by a high force event, leading to an inflammatory response in the joint. This inflammatory response causes an imbalance in the catabolic and anabolic processes, ultimately resulting in tissue turnover and altered biomechanics and biochemical changes that affect the joint and the entire limb.\textsuperscript{5,30} The natural response that takes place increases pro-inflammatory mediators, it is unknown how long it takes for levels of these inflammatory mediators to return to pre-injury levels, if ever.\textsuperscript{5} This change from homeostasis causes a metabolic crisis from the imbalanced catabolic and anabolic activity.\textsuperscript{5,30}

Pro-inflammatory biomarkers within the synovial fluid increase as they attempt to form new blood vessels and osteophytes and activate catabolic enzymes.\textsuperscript{5,31,32} The catabolic enzymes begin to breakdown the components within the extracellular matrix of the articular cartilage, increasing permeability and articular water content.\textsuperscript{2,5} This causes biomechanical and biochemical changes in the properties of the articular cartilage, despite attempts to control the catabolic enzymes biosynthetically.\textsuperscript{2,5,31,32} Chondrocytes begin to stimulate additional cartilage degeneration, causing ossification of the deep regions of the articular cartilage.\textsuperscript{5} Fragments of the articular cartilage begin entering the synovial fluid simultaneously stimulating more catabolic pathways, leading to an endless cycle.\textsuperscript{5}
Damage or biomechanical changes to a joint can occur from an acute event or from repetitive overloading. Microtrauma can occur from repetitive overloading of the same structures, as well as secondary to macrotrauma of a joint. Microtraumas that frequently accompany macrotraumas include subchondral or cartilage “bone bruises,” and osteochondral or bone marrow lesions. While the purpose of surgical reconstruction is to preserve the knee joint and prevent early onset OA, surgical intervention could be a risk factor. After surgery the joint will have a new loading pattern due to either instability or compensatory movements, which can lead to microtrauma and increased risk of OA.

ACL ruptures are associated with an increased risk for developing OA and an earlier onset than expected in the general population. A case series conducted by Murray et al. looked at the association between ACL reconstruction and early onset OA in 114 patients with patellar tendon grafts, with a mean follow up of 13 years. All patients had unilateral ACL tears, the same surgeon perform their surgeries, and the same rehabilitation protocol. A higher than normal incidence rate of radiographic change was seen: 33% of injured knees compared to 21% of uninjured knees. Poor radiological outcome was associated with meniscectomy, meniscal injury, and chondral injury at the time of surgery. Poor subjective outcome was associated with chondral injury and previous surgery at the time of surgery, lower International Knee Documentation Committee (IKDC) score and prolonged or no return to sport at follow-up. It was found that the medial compartment had the worst OA progression, however the lateral and patellofemoral compartments tended to have worse Kellgren and Lawrence grading in the patient’s injured knee compared to their uninjured knee. These observations show the presence of degenerative disease throughout the entire knee joint.
There are multiple genetic factors that are risk factors for OA. Researchers have identified genes that predispose individuals to OA, many of which encode for regulatory proteins. There is an increased risk of hip and knee OA in siblings of patients with OA. This increased risk is also passed on to their offspring. This familial link is not only related to the development of OA, but also the progression of the disease. Genotyping may have implications for identification of at-risk patients as well as the prevention, treatment, and management of OA.

Females have an increased risk of knee OA. There are multiple factors that contribute to this increased risk, including anatomic factors, kinematic factors, history of injury, and hormonal factors. Females have narrower femurs and smaller patellae, differences in tibial condyle size, and larger Q-angles anatomically compared to males. These differences are also associated with decreased knee cartilage volume, which increases the risk of knee OA. Females have repeatedly demonstrated altered kinematics and increased valgus stress compared to males within studies. It is also well established that females have an increased risk of certain injuries, specifically ACL sprains, due to these anatomic and kinematic differences, which cause increased risk of OA.

Estrogen is the primary hormone linked with OA risk. Post-menopausal estrogen changes have shown to drastically increase OA risk in women. It is not well established why the estrogen changes cause an increased OA risk in women despite being well documented. White post-menopausal women that took an estrogen replacement therapy had a decreased chance of developing radiographic evidence of knee arthritis, compared to their non-estrogen replacement counterparts.
Treatment. There are four gradual phases for OA treatment: 1. non-pharmacological, 2. pharmacological, 3. complementary and alternative, and 4. surgical. Treatment usually begins with non-pharmacological, the least invasive, which starts with exercise, bracing, splinting, or a cane. Thomas et al. conducted a randomized control trial studying home based exercise programs and outcomes in patients with knee pain. Two years of home-based exercise programs significantly reduced self-reported knee pain compared to the non-exercise psychosocial group, and the control group with no intervention. Non-pharmacological treatment also includes weight loss. A meta-analysis conducted by Christensen, Bartels, Astrup & Biddal assessed clinical benefits of weight loss in overweight knee OA patients. They reported that when overweight individuals lost 5.1% of their weight it significantly reduced their disability.

Pharmacological options are often chosen after non-pharmacological interventions are ineffective. Pharmacological treatments typically start with acetaminophen, progressing to nonsteroidal anti-inflammatory drugs (NSAIDs) and then intra-articular injections. Two types of intra-articular injections are often used, corticosteroids have proven effectiveness on knee OA and are shown to have short term relief (4-8 weeks), while hyaluronic acid has shown relief for up to four months with knee OA. Complementary and alternative medicines are frequently used if patients have no relief from pharmacological treatment as the last conservative method before surgical treatment. Acupuncture, glucosamine, and chondroitin supplementation are methods commonly seen in this phase of treatment. Acupuncture has only shown to have short-term benefits in pain reduction, whereas glucosamine and chondroitin supplementation have shown to be effective for moderate to severe knee OA. However, due to lack of regulation there is a considerable amount of variability in ingredients of supplements, leading to inconsistent
outcomes and uncertain viability. Surgical treatment is reserved for patients with persistent pain despite all conservative treatment efforts. The most effective surgical intervention is total joint replacement. However, some patients, particularly younger, may opt for arthroscopic debride ment.

Acute Femoral Cartilage Deformation

Acute femoral cartilage deformation is a normal physiologic process that helps to absorb force and provide nutrients to the cartilage. Cartilage deformation is regulated by the extracellular matrix. The amount of cartilage deformation following acute activity, as well as the time it takes to return to normal, can be used as surrogate measures of cartilage composition and health. Previous research has studied acute femoral cartilage deformation following walking, running, and drop landing, and a few researchers have used a combination of these activities.

Magnetic Resonance Imaging. Researchers have used MRI to measure acute femoral cartilage deformation. One study looked at knee cartilage volume changes utilizing both MRI and serum COMP concentrations. After running for 60 minutes at maximal sustainable speed, cartilage volume decreased in healthy, trained male and female runners. This change in cartilage volume was significantly correlated with baseline COMP levels and with the change in COMP levels after the run. A similar study assessed the deformational behavior of knee cartilage and changes in serum COMP after running for 30 minutes at 2.2m/s and 100 vertical drop landings using MRI in healthy males and females with a sedentary lifestyle. Similar results were found, and the average serum COMP concentration remained significantly elevated 1 hour after both the running and drop landing interventions. There was a significant correlation between changes in serum COMP levels and total cartilage deformation following
drop landing, but not running concentration. Interestingly, the correlation showed greater increases in serum COMP concentrations were associated with less cartilage deformation.

While some researchers combined activities, others focused on acute femoral cartilage deformation after one specific activity. Boocock et al. looked at the short-term effects of running on the deformation of knee articular cartilage using MRI. They examined the relationship between changes in knee cartilage volume and biomechanical modulators of knee joint load. They used healthy male and female recreational runners as their participants, each participating in a control condition where they sat for 30 minutes, and an experimental running condition where they ran at a self-selected pace for 5000 steps, using a pedometer. Their results showed significant changes in knee cartilage volume were present after running and that there were no significant differences between males and females, when controlling for body weight. A similar study by Lad et al. measured the normal gait-induced compressive strains from walking in tibiofemoral cartilage in healthy male and females. Using a combination of MRI and 3-dimensional models they found that normal walking causes significant compressive strains in the articular cartilage of both medial and lateral compartments of the tibial plateau and femoral condyles. Tibial cartilage experienced significantly higher overall strain than femoral cartilage. Males demonstrated an average of 17% thicker baseline cartilage than females, however they did not mention anything about controlling for bodyweight and they did not present their participant’s demographics. Boocock et al. found differences between sex, but once they controlled for bodyweight, the differences were not significant.

MRI has also been used to compare the articular cartilage of individuals with post-operative ACL reconstruction to the articular cartilage in healthy individuals. Van Ginckel et al. used MRI with 3-dimensional morphology and T2/T2* quantification to evaluate the
cartilage status in ACL-reconstructed patients 6 months after surgery compared to matched controls after running at a self-selected pace for 30 minutes.\textsuperscript{57} They also explored the role of time to return to play and/or surgical delay on cartilage status.\textsuperscript{57} There were no significant differences in cartilage volume and thickness between ACL-reconstructed knees and healthy matched controls.\textsuperscript{57} However, when examining the 3D morphological characteristics, differences were apparent in biochemical composition of ACL-reconstructed individuals compared to healthy controls, suggesting a decrease in cartilage quality in ACL-reconstructed individuals.\textsuperscript{57} A shorter surgical delay was associated with slower cartilage recovery after running.\textsuperscript{57} This finding is important for clinicians as it implies individuals who have surgery sooner have a worse prognosis. From this, it can be inferred that time prior to surgery, whether it be used for rehabilitation or just letting the tissues re-equalibrate to their new normal, may be a critical factor in long-term cartilage health. This was the first study to associate an early return to sports with trends toward increased cartilage deformation and diminished cartilage function at 6 months after surgery.\textsuperscript{57}

Ultrasound. Researchers have previously relied on MRI to measure acute cartilage deformation but have recently used high frequency ultrasound instead. Ultrasound has been used as a tool for assessing acute femoral cartilage deformation, as well as cartilage quality using wavelet magnitude and echo intensity.\textsuperscript{2} It is inexpensive and non-invasive compared to other methods of assessment such as MRI.\textsuperscript{60} Ultrasound has been validated in the measurement of knee cartilage by multiple authors, one study states that in normal to moderately damaged cartilage, ultrasound produces accurate and reproducible measurements,\textsuperscript{60} and another study states that it is a reliable and sensitive imaging modality for medial femoral cartilage deformation.\textsuperscript{58}
Ultrasound can detect acute medial femoral cartilage response to load. Harkey et al.\textsuperscript{52} assessed medial femoral cartilage deformation with ultrasound following 30 minutes of walking, and its possible association to habitual walking speed in healthy male and female participants females.\textsuperscript{52} Medial condyle deformation was significantly, positively associated with habitual walking speed, meaning greater walking speed was significantly associated with greater acute medial femoral cartilage deformations.\textsuperscript{52} The findings of this study reveal that ultrasound is capable of detecting an acute medial femoral cartilage response to walking, and that this deformation is associated with habitual walking speed.\textsuperscript{52} A similar study was conducted by Harkey et al.\textsuperscript{58} comparing ultrasonographic assessment of medial femoral cartilage deformation after walking and running in healthy males and females. Both the running condition and walking condition lasted 30 minutes.\textsuperscript{58} There was significant medial femoral cartilage deformation following each walking and running condition compared to the control condition (rest), however there was no significant difference between the walking and running conditions.\textsuperscript{58} This study concluded that ultrasound is a sensitive imaging technique for detecting acute medial femoral cartilage deformation after walking and running in healthy individuals.\textsuperscript{58} This study also introduced the idea of monitoring cartilage health as a cost-effective strategy to identify individuals with underlying cartilage pathologies.\textsuperscript{58} Such a tool would be useful in post-operative patients, such as after an ACL reconstruction, as an objective measurement of cartilage deformation and recovery to help decide when to progress rehabilitation and ultimately clear for return to play.

Acute cartilage deformation is load-dependent. Harkey et al.\textsuperscript{61} assessed the acute femoral cartilage response and recovery after walking and drop landing, in healthy males and females.\textsuperscript{61} There was significant deformation after walking and drop landing compared to the control
Between the two conditions there was greater medial thickness deformation after drop landing than after walking immediately after condition, and 15 minutes after condition, indicating that the deformation from the drop landing required more time to recover compared to walking. These results confirm that deformation is load-dependent in healthy individuals and indicate that ultrasound is an accessible assessment of femoral cartilage response.

Foot Strike

Foot strike, or how the foot contacts the ground during gait, is often categorized into three patterns: rearfoot strikers, midfoot strikers, and forefoot strikers. Rearfoot striking, when initial contact with the ground is made with the heel or posterior foot, is the most common foot strike, with up to 89% of runners rearfoot striking. Midfoot striking is classified by initial contact by both the posterior and anterior portions of the foot. When initial contact occurs only with the anterior portion of the foot, it is considered a forefoot strike. Due to similarity of foot angles between midfoot and forefoot strikes, they are often grouped together in research. In a systematic review and meta-analysis conducted by Almeida et al., 12 out of the 16 articles included grouped participants into either rearfoot or forefoot strike, three articles grouped participants into rearfoot or midfoot strike, while only one article grouped participants into rearfoot, midfoot, or forefoot strike.

There are biomechanical alterations associated with each foot strike due to differences in foot angle at initial contact. These biomechanical differences have been studied by many researchers. Kulmala et al. examined lower limb loading profiles in both rearfoot and forefoot strike female runners. It was found that forefoot strike runners had lower patella femoral contact force and patella femoral stress compared to rearfoot strike runners. Less dorsiflexion at initial contact and a higher peak plantar flexion moment was also seen in forefoot strike runners.
Rearfoot strike runners exhibited higher peak vertical ground reaction forces, longer contact time, and significantly greater peak knee flexion angle during stance phase.\textsuperscript{63} Interestingly, forefoot strike runners showed a lower peak knee abduction moment,\textsuperscript{63} meaning forefoot strikers showed greater movement within the frontal plane than rearfoot strikers. This has been shown to correspond with increased medial compartment knee loading,\textsuperscript{63,69,70} which has been linked with degenerative knee disorders.\textsuperscript{63,71,72} Knorz et al.,\textsuperscript{73} used 3-dimensional motion analysis to analyze the stress patterns of the ankle, knee, and hip in forefoot and rearfoot strike runners. Participants in this study first ran with their habitual running form, and then were asked to purposely run in their non-habitual foot strike. Through this research it was observed that independent of participant’s habitual foot strike, running with a forefoot strike lead to significantly higher vertical maximum peak force values and resultant forces compared to a rearfoot strike.\textsuperscript{73} However, loading rates of these vertical and resultant forces were significantly lower in forefoot compared to rearfoot strike running.\textsuperscript{73}

Gait modifications, while often unintentional, can purposely be used to treat injuries by unloading injured structures and tissues. A systematic review conducted by Napier et al.,\textsuperscript{74} attempted to determine which gait modification interventions would be effective in treating running-related injuries. The results of this systematic review showed conflicting evidence for knee kinematics, vertical peak impact, average loading rate and shock attenuation when comparing rearfoot and forefoot strike running.\textsuperscript{74} It was supported with strong evidence that foot strike manipulation caused changes in ankle kinematics, however, no evidence was found to support the use of foot strike manipulation to change vertical or leg stiffness.\textsuperscript{74} This data coincides with the previously mentioned systematic review and meta-analysis conducted by Almeida et al.,\textsuperscript{62} which found that forefoot strike runners contacted the ground in a plantar
flexed position while rearfoot strike runners made contact in a dorsiflexed position, thus changing ankle kinematics.

Lower Body Positive Pressure Treadmills

Lower body positive pressure treadmills (LBPPTs) are used to reduce load on the musculoskeletal system while walking or running. The Alter-G® is a LBPPT consisting of a treadmill that is encased in a chamber that becomes airtight when the individual using the treadmill steps into it. Individuals using an Alter-G® wear neoprene shorts that have a skirt similar to a kayak that gets zipped into the chamber itself, creating the airtight seal (Figure 1). Unloading occurs in 1% intervals of bodyweight percentage, individuals can run at full (100%) body weight (BW) to as little as 20% BW. A fan in the front of the treadmill blows air into the chamber, creates a lifting force at the individual’s hips, thus unweighting them (Figure 2). This process is monitored by a calibrated pressure sensor measures the chamber pressure and the percentage of bodyweight experienced. Originally created to simulate anti-gravity conditions faced by astronauts while in space,75 LBPPTs are now available commercially and have been integrated into athletic performance training and rehabilitation settings.76-79

Researchers have investigated the body’s physiological and biomechanical responses to LBPPT unloading. A studied conducted by Grabowski and Kram,80 aimed to quantify the effects of running velocity and body weight support on ground reaction forces and metabolic power. Participants ran at three different running velocities and four different body weight percentages.80 It was found that when body weight percentage was decreased, there was a linear decrease in vertical impact peak ground reaction force, active peak ground reaction force, and loading rate at all velocities.80 Velocity and body weight percentage found to be significant predictors of gross metabolic work.80 A similar study was conducted by Smoliga et al.81 where
participants wore pressure insoles within their shoes to look at regional loading of the foot.\textsuperscript{81} Participants ran at three different speeds and five different body weight percentages.\textsuperscript{81} It was discovered that there was a significant effect for body weight percentage on forefoot to rearfoot relative load; running at bodyweight percentages less than 80% caused a significant shift towards forefoot loading.\textsuperscript{81} However, there were no significant differences in regional loading between 80\% BW and 100\% BW, indicating that running at 80\% BW does not substantially alter regional plantar loading, and therefore should not significantly alter running mechanics.\textsuperscript{81}

There are also numerous studies that investigated the physiological responses in combination with the biomechanical responses to LBPPTs. Farina et al.\textsuperscript{76} conducted a systematic review of six studies included examining kinetics, all agreed running that decreased body weight percentage consistently decreased peak ground reaction force.\textsuperscript{80-85} All studies included that examined VO\textsubscript{2} and metabolic cost agreed that at a given velocity, if body weight percentage decreased, VO\textsubscript{2} levels and metabolic cost significantly decreased.\textsuperscript{76,83,84,86-89} Heart rate,\textsuperscript{82,84,90} and rating of perceived exertion (RPE) also decreased at a given velocity when body weight percentage decreased.\textsuperscript{76,83,89} These results agree with research conducted by Barnes and Janecke,\textsuperscript{91} that found decreased VO\textsubscript{2}, heart rate, and RPE as body weight percentage decreased while running on an LBPPT in highly-trained distance runners. This study also revealed that as body weight percentage decreased, stride length and flight duration increased while stride rate and contact time decreased, which was also seen in a study included in the systematic review.\textsuperscript{85,91}

While most research on LBPPTs effects is with set parameters for experimental conditions, some studies have taken participants’ normal training schedule and transitioned their training be done on an LBPPT. Studies included in the systematic review investigating differences between training at 100\% BW and decreased body weight found greater training
speeds and duration, as well as greater time to exhaustion running at decreased body weight percentages on LBPPTs. The systematic review concluded that LBPPTs do achieve their primary goal of reducing forces on the musculoskeletal system, as shown by a decrease in ground reaction forces, by providing an upward vertical force to counter gravity. This claim is further supported by research conducted by Denning et al., examining the independent effects of body weight on articular cartilage catabolism associated with walking. Participants walked at control (100% BW), decreased body weight (60% BW on LBPPT), or increased body weight via weighted vest (140% BW) and serum COMP were tested immediately before and after walking. Participant serum COMP levels significantly after walking at 100% BW and 140% BW, but not after walking at 60% BW, while no significant differences in heart rate and RPE were seen between 100% BW and 60% BW. These results indicate that LBPPTs allow maintenance of cardiovascular responses to walking while reducing articular cartilage catabolism. Due to the decreased load on the musculoskeletal system and decreased serum COMP levels seen after walking at decreased body weight percentage, LBPPTs could be beneficial to the knee OA population.

LBPPTs have also been utilized in patients with knee OA. Takacs et al., had knee OA participants walk for 20 minutes at 100% BW and then again on a LBPPT at whatever body weight percentage the kept the participant’s affected knee pain-free. Using a visual analog scale (VAS) and recording the percentage of body weight participants were on every five minutes, it was concluded that in the population tested, a mean of 87.6% BW on the LBPPT provided significant pain relief during walking and prevented exacerbation of acute knee pain. The results of this study suggest LBPPTs can be used to safely and effectively simulate weight loss, by reducing body weight percentage, and reduce knee pain while walking in the overweight knee
A similar study conducted by Kawae et al. had lower limb OA patients walk on level ground for eight minutes, and then walked on the Alter-G® LBPPT for eight minutes at a self-selected pace, at whatever body weight percentage allowed them to walk pain-free. Participants reported significantly greater pain after walking on level ground than after walking on the Alter-G®, and walking speed was significantly faster during Alter-G® walking. These results suggest that LBPPTs have acute effects on knee/lower limb OA patients while walking, allowing for reduced pain and increased comfortable walking speed compared to 100%BW or level ground walking.

Chronic effects of LBPPTs have also been studied using 12-week walking programs. Peeler et al. implemented a 12-week LBPPT walking program in overweight patients with knee OA while monitoring knee joint pain and function, and quadriceps and hamstring strength. After the program concluded, participants reported significantly higher scores in all five Knee Injury and Osteoarthritis Outcome Score (KOOS) subscales, with the greatest increase in the quality of life subscale, as well as significantly lower acute knee pain at follow-up compared to baseline. Significant strength increases were seen in both the quadriceps and hamstring muscle groups at follow-up compared to baseline, and by the end of the program the average body weight percentage needed for pain-free walking was significantly lower than at the start of the 12-weeks. It was concluded that an LBPPT exercise regimen can be used in the overweight knee OA population to significantly decrease knee pain, enhance joint function, and strengthen quadriceps and hamstring musculature by safely promoting pain-free walking exercise. A similar study conducted by Peeler and Ripat strengthened the findings of the previous study by adding the Canadian Occupational Performance Measure (COPM), another patient-rated outcome measure, to the data collected. Using the same 12-week program in knee OA patients it
was shown that both KOOS and COPM scores improved at follow-up, as well as quadriceps strength. Participants similarly reported significantly decreased acute knee pain during 100% BW walking following the program, leading to the conclusion that an LBPPT walking regimen allowed knee OA patients to participate in regular exercise without exacerbation of symptoms, while safely and effective managing joint pain and symptoms. Evidence of LBPPT’s reduction on musculoskeletal load is further strengthened by research conducted by Patil et al., using custom electronic tibial prostheses, for a total knee arthroplasty, to measure joint forces in patients on an LBPPT. Patients were tested at two different treadmill speeds, four body weight percentage settings, and various incline and decline settings that were all randomized. The data showed peak axial loading on the tibial plateau was consistently reduced at lower body weight percentage settings, and also revealed that knee forces, which can reach upwards of five-times body weight during unsupported (100% BW) jogging, can be reduced to less than two-times body weight while jogging on the LBPPT. These results suggest that LBPPTs can allow for exercise at running speeds while decreasing joint loads to levels below that of comfortable walking. Patil et al. concluded that LBPPTs may be an effective tool for rehabilitation of patients following lower extremity surgery due to its ability to decrease joint forces in a controlled manner.
The Effects of Lower Body Positive Pressure Treadmill Running on Acute Femoral Cartilage Deformation in Healthy Males and Females

INTRODUCTION

Lower body positive pressure treadmills (LBPPTs) are used to reduce load on the musculoskeletal system while walking or running. Their use in athletic performance training and rehabilitation settings is increasing.\textsuperscript{76-79} LBPPTs are commonly used in the OA and the athletic populations. Researchers have studied the physiologic effects of LBPPT unloading, including regional plantar loading, and have concluded that LBPPTs may be an effective tool for rehabilitation of patients following lower extremity surgery due to its ability to decrease joint forces in a controlled manner.\textsuperscript{98} Researchers have cautioned, however, that running at less than 80% BW causes a shift in running and foot strike mechanics.\textsuperscript{81} Researchers have also examined the systemic effects of body weight on articular cartilage while walking at different body weight percentages on an LBPPT assessing serum COMP levels.\textsuperscript{93}

Acute femoral cartilage deformation is a normal physiologic process that can be used as a surrogate measure of cartilage composition and health following activity since acute cartilage is load dependent.\textsuperscript{51} Acute cartilage deformation is load dependent. Ultrasound has frequently been used as a tool for assessing acute femoral cartilage deformation.\textsuperscript{2} This assessment method is inexpensive and non-invasive compared to other methods of assessment such as MRI or blood samples.\textsuperscript{60} Ultrasound has been validated as an accurate and reliable measure of femoral articular cartilage thickness,\textsuperscript{60} and is capable of detecting an acute femoral cartilage response to walking, running, and drop landing.\textsuperscript{58,61,99} However, no research has been conducted on using ultrasound to assess acute femoral cartilage deformation after using a LBPPT. Therefore, the primary purpose of the current study was to compare the effects of running at 100% and 80% body
weight (BW) on a LBPPT on femoral articular cartilage and gait biomechanics between sexes and limbs in healthy, physically active participants. A secondary purpose was to examine relationships between patient reported outcomes and cartilage deformation for each trial.

METHODS

Research Design

This study used a two-group crossover design to assess the acute femoral deformation after two running conditions. One group was males and one was females. Due to the nature of crossover studies, participants acted as their own controls. The independent variables were group (sex) and running condition. The dependent variables were vertical ground reaction forces (vGRF), Knee Injury and Osteoarthritis Outcome Score (KOOS), Borg’s Rating of Perceived Exertion (RPE), and femoral cartilage deformation. Potential covariates included foot strike, height, and weight.

Participants

20 physically active participants, between the ages 18 to 25 were recruited and participated in this study (Table 1). Participants were recruited using written flyers that were shared electronically, via email, and through oral requests. Inclusion criteria were: between 18 and 25 years old, recreationally active, and the ability to run for 30 minutes at 2.68 m/s. Exclusion criteria were: history or symptoms of any type of arthritis in the knee, previous lower extremity surgery or severe injury, intra-articular injection within the last 6 months, osteochondral lesions or defects, and previously diagnosed osteochondritis dissecans.

Instrumentation

Lower body positive pressure treadmill (LBPPT). This study used an Alter-G Via X® (Alter-G Inc., Fremont, CA) LBPPT for both conditions. The Alter-G® requires specific
Alter-G® shorts that were also used in this study. These Alter-G® neoprene shorts have a skirt with a zipper that creates an airtight seal with the chamber. Once zipped into the chamber, the fan within the Alter-G® pushes air into the chamber, creating a vertical lifting force that acts on the waist of the individual, thus lifting them up and supporting them, reducing their acting body weight. Every time anyone uses an Alter-G® treadmill it must be calibrated to them each time. Once calibrated, the Alter-G Via X® can reduce bodyweight in increments of 1%, with a maximum reduction to 20% body weight. The Via X® model treadmill can go forwards and reverse, with a maximum forward speed of 15mph, and a maximum speed of 5mph in reverse. Alter-G® treadmills have been used in previous research, and is a valid and reliable means to achieve a given metabolic stimulus with reduced musculoskeletal loading.

Ultrasound. This study used a GE Logiq e NEXTGEN 7 Ultrasound unit (General Electric Co., Boston, MA) with a 12 MHz linear probe. ImageJ software (National Institutes of Health, Bethesda, MD) was used to analyze the ultrasonographic images. This software has been used in multiple ultrasonographic studies of acute femoral cartilage deformation, at West Chester University and at various other sites. Ultrasound has been validated as an accurate and reliable measure of femoral articular cartilage thickness, and is capable of detecting an acute femoral cartilage response to walking, running, and drop landing.

Two mass model. Vertical ground reaction force was calculated using a two-mass model, which has been validated by Clark et al.. The two-mass model only requires body mass, contact time, aerial time, and lower limb acceleration to predict vGRF. These stride measurements can be easily obtained with a slow motion video set at 240 frames/second, on devices such as an iPad or iPhone. The two-mass model is based off the fundamental theory that the total vertical ground reaction force waveform is composed of two overlapping
bell-shaped impulses due to the vertical collision of the lower limb with the running surface, and the simultaneous accelerations of the rest of the body during ground contact.\textsuperscript{100}

Knee Osteoarthritis Outcome Score (KOOS). The KOOS was used as a patient reported outcome measure to assess participant’s opinion about their knees and any associated problems. It is a 42-question survey with every question using a five-point Likert scale, 0 = never, 1 = rarely, 2 = sometimes, 3 = often, and 4 = always. The KOOS has five subscales, each measuring a specific aspect; symptoms, pain, activities of daily living, sports and recreation, and quality of life. The KOOS has been validated and is reliable in both acute injury consequences in the young and physically active population as well as chronic outcomes in the elderly population,\textsuperscript{101} especially knee OA.\textsuperscript{102}

Procedures

Recruitment. Participants were recruited for this study via flyers (Appendix A) that were shared via email (Appendix B). All potential participants met with the investigator and discussed the purpose, procedures, and informed consent form (Appendix C). This study was approved by West Chester University International Review Board (Protocol ID # 20190925A, Appendices D and E).

Pre-exercise Assessment Protocol. Data collection consisted of two days, exactly one week apart, both scheduled at the same time of the day. The order of the conditions was be randomized using two-block randomization. Upon arrival of the first scheduled data collection, participants were fitted for Alter-G® shorts, and then sat for 30 minutes in a long sit position (Figure 3) on a treatment table against a wall, with the shorts on to allow for decompression of femoral cartilage as established in previous research.\textsuperscript{58} The treatment table had two tape measures taped to it, one for each limb. During these 30 minutes, each participant completed a
healthy history questionnaire (Appendix F) and a KOOS (Appendix G). They also familiarized themselves with the Borg’s Rating of Perceived Exertion (RPE, Appendix H). Once 30 minutes had passed, the participant’s baseline acute femoral cartilage thickness was assessed using ultrasound, one leg at a time. While remaining seated, the participant’s knee was flexed to 140º, this measurement was checked by a goniometer. Once placed at 140º of flexion, the investigator noted where the participant’s calcaneus was on the tape measure. This measurement was used to easily recreate this position for future measurements. While remaining in 140º of knee flexion, the ultrasound head was placed transversely, in line with the lateral and medial femoral condyles, just above the superior line of the patella (Figure 4). Three images were taken of the femoral cartilage for analysis. This process was then be repeated for the other limb. Once baseline images had been taken of both limbs, the participant was setup on the Alter-G® by the investigator and began their assigned exercise condition. These procedures have been used in previous research.58

Exercise Protocol. The experimental condition consisted of running at 80% bodyweight (BW) for 30 minutes, at 2.68 meters per second (m/s) or 6 miles per hour (mph) on the Alter-G®. The control condition consisted of running at full (100%) BW for 30 minutes at 2.68 m/s on the Alter-G®. 2.68 m/s was selected because it has been used in research conducted by Cutuk et al.,82 as well as previous research conducted at West Chester University. During each condition, participants were asked to rate their exertion using the Borg’s RPE scale every five minutes until the completion of the 30-minute condition. Halfway through each condition, at 15 minutes, a short video (approximately 10 seconds in length) was taken of the participant’s gait to analyze their gait and foot strike and determine their vGRF using a two-mass model calculation.100 Upon the completion of the 30-minute condition, participants were taken off the Alter-G® with help from the investigator and instructed to sit back on the table.
Post-exercise Assessment Protocol. Ultrasonographic assessment of cartilage occurred immediately after the exercise condition had ended and the participant was seated. The participant was placed into 140º of knee flexion again and three images were taken of each limb again. After the post activity images were taken, the participant left. The same routine was used on the second day of data collection, the only difference being which condition (80% or 100% BW) the participant completed that day.

Cartilage thickness. Femoral cartilage thickness for the intercondylar compartment was measured at the mid-point of the intercondylar notch. Medial and lateral compartment cartilage thickness was measured at the mid-point of the medial and lateral condyles. These methods have been used in multiple ultrasonographic studies on acute femoral cartilage deformation.\(^52,58,61,99\) Percent change of cartilage width was calculated for each compartment after each condition:

\[
\text{Percent change} = \left( \frac{\text{mean}_{\text{post}} - \text{mean}_{\text{baseline}}}{\text{mean}_{\text{baseline}}} \right) \times 100
\]

A negative percent change in thickness signifies the post measurement was less than baseline measurement, therefore a greater negative percent change indicates greater cartilage deformation.

Data Analyses. All statistics were conducted using SPSS v24 (SPSS Inc., Chicago, IL) with a priori significance set at \(p \leq 0.05\). Dependent T-Tests were used to compare the cartilage width and percent change of each compartment before and after each condition, as well as between conditions. Independent T-Tests were used to compare cartilage width and percent change per compartment between sexes. Dependent T-Tests were used to compare gait biomechanics between conditions, while Pearson’s Correlations examined the relationship between vGRF and cartilage deformation. Pearson’s Correlation were also used to examine
relationships between cartilage width percent change and the KOOS and Borg’s RPE patient reported outcomes.

RESULTS

Ultrasonographic cartilage response

After activity. A statistically significant decrease in both right (p=0.048; Table 2) and left (p=0.030; Table 3) medial compartment cartilage width was seen after running at 100% BW ([40.99±21.27] and [39.04±15.71]) compared to baseline measurements ([45.11± 22.20] and [43.08±19.62]). A statistically significant (p=0.005) decrease in right intercondylar compartment cartilage width was seen post 100% BW running (40.13±16.43) compared to baseline (45.31±18.66) measurements (Table 4). No significant differences were seen within the medial compartment between post 80% BW and baseline measurements in either the right (Table 2) or left (Table 3) limbs. No other significant differences were found between pre and post measurements of the intercondylar compartment in either condition or limb (Tables 4 & 5).

Lateral compartment cartilage significantly decreased in both right (p=0.024; Table 6) and left (p=0.045; Table 7) limbs after running at 100% BW ([39.57±17.66] and [38.54±16.98]) compared to baseline measurements ([44.15±23.84] and [43.46±22.14]). Right lateral compartment cartilage width significantly decreased (p=0.006) post 80% BW running (39.37±14.75) compared to baseline (45.11±20.34; Table 6), however the left lateral compartment cartilage showed no significant differences (Table 8).

Between conditions. Right medial compartment cartilage showed statistically significant (p=0.03) greater percentage cartilage width reduction for the medial compartment at 100% (-8.85±17.86) compared to 80% (0.66±11.87; Table 2). No statistically significant differences were found for the left medial compartment cartilage width between conditions (Table 3). Right
intercondylar cartilage showed statistically significant (p=0.042) greater reduction in cartilage width for the intercondylar compartment at 100% (-10.58±13.35) compared to 80% (-0.73±17.47; Table 4). No statistically significant differences were found between left intercondylar cartilage width between conditions (Table 5). No significant differences were found in cartilage deformation between conditions in both the right (Table 6) and left (Table 7) lateral compartments.

Between sexes. There were statistically significant differences in percent change between sexes in both the medial (p=0.04, 16.07± 7.3) and intercondylar (p=0.043, 11.86±5.46) compartments after running at 100% BW, with females showing significantly greater percent reduction. No statistically significant difference was found in percent change of lateral compartment after running at 100% BW. No statistically significant differences were found between sexes in the medial, intercondylar, or lateral compartment’s percent change after running at 80% BW (see Tables 8-11).

Between limbs. No statistically significant differences in cartilage percent change were found between limbs for any compartment after either condition.

Biomechanics

Ground contact time. Statistically significant greater contact times were found in both the right (p=0.004; Table 12) and left limbs (p<0.001; Table 13) in 100% BW compared to 80% BW.

Flight time. Statistically significant (p<0.001) decreased flight times were seen at 100% BW compared to 80% BW in both the right ([0.08±0.02] to [0.10±0.02]; Table 12) and left ([0.08±0.02] to [0.10±0.02]; Table 13) limbs, respectively.
Step rate. Statistically significant greater step rates were found in both the right (p=0.018) and left limbs (p=0.001) in 100% BW compared to 80% BW, (2.76±0.15) compared to (2.70±0.18) in the right (Table 12), and (2.71±0.14) compared to (2.63±0.12) in the left (Table 13) limb, respectively.

Step length. Running at 100% BW had statistically significant shorter step length in comparison to running at 80% BW, in both the right (p=0.016; Table 12) and left limbs (p=0.002; Table 13).

Vertical ground reaction force. 100% BW had statistically significant (p<0.001) greater vGRF was seen at 100% BW compared to 80% BW in both the right ([814.71±95.13] to [694.54±83.11]; Table 12) and left ([809.06±88.80] to [696.48±83.67]; Table 13) limbs, respectively.

Loading rate. Statistically significant decreased rates of loading were found in both limbs between conditions. Rates of loading were significantly less in the right (p=0.001) and left limbs (p<0.001) in 100% BW compared to 80% BW, (4.48±0.58) compared to (5.00±0.73) in the right (Table 12), and (4.34±0.52) compared to (4.90±0.73) in the left (Table 13) limb, respectively.

Patient reported outcomes

Borg’s RPE. No statistical significance was found between average Borg’s RPE during the 100% BW trial and femoral cartilage deformation of any compartment of either the right or left limbs. No statistical significance found between average rating of Borg’s RPE during the 80% BW trial and right femoral cartilage deformation of any compartment. A statistically significant moderately strong (p=0.02, r=-0.514) negative correlation was found between average Borg’s RPE during the 80% BW trial and left intercondylar cartilage percent change of the 80%
BW trial. No statistical significance found between average Borg’s RPE during the 80% BW trial and left medial or lateral compartment cartilage percent change.

KOOS scores. No statistical significance was found between KOOS pain scores and left and right cartilage percent change of any compartment after running at 100% BW. Statistically significant negative correlations were found between KOOS Pain score and right medial (moderately strong) (p=0.021, r=-0.513), and intercondylar (strong) (p=0.005, r=-0.604) compartment cartilage percent change after the 80% BW trial. No statistical significance was found between KOOS Pain score and right lateral compartment cartilage percent change or any compartment cartilage percent change in the left limb. A statistically significant (p=0.01) moderately strong (r=-0.559) negative correlation was found between KOOS Symptom score and right medial 100% BW cartilage percent change. No statistically significant correlations were found between KOOS Symptom score and right 100% BW intercondylar, lateral, or any compartment percent change in the left limb. No statistical significance was found between KOOS Symptom score and any 80% BW compartment cartilage percent change from either limb. KOOS Activities of Daily Living (ADL) scores showed statistically significant negative correlations to right limb 100% BW intercondylar (moderately strong) (p=0.044, r=-0.455), and lateral (moderately strong) (p=0.02, r=-0.517) cartilage percent change. No statistical significance was found between KOOS ADL score and any left limb 100% compartment cartilage percent change, nor any compartment cartilage percent change in either limb for 80% BW. KOOS Sport/Recreation scores showed no statistical significance to any compartment cartilage percent change in either limb at 100% BW. A statistically significant (p=0.038) moderately strong (r=-0.468) negative correlation was found between KOOS Sport/Recreation score and right 80% BW intercondylar cartilage percent change. No statistically significant
correlations were found between KOOS Sport/Recreation score and right 80% medial or lateral, nor any left limb compartment cartilage percent change. KOOS Quality of Life scores showed no statistical significance to any compartment cartilage percent change in either limb in either BW conditions.

DISCUSSION

This is the first study to assess and compare acute ultrasonographic cartilage deformation after running on a LBPPT at 100% BW and 80% BW, as well as between sexes. As expected, medial and lateral compartment femoral cartilage width decreased significantly in limbs after running at 100% BW. These findings are consistent with MRI evidence from Boocock et al., and Lad et al. in which significant decreases in medial and lateral femoral cartilage volume was seen after running 5,000 steps at a self-selected pace, and significant compression of the medial and lateral femoral compartment cartilage after walking for 20 minutes on a treadmill at 1.1m/s. Our medial compartment cartilage width reduction is also consistent with US evidence from Harkey et al. on acute femoral cartilage deformation after walking (0.99 m/s ± 0.26) and running (2.26 m/s ± 0.64) at self-selected paces for 30 minutes, and MRI and biomarker evidence from Niehoff et al. which found a significant decrease in medial compartment femoral cartilage thickness and volume and a significant increase in serum COMP levels after running at 2.2 m/s for 30 minutes.

Interestingly, in our study, intercondylar compartment cartilage width decreased significantly in the right limb, but not the left after running at 100% BW. This could be due to limb dominance, which was not assessed in our questionnaires. In the study conducted by Harkey et al. on acute femoral cartilage deformation using ultrasound, only the dominant limb was assessed and significant decreases were found in the width of the medial, intercondylar, and
lateral compartments of the femoral cartilage after both walking and drop landing compared to rest.\textsuperscript{61}

We found no significant change in medial and intercondylar compartment cartilage width between baseline measurements and after running at 80\% BW. No other study has looked at acute femoral cartilage deformation after running on an LBPPT using ultrasound or MRI. However, Denning et al. saw similar results in serum COMP levels after running at 60\% BW.\textsuperscript{93} Denning et al. assessed serum COMP levels after running at 60\% BW, 100\% BW, and 140\% BW.\textsuperscript{93} Serum COMP levels significantly increased after running at 100\% BW and 140\% BW, but not 60\% BW,\textsuperscript{93} suggesting that walking at 60\% BW reduced the musculoskeletal load enough to not cause any significant increase in serum biomarkers (reflective of reduced cartilage width). Our findings were similar, therefore if we had assessed serum biomarkers, it could be inferred that we would not have found a significant increase in serum biomarkers as well.

In addition to the decreased cartilage width reductions at 80\% BW, all biomechanical variables significantly changed, indicating reduced musculoskeletal load. These findings could explain the decreased pain OA patients have reported during and after walking on an LBPPT at decreased bodyweight in multiple studies.\textsuperscript{94,95} Overweight knee OA patients in Takacs et al. study reported significant pain relief while walking and prevention of exacerbation of acute knee pain while walking for 20 minutes at a mean 87.6\% BW compared to 100\% BW.\textsuperscript{94}

The amount of unloading is not consistent across studies. Participants in the Denning et al. study were unweighted 20\% more than ours (60\% BW compared to 80\% BW), more research evidence is needed to fully support the idea that running at 80\% BW unloads the femoral cartilage and does not lead to deformation. We chose 80\% BW for our experimental trial due to existing evidence in the literature that anything less than 80\% BW would alter gait kinematics.\textsuperscript{81}
However, we descriptively observed a shift away from heel striking at 80% BW in many of our participants who had heel strikes while running at 100% BW.

We found a significant decrease in right lateral compartment cartilage thickness after running at 80% BW. However, this acute cartilage deformation was unilateral, and was not seen in the left limb. We speculate that this change may be a result of the observed altered gait kinematics or could potentially be explained by limb dominance. However, when comparing acute femoral cartilage deformation per compartment between limbs, we found no statistically significant differences in cartilage percent change in any compartment between limbs. These findings contradict those of Smoliga et al., who indicated that running mechanics were not altered when running at 80% BW. Therefore, future research should focus on possible causes of these unilateral discrepancies or asymmetries in acute cartilage deformation such as kinematics and kinetics.

We found significantly greater reduction in cartilage width of the medial and intercondylar femoral compartments of the right limb after 100% BW than 80% BW running. No statistically significant differences were seen in these compartments of the left limb, however there was still greater reduction in cartilage after 100% BW than 80% BW running which is clinically significant. While no other study has looked at acute femoral cartilage deformation using ultrasound, we can extrapolate that our findings reinforce the findings of Denning et al. that saw no significant changes in serum COMP levels before and after walking at 60% BW, but significant increases in serum COMP after 100% and 140% BW walking. However, Denning et al. did not investigate local joint compartmental changes, they looked at systemic serum changes. The percent change of lateral compartment cartilage thickness did not show statistically significant differences between trials, but interestingly, the right lateral compartment showed
greater deformation after 80% BW than compared to 100% BW running. This was the only compartment in either right or left limbs to have increased percent change after 80% BW compared to 100% BW, which could be significant clinically and may be something practitioners should be aware of before deciding to use an LBPPT.

We found significant biomechanical differences between 100% BW and 80% BW. Ground contact time, step rate, flight time, and step length were all significantly different between the two body weight conditions. Our biomechanical findings are consistent with Barnes and Janecke, who found that ground contact time and step rate was greatest at 100% BW, and decreased as percent BW decreased during interval series at various body weight settings on an LBPPT. Flight time was greater at 80% BW than 100% BW in our study, which also agrees with Barnes and Janecke, as well as Sainton et al. In Sainton’s study, participants ran at 100%, and 60% BW or 80% BW. Our data showed step length was greater at 80% BW than 100% BW which supports the findings of with Barnes and Janecke, as well as similar evidence from Cutuk et al. where participants walked and ran at 6mph at 20%, 60%, and 100% BW, and step length increased as percent BW increased. Our vGRF data showed greater forces at 100% BW than 80% BW which agrees with various studies in which participants ran at multiple percent BW settings on an LBPPT which all concluded vGRFs decrease as percent BW setting decreases. Our findings on increased loading rate at 80% BW compared to 100% BW agree with Grabowski and Kram. Contrarily, Sainton et al., who found loading rates decreased at 60% and 80% BW compared to 100% BW. This discrepancy could be due to the difference in running velocities. Participants in our study ran at 2.68 m/s. Participants in Grabowski and Kram’s study participants ran at faster paces (3, 4, and 5 m/s), while participants in the study conducted by Sainton et al. ran at self-selected paces, however – the average pace
2.48m/s±0.17m/s was close to our prescribed running pace. Since participants selected their own pace in the Sainton et al. study, they could also have chosen a pace that they felt was more natural and therefore may not have altered their gait mechanics as much as faster velocities potentially would have. It is important to note that while loading rates increased at 80% BW, the load itself was less compared to 100% BW. Future research should focus on loading rates across various percent BW settings and running velocities.

We found a statistically significant moderately strong negative correlation between vGRF and right lateral compartment cartilage percent change for the 100% BW condition. We also found statistically significant strong negative correlations between vGRF and left and lateral compartment cartilage percent change for the 80% BW condition. For our percent change calculation, a greater negative percent change in thickness indicates greater cartilage deformation (thinning). Therefore, as vGRF increased at 100% BW, we saw greater deformation in the lateral compartment cartilage of the right leg. The same was found to be true in the left intercondylar and lateral compartments at 80% BW.

Females had significantly greater cartilage deformation in the right medial and intercondylar compartments compared to males, at 100% BW. Our findings strengthen those of Boocock et al. who found percent change in femoral cartilage volume was greater in females compared to males, but not significantly greater. While we did not assess anatomical or kinematic differences in our study, they may be a plausible explanation for the differences between sex. Anatomical differences such as increased Q-angle in females compared to males. Kinematic differences may also be responsible for this disparity, as females have repeatedly shown altered mechanics and increased valgus stress compared to males. No significant
differences were seen in any other compartments at 100% BW, and no significant differences were seen between sexes at 80% BW.

Examining the relationship between Borg’s RPE for each condition and cartilage percent change, we found a statistically significant moderately strong negative correlation between RPE of the 80% BW condition and left 80% BW intercondylar cartilage percent change. Again, since a greater negative percent change in thickness indicates greater cartilage deformation, this signifies that as RPE increased during 80% BW running, left intercondylar cartilage became thinner. No other significant correlations were found between RPE of either running condition. Our study is the first to find correlations between RPE and acute femoral cartilage deformation, however multiple studies\(^{88,89}\) have shown decreased RPE during submaximal running at decreased body weight compared to 100% body weight.

Examining the relationships between the five KOOS sub scores and cartilage percent change we found multiple significant correlations, all of which were negative, signifying that participants who reported greater symptoms in that specific sub scale (had worse scores) had greater cartilage deformation in the compartments mentioned. Our results support those of Cattano et al.\(^{103}\) Looking at serum biomarkers before and after running at 2.2 m/s for 30 minutes, Cattano et al. found KOOS QOL were negatively correlated to changes in serum IL-1β levels, a biomarker for inflammatory response, signifying that lower KOOS QOL scores were associated with greater inflammatory response after running.\(^{103}\)

In our study, KOOS Pain scores showed a significant negative moderately strong correlation with right 80% BW medial cartilage percent change, and a strong correlation between right 80% BW intercondylar cartilage percent change. No other cartilage compartment percent change of either conditions were found to be correlated with KOOS Pain scores. KOOS
Symptom score was found to have a significant moderately strong negative correlation with right 100% BW medial cartilage percent change. No other cartilage compartment percent change of either conditions were found to be correlated with KOOS Symptom scores. KOOS ADL score was found to have significant moderately strong negative correlations with right 100% BW intercondylar and lateral compartment cartilage percent changes. No other cartilage compartment percent change of either conditions were found to be correlated with KOOS ADL scores. KOOS Sport/Recreation score was found to have a significant moderately strong negative correlation with right 80% BW intercondylar cartilage percent change. No other cartilage compartment percent change of either conditions were correlated with KOOS Sport/Recreation scores.

LIMITATIONS

While the findings of this research study are very interesting, there are some limitations that should be noted. The external generalizability is yet to be determined. The accuracy of the unloading of a lower body positive pressure treadmill is not well known, this limitation could have very large implications to our data. While we chose a similar running velocity as previous research, 2.68 m/s may not have been demanding enough to have a large effect size on our participants since they were all physically active individuals. This may have impacted our effect size. As previously mentioned, limb dominance was not determined. Knowing whether participants were right or left limb dominant might have been used to explain some of the unilateral discrepancies. Foot strike was also not determined for participants, which could have affected differences between groups (males and females). Our biomechanical findings were similar to previous research, this data was collected in a 10 second window at the 15-minute mark, halfway through each running condition. Therefore, the gait biomechanics and ground reaction force data may not be representative of participant’s gait throughout the entire session,
due to alterations in gait caused by fatigue. Lastly, the KOOS questionnaire was only administered to participants during their first data session, these scores might have changed if we had administered the KOOS again during the second data session.

FUTURE RESEARCH

Extensions of the findings of this study should examine the effects of running at various percent body weight settings on femoral articular cartilage, loading rates, and gait biomechanics. The same should be examined at faster running velocities. Limb dominance and foot strike should be determined in all participants and causes for unilateral discrepancies should be examined as well. These should be researched in healthy populations as well as unhealthy populations, specifically those that are known to have compromised joint health.

CONCLUSION

This was the first study to assess and compare acute femoral cartilage deformation, using ultrasonography, after running on a LBPPT. Running at 80% BW on a LBPPT caused enough reduction in musculoskeletal load to significantly reduce cartilage deformation and alter biomechanics. These results provide support for the use of LBPPTs in rehabilitation or athletic performance training for specific populations and patients looking to decrease musculoskeletal load and the accompanying stress on femoral cartilage.

Females had significantly greater reduction in cartilage deformation than males, specifically in cartilage compartments that are consistent with altered gait biomechanics. Vertical ground reaction forces were correlated with unilateral cartilage deformation at both body weight conditions, suggesting they may have predictive value in cartilage deformation. This was the first study to find correlations between patient reported outcomes and acute femoral cartilage deformation using ultrasonography.
REFERENCES


23. King KB, Lindsey CT, Dunn TC, Ries MD, Steinbach LS, Majumdar S. A study of the relationship between molecular biomarkers of joint degeneration and the magnetic


96. Peeler J, Christian M, Cooper J, Leiter J, MacDonald P. Managing Knee Osteoarthritis: The Effects of Body Weight Supported Physical Activity on Joint Pain, Function, and...
46


**Table 1.** Demographic Information for Study Participants

<table>
<thead>
<tr>
<th>Demographic</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of subjects</td>
<td>10</td>
<td>10</td>
<td>20</td>
</tr>
<tr>
<td>Age (years)</td>
<td>22 ± 1.33</td>
<td>21.6 ± 1.35</td>
<td>21.8 ± 1.32</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.75 ± 0.06</td>
<td>1.62 ± 0.04</td>
<td>1.68 ± 0.08</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>67.72 ± 8.59</td>
<td>62.96 ± 5.85</td>
<td>65.34 ± 7.56</td>
</tr>
</tbody>
</table>

Mean ± SD (range), m=meters, kg=kilograms

**Table 2.** Right Medial Compartment Average Cartilage Width (mm)

<table>
<thead>
<tr>
<th></th>
<th>100% BW</th>
<th>80% BW</th>
<th>CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre</td>
<td>45.11 ± 22.20</td>
<td>46.69 ± 23.98</td>
<td>-6.30 – 3.15</td>
<td>0.494</td>
</tr>
<tr>
<td>Post</td>
<td>40.99 ± 21.27</td>
<td>46.38 ± 22.95</td>
<td>-10.55 - -0.24</td>
<td>0.041*</td>
</tr>
<tr>
<td>Percent change</td>
<td>-8.85 ± 17.86</td>
<td>0.66 ± 11.87</td>
<td>-18.01 - -1.00</td>
<td>0.030*</td>
</tr>
<tr>
<td>CI</td>
<td>0.03 – 8.22</td>
<td>-2.40 – 3.01</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P value</td>
<td>0.048*</td>
<td>0.817</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Mean ± SD, BW = body weight, mm = millimeters, CI = confidence interval. Columns denote within conditions; Rows denote between conditions. * Indicates significance at the 0.05 level.
### Table 3. Left Medial Compartment Average Cartilage Width (mm)

<table>
<thead>
<tr>
<th></th>
<th>100% BW</th>
<th>80% BW</th>
<th>CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre</td>
<td>43.08 ± 19.62</td>
<td>43.12 ± 18.46</td>
<td>-2.91 – 2.82</td>
<td>0.974</td>
</tr>
<tr>
<td>Post</td>
<td>39.04 ± 15.71</td>
<td>43.32 ± 19.34</td>
<td>-9.08 – 0.54</td>
<td>0.079</td>
</tr>
<tr>
<td>Percent change</td>
<td>-6.07 ± 17.69</td>
<td>0.87 ± 10.25</td>
<td>-14.19 – 0.33</td>
<td>0.060</td>
</tr>
<tr>
<td>CI</td>
<td>0.43 – 7.63</td>
<td>-2.70 – 2.31</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P value</td>
<td>0.030*</td>
<td>0.873</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Mean ± SD, BW = body weight, mm = millimeters, CI = confidence interval. Columns denote within conditions; Rows denote between conditions. * Indicates significance at the 0.05 level.

### Table 4. Right Intercondylar Compartment Average Cartilage Width (mm)

<table>
<thead>
<tr>
<th></th>
<th>100% BW</th>
<th>80% BW</th>
<th>CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre</td>
<td>45.31 ± 18.66</td>
<td>46.87 ± 23.61</td>
<td>-6.01 – 2.89</td>
<td>0.472</td>
</tr>
<tr>
<td>Post</td>
<td>40.13 ± 16.43</td>
<td>45.67 ± 22.69</td>
<td>-9.73 - -1.35</td>
<td>0.012*</td>
</tr>
<tr>
<td>Percent change</td>
<td>-10.53 ± 13.35</td>
<td>-0.73 ± 17.47</td>
<td>-19.30 - -0.40</td>
<td>0.042*</td>
</tr>
<tr>
<td>CI</td>
<td>1.74 – 8.63</td>
<td>-2.38 – 4.79</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P value</td>
<td>0.005**</td>
<td>0.491</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Mean ± SD, BW = body weight, mm = millimeters, CI = confidence interval. Columns denote within conditions; Rows denote between conditions. * Indicates significance at the 0.05 level, ** indicates significance at the 0.01 level.
Table 5. Left Intercondylar Compartment Average Cartilage Width (mm)

<table>
<thead>
<tr>
<th></th>
<th>100% BW</th>
<th>80% BW</th>
<th>CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre</td>
<td>41.80 ± 19.22</td>
<td>43.69 ± 20.35</td>
<td>-5.33 – 1.55</td>
<td>0.265</td>
</tr>
<tr>
<td>Post</td>
<td>39.44 ± 15.73</td>
<td>42.90 ± 18.17</td>
<td>-5.96 – -0.96</td>
<td>0.009**</td>
</tr>
<tr>
<td>Percent change</td>
<td>-1.95 ± 18.71</td>
<td>0.67 ± 13.65</td>
<td>-12.83 – 7.58</td>
<td>0.596</td>
</tr>
<tr>
<td>CI</td>
<td>-0.85 – 5.56</td>
<td>-2.80 – 4.38</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P value</td>
<td>0.140</td>
<td>0.652</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Mean ± SD, BW = body weight, mm = millimeters, CI = confidence interval. Columns denote within conditions; Rows denote between conditions. * Indicates significance at the 0.05 level, ** indicates significance at the 0.01 level.

Table 6. Right Lateral Compartment Average Cartilage Width (mm)

<table>
<thead>
<tr>
<th></th>
<th>100% BW</th>
<th>80% BW</th>
<th>CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre</td>
<td>44.15 ± 23.84</td>
<td>45.11 ± 20.34</td>
<td>-5.62 – 3.69</td>
<td>0.669</td>
</tr>
<tr>
<td>Post</td>
<td>39.57 ± 17.66</td>
<td>39.37 ± 14.75</td>
<td>-3.15 – 3.56</td>
<td>0.901</td>
</tr>
<tr>
<td>Percent change</td>
<td>-6.98 ± 14.07</td>
<td>-10.15 ± 12.48</td>
<td>-3.94 – 10.27</td>
<td>0.363</td>
</tr>
<tr>
<td>CI</td>
<td>0.68 – 8.49</td>
<td>1.89 – 9.61</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P value</td>
<td>0.024*</td>
<td>0.006**</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Mean ± SD, BW = body weight, mm = millimeters, CI = confidence interval. Columns denote within conditions; Rows denote between conditions. * Indicates significance at the 0.05 level, ** indicates significance at the 0.01 level.
**Table 7.** Left Lateral Compartment Average Cartilage Width (mm)

<table>
<thead>
<tr>
<th></th>
<th>100% BW</th>
<th>80% BW</th>
<th>CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre</td>
<td>43.46 ± 22.14</td>
<td>45.89 ± 23.75</td>
<td>-7.40 – 2.52</td>
<td>0.317</td>
</tr>
<tr>
<td>Post</td>
<td>38.54 ± 16.98</td>
<td>40.59 ± 17.97</td>
<td>-6.29 – 2.19</td>
<td>0.324</td>
</tr>
<tr>
<td>Percent change</td>
<td>-8.45 ± 17.37</td>
<td>-5.95 ± 21.65</td>
<td>-14.37 – 9.37</td>
<td>0.664</td>
</tr>
<tr>
<td>CI</td>
<td>0.11 – 9.72</td>
<td>-1.88 – 12.48</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P value</td>
<td>.045*</td>
<td>0.139</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Mean ± SD, BW = body weight, mm = millimeters, CI = confidence interval. Columns denote within conditions; Rows denote between conditions. * Indicates significance at the 0.05 level.

**Table 8.** Right 100% BW Cartilage Percent Change Differences Between Sexes by Compartment.

<table>
<thead>
<tr>
<th></th>
<th>Male</th>
<th>Female</th>
<th>CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medial</td>
<td>-0.81 ± 21.41</td>
<td>-16.88 ± 8.43</td>
<td>0.78 – 31.36</td>
<td>0.040*</td>
</tr>
<tr>
<td>Intercondylar</td>
<td>-4.66 ± 14.24</td>
<td>-16.51 ± 9.75</td>
<td>0.39 – 23.32</td>
<td>0.043*</td>
</tr>
<tr>
<td>Lateral</td>
<td>-10.74 ± 13.24</td>
<td>-3.22 ± 14.53</td>
<td>-20.58 – 5.54</td>
<td>0.242</td>
</tr>
</tbody>
</table>

Mean ± SD. * Indicates significance at the 0.05 level.
**Table 9.** Left 100% BW Cartilage Percent Change Differences Between Sexes by Compartment.

<table>
<thead>
<tr>
<th>Compartment</th>
<th>Male</th>
<th>Female</th>
<th>CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medial</td>
<td>-7.84 ± 10.81</td>
<td>-4.31 ± 11.72</td>
<td>-20.52 – 13.45</td>
<td>0.667</td>
</tr>
<tr>
<td>Intercondylar</td>
<td>-6.81 ± 11.72</td>
<td>2.91 ± 23.44</td>
<td>-27.13 – 7.69</td>
<td>0.256</td>
</tr>
</tbody>
</table>

Mean ± SD. * Indicates significance at the 0.05 level

**Table 10.** Right 80% BW Cartilage Percent Change Differences Between Sexes by Compartment.

<table>
<thead>
<tr>
<th>Compartment</th>
<th>Male</th>
<th>Female</th>
<th>CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medial</td>
<td>0.36 ± 9.42</td>
<td>0.96 ± 14.43</td>
<td>-12.05 – 10.85</td>
<td>0.913</td>
</tr>
<tr>
<td>Intercondylar</td>
<td>-4.03 ± 12.14</td>
<td>2.56 ± 11.73</td>
<td>-23.14 – 9.94</td>
<td>0.413</td>
</tr>
<tr>
<td>Lateral</td>
<td>-13.96 ± 11.74</td>
<td>-6.33 ± 12.59</td>
<td>-19.06 – 3.81</td>
<td>0.178</td>
</tr>
</tbody>
</table>

Mean ± SD. * Indicates significance at the 0.05 level
Table 11. Left 80% BW Cartilage Percent Change Differences Between Sexes by Compartment.

<table>
<thead>
<tr>
<th>Compartment</th>
<th>Male</th>
<th>Female</th>
<th>CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medial</td>
<td>2.04 ± 8.77</td>
<td>-0.33 ± 11.90</td>
<td>-7.45 – 12.19</td>
<td>0.619</td>
</tr>
<tr>
<td>Intercondylar</td>
<td>-1.72 ± 16.52</td>
<td>3.07 ± 10.37</td>
<td>-17.76 – 8.16</td>
<td>0.447</td>
</tr>
</tbody>
</table>

Mean ± SD. * Indicates significance at the 0.05 level

Table 12. Right Limb Biomechanical Variables and Ground Reaction Forces

<table>
<thead>
<tr>
<th></th>
<th>100% BW</th>
<th>80% BW</th>
<th>CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GCT (s)</td>
<td>0.287 ± 0.021</td>
<td>0.275 ± 0.024</td>
<td>0.00 – 0.02</td>
<td>0.004**</td>
</tr>
<tr>
<td>Flight time (s)</td>
<td>0.077 ± 0.019</td>
<td>0.097 ± 0.019</td>
<td>-0.03 - 0.01</td>
<td>&lt;0.001**</td>
</tr>
<tr>
<td>Step rate (step/s)</td>
<td>2.76 ± 0.15</td>
<td>2.70 ± 0.18</td>
<td>0.01 – 0.09</td>
<td>0.018*</td>
</tr>
<tr>
<td>Step length (m)</td>
<td>0.98 ± 0.05</td>
<td>0.99 ± 0.06</td>
<td>-0.04 - 0.00</td>
<td>0.016*</td>
</tr>
<tr>
<td>Fz (N)</td>
<td>814.71 ± 95.13</td>
<td>694.54 ± 83.11</td>
<td>96.50 – 143.85</td>
<td>&lt;0.001**</td>
</tr>
<tr>
<td>LR (N/s)</td>
<td>4.48 ± 0.58</td>
<td>5.00 ± 0.73</td>
<td>-0.79 - 0.24</td>
<td>0.001**</td>
</tr>
</tbody>
</table>

Mean ± SD, BW = body weight, GCT = ground contact time, Fz = force, LR = loading rate, s = seconds, step/s = steps per second, m = meters, N = newtons, N/s = newtons per second. * Indicates significance at the 0.05 level, ** indicates significance at the 0.01 level.
### Table 13. Left Limb Biomechanical Variables and Ground Reaction Forces

<table>
<thead>
<tr>
<th></th>
<th>100% BW</th>
<th>80% BW</th>
<th>CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GCT (s)</td>
<td>0.293 ± 0.022</td>
<td>0.281 ± 0.022</td>
<td>0.01 – 0.02</td>
<td>&lt;0.001**</td>
</tr>
<tr>
<td>Flight time (s)</td>
<td>0.077 ± 0.018</td>
<td>0.100 ± 0.023</td>
<td>-0.03 - -0.01</td>
<td>&lt;0.001**</td>
</tr>
<tr>
<td>Step rate (step/s)</td>
<td>2.71 ± 0.14</td>
<td>2.63 ± 0.12</td>
<td>0.03 – 0.12</td>
<td>0.001**</td>
</tr>
<tr>
<td>Step length (m)</td>
<td>0.99 ± 0.05</td>
<td>1.02 ± 0.04</td>
<td>-0.04 - -0.01</td>
<td>0.002**</td>
</tr>
<tr>
<td>Fz (N)</td>
<td>809.06 ± 88.80</td>
<td>696.48 ± 83.67</td>
<td>92.60 – 132.56</td>
<td>&lt;0.001**</td>
</tr>
<tr>
<td>LR (N/s)</td>
<td>4.35 ± 0.52</td>
<td>4.90 ± 0.73</td>
<td>-0.77 - -0.34</td>
<td>&lt;0.001**</td>
</tr>
</tbody>
</table>

Mean ± SD, BW = body weight, GCT = ground contact time, Fz = force, LR = loading rate, s = seconds, step/s = steps per second, m = meters, N = newtons, N/s = newtons per second.

* Indicates significance at the 0.05 level, ** indicates significance at the 0.01 level.
FIGURES

Figure 1: Participant Positioning in Alter-G®

![Image of participant positioning in Alter-G®](image1.png)

Figure 2: Alter-G® Calibration Process

![Image of Alter-G® calibration process](image2.png)

Written consent for the use of these photos was obtained from participant.
Figure 3: Long Sit Position

Figure 4: Femoral Cartilage Thickness Measurement Procedure

Written consent for the use of these photos was obtained from participant.
Appendix A: Recruitment Flyer

Participants needed for study investigating anti-gravity treadmill running!

Research Description & Purpose: This research study will compare the effects of running at 100% bodyweight and 80% bodyweight on the articular cartilage of the knee.

This study is for West Chester University students, ages 18-25, who identify as recreationally active. Research is always voluntary!

Would the study be a good fit for me? This study may be a good fit for you if you:
- Are recreationally active
- Can run for 30 minutes at 6mph
- Have no previous lower leg surgeries or severe injuries

What would happen if I took part in the study? If you decide to take part in the research study, you would attend two separate data collection sessions, exactly one week apart, in which you would:
- Be fitted for Alter-G shorts
- Sit for 30 minutes
- Take questionnaire while sitting
- Get baseline ultrasonographic images taken of your knee
- Run for 30 minutes at 6mph
- Get post-activity ultrasonographic images taken of your knee

Specify Location of Research: This research will take place in the West Chester University Athletic Training Facility in the Sturzebecker Health Science Center, located at: 855 S New Street West Chester, PA 19382

Contact Information: To take part in this anti-gravity treadmill running research study or for more information, please contact Megan Graff at MG910582@wcupa.edu

PI Name, department & address: The principal researcher for this study is Megan Graff at West Chester University. Study IRB#: 20190925A
Appendix B: Script for Email Recruitment

Subject Line: Master’s Thesis Participants Needed

Hello Students!

I hope that this email finds everyone well. My name is Megan Graff and I am conducting research on running on an antigravity treadmill and need participants.

I am hoping that you may be able to help! If you can personally participate or if you know of any friends that may be able to participate… please email me at MG910582@wcupa.edu!

I am looking for healthy and recreationally active males and females, age 18-25 years old. You cannot participate if you have had any lower limb surgeries or severe injuries.

Please help spread the word! If you know anyone that may be interested in participating, please have them email me at MG910582@wcupa.edu

Thank you for any help you can provide!
Megan Graff

Megan Graff, MS Candidate, LAT, ATC
Graduate Assistant Athletic Trainer
West Chester University
(516) 974-3169
Appendix C: Informed Consent Form

Project Title: The Effects of Lower Body Positive Pressure Treadmill Running on Acute Femoral Cartilage Deformation in Healthy Males and Females

Investigator(s): Megan Graff; Kenneth Clark; John Smith; Nicole Cattano

Project Overview:

Participation in this research project is voluntary and is being done by Megan Graff as part of their Master's Thesis to compare the effects of running at 100% bodyweight and 80% body weight on an anti-gravity treadmill on the articular cartilage of the knee in healthy individuals. Your participation will take about two 65 minute sessions to get fitted with Alter-G shorts, sit for 30 minutes, take questionnaires while sitting, take baseline ultrasonographic images, run for 30 minutes, take post activity ultrasonographic images. There is a minimal risk of mild discomfort while running on the Alter-G (anti-gravity treadmill). As the participant, you will have the opportunity to gain experience running on an Alter-G anti-gravity treadmill. This research will help to collect objective data on how anti-gravity running affects acute femoral cartilage deformation, and to understand the collected objective data that will either support or oppose the use of anti-gravity treadmills in rehabilitation.

The research project is being done by Megan Graff as part of her Master's Thesis to compare the effects of running at 100% bodyweight and 80% body weight on an anti-gravity treadmill on the articular cartilage of the knee in healthy individuals. If you would like to take part, West Chester University requires that you agree and sign this consent form.

You may ask Megan Graff any questions to help you understand this study. If you don’t want to be a part of this study, it won’t affect any services from West Chester University. If you choose to be a part of this study, you have the right to change your mind and stop being a part of the study at any time.

1. What is the purpose of this study?

   - To compare the effects of running at 100% bodyweight and 80% body weight on an anti-gravity treadmill on the articular cartilage of the knee in healthy individuals.

2. If you decide to be a part of this study, you will be asked to do the following:

   - Be fitted with Alter-G shorts
   - Sit for 30 minutes
   - Take questionnaire while sitting
   - Baseline ultrasonographic images
   - Run for 30 minutes
   - Post activity ultrasonographic images
• Return in 1 week to repeat the procedures with a different body weight setting on the treadmill
• This study will take a total of 2 hours and 10 minutes (two 65 min. sessions) of your time.

3. Are there any experimental medical treatments?

• No

4. Is there any risk to me?

• Possible risks or sources of discomfort include: Mild discomfort while running on the Alter-G (anti-gravity treadmill)
• If you become upset and wish to speak with someone, you may speak with Megan Graff
• If you experience discomfort, you have the right to withdraw at any time.

5. Is there any benefit to me?

• Benefits to you may include: experience running on an Alter-G anti-gravity treadmill.
• Other benefits may include: collect objective data on how anti-gravity running affects acute femoral cartilage deformation, and to collect objective data that will either support or oppose the use of anti-gravity treadmills in rehabilitation.

6. How will you protect my privacy?

• The session will not be recorded.
• Your records will be private. Only Megan Graff, Kenneth Clark, John Smith, Nicole Cattano, and the IRB will have access to your name and responses.
• Your name will not be used in any reports.
• Records will be stored:
  o Password Protected File/Computer

• Participants names will not be attached to the data collected. Participants names will only be written on their signed informed consent forms, which will be locked away in a filing cabinet inside a locked office.
• Records will be destroyed Three Years After Study Completion

7. Do I get paid to take part in this study?

• No

8. Who do I contact in case of research related injury?

• For any questions with this study, contact:
  o Primary Investigator: Megan Graff at 516-974-3169 or mg910582@wcupa.edu
Secondary Investigator and Faculty Sponsor: Nicole Cattano at 610-436-2250 or Ncattano@wcupa.edu
Tertiary Investigator: Kenneth Clark at 610-436-2109 or KClark@wcupa.edu

9. What will you do with my Identifiable Information/Biospecimens?

- Not applicable.

For any questions about your rights in this research study, contact the ORSP at 610-436-3557.

I, _________________________________ (your name), have read this form and I understand the statements in this form. I know that if I am uncomfortable with this study, I can stop at any time. I know that it is not possible to know all possible risks in a study, and I think that reasonable safety measures have been taken to decrease any risk.

_________________________________
Subject/Participant Signature Date:________________

_________________________________
Witness Signature Date:________________
Appendix D: IRB Approval Letter

TO: Megan Graff, Nicole Cattano, John Smith, Kenneth Clark
FROM: Nicole M. Cattano, Ph.D.
Co-Chair, WCU Institutional Review Board (IRB)
DATE: 9/24/2019

Project Title: The Effects of Lower Body Positive Pressure Treadmill Running on Acute Femoral Cartilage Deformation in Healthy Males and Females.
Date of Approval: 9/24/2019

☒ Expedited Approval
This protocol has been approved under the new updated 45 CFR 46 common rule that went in to effect January 21, 2019. As a result, this project will not require continuing review. Any revisions to this protocol that are needed will require approval by the WCU IRB. Upon completion of the project, you are expected to submit appropriate closure documentation. Please see www.wcupa.edu/research/irb.aspx for more information.

Any adverse reaction by a research subject is to be reported immediately through the Office of Research and Sponsored Programs via email at irb@wcupa.edu.

Signature:

Co-Chair of WCU IRB

WCU Institutional Review Board (IRB)
IORG#: IORG0004242
IRB#: IRB00005030
FWA#: FWA00014155

West Chester University is a member of the State System of Higher Education
Appendix E: IRB Revision Approval Letter

TO: Megan Graff, Nicole Cattano, John Smith, Kenneth Clark
FROM: Melissa A. Reed, Ph.D.
Co-Chair, WCU Institutional Review Board (IRB)
DATE: 11/26/2019

Project Title: The Effects of Lower Body Positive Pressure Treadmill Running on Acute Femoral Cartilage Deformation in Healthy Males and Females
Date of Approval for Revision**: 11/26/2019
**Please note that the original end date of your approved protocol still applies**

☑ Expedited Approval
This protocol has been approved under the new updated 45 CFR 46 common rule that went into effect January 21, 2019. As a result, this project will not require continuing review. Any revisions to this protocol that are needed will require approval by the WCU IRB. Upon completion of the project, you are expected to submit appropriate closure documentation. Please see www.wcupa.edu/research/irb.aspx for more information.

Any adverse reaction by a research subject is to be reported immediately through the Office of Research and Sponsored Programs via email at irb@wcupa.edu.

Signature: Melissa Reed
Co-Chair of WCU IRB

WCU Institutional Review Board (IRB)
IORG#: IORG0004242
IRB#: IRB00005030
FWA#: FWA00014155

West Chester University is a member of the State System of Higher Education
Appendix F: Health History Questionnaire

Health History Questionnaire

Participant Number: ____________________________ Date: ________________

DOB: _____/_____/_____

Please answer the following questions to the best of your ability.

YES  NO
1. Are you between the ages of 18 and 25?
   Age: __________

YES  NO
2. Do you currently participate in moderate physical activity?
   (Participating a minimum of 2x/wk for a total of 80 minutes at moderate intensity)

YES  NO
3. Have you ever had a significant lower extremity injury within the last 3 months?
   (e.g., missed physical activity for >2 weeks, use of crutches for >1 week)

YES  NO
4. Have you ever been diagnosed with arthritis (e.g., rheumatoid) by a physician?

YES  NO
5. Have you ever had an intra-articular injection within the past 30 days?

YES  NO
6. Have you played sports in the past?
   If yes, please list the sport(s) and # years participated:

YES  NO
7. Have you ever been diagnosed with a concussion?
   If yes, please list dates of each concussion:

YES  NO
8. Does your knee ever swell?
   If yes, how often?

YES  NO
9. Does your knee ever swell?

10. How many days a week are you physically active? _______________
    How many minutes per day? _______________

YES  NO
11. Is running part of your regular physical activity?
    How many times per week? ___________ Average distance ___________
**Orthopedic Medical History**

Have you ever had any injuries or problems to the following? (If yes – specify WHEN & What)

<table>
<thead>
<tr>
<th>YES</th>
<th>NO</th>
<th>Not Sure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Pelvis or Hip</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Thigh</td>
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<tr>
<td></td>
<td></td>
<td>Knee Ligament</td>
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<tr>
<td></td>
<td></td>
<td>Knee Meniscus</td>
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<tr>
<td></td>
<td></td>
<td>Chronic Knee</td>
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<tr>
<td></td>
<td></td>
<td>Leg Fracture</td>
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<tr>
<td></td>
<td></td>
<td>Chronic Leg</td>
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<tr>
<td></td>
<td></td>
<td>Stress Fractures</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Low Back Pain</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Chronic Knee Pain</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ankle Sprain</td>
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<tr>
<td></td>
<td></td>
<td>Chronic Lower Leg</td>
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<td></td>
<td></td>
<td>Chronic Low Back</td>
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<td></td>
<td></td>
<td>Acute Low Back</td>
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<tr>
<td></td>
<td></td>
<td>Shoulder</td>
</tr>
</tbody>
</table>

- Do you take any anti-inflammatory medications regularly? (e.g., Advil, Aleve)  
  If yes, What:  
  What for:  

- Do you take any supplements regularly? (e.g., Glucosamine, Fish Oil)  
  If yes, What:  
  What for:  

Thank you for completing this health history questionnaire. Your participation is much appreciated!
Appendix G: Knee Osteoarthritis Outcome Score (KOOS)

KOOS KNEE SURVEY

Today’s date: _____/_____/_____

Participant Number

INSTRUCTIONS: This survey asks for your view about your knee. This information will help us keep track of how you feel about your knee and how well you are able to perform your usual activities. Answer every question by ticking the appropriate box, only one box for each question. If you are unsure about how to answer a question, please give the best answer you can.

Symptoms
These questions should be answered thinking of your knee symptoms during the last week.

S1. Do you have swelling in your knee?
   Never  Rarely  Sometimes  Often  Always

S2. Do you feel grinding, hear clicking or any other type of noise when your knee moves?
   Never  Rarely  Sometimes  Often  Always

S3. Does your knee catch or hang up when moving?
   Never  Rarely  Sometimes  Often  Always

S4. Can you straighten your knee fully?
   Always  Often  Sometimes  Rarely  Never

S5. Can you bend your knee fully?
   Always  Often  Sometimes  Rarely  Never

Stiffness
The following questions concern the amount of joint stiffness you have experienced during the last week in your knee. Stiffness is a sensation of restriction or slowness in the ease with which you move your knee joint.

S6. How severe is your knee joint stiffness after first wakening in the morning?
   None  Mild  Moderate  Severe  Extreme

S7. How severe is your knee stiffness after sitting, lying or resting later in the day?
   None  Mild  Moderate  Severe  Extreme
Knee injury and Osteoarthritis Outcome Score (KOOS), English version LK1.0

**Pain**

P1. How often do you experience knee pain?
- Never
- Monthly
- Weekly
- Daily
- Always

What amount of knee pain have you experienced the **last week** during the following activities?

P2. Twisting/pivoting on your knee
- None
- Mild
- Moderate
- Severe
- Extreme

P3. Straightening knee fully
- None
- Mild
- Moderate
- Severe
- Extreme

P4. Bending knee fully
- None
- Mild
- Moderate
- Severe
- Extreme

P5. Walking on flat surface
- None
- Mild
- Moderate
- Severe
- Extreme

P6. Going up or down stairs
- None
- Mild
- Moderate
- Severe
- Extreme

P7. At night while in bed
- None
- Mild
- Moderate
- Severe
- Extreme

P8. Sitting or lying
- None
- Mild
- Moderate
- Severe
- Extreme

P9. Standing upright
- None
- Mild
- Moderate
- Severe
- Extreme

**Function, daily living**

The following questions concern your physical function. By this we mean your ability to move around and to look after yourself. For each of the following activities please indicate the degree of difficulty you have experienced in the **last week** due to your knee.

A1. Descending stairs
- None
- Mild
- Moderate
- Severe
- Extreme

A2. Ascending stairs
- None
- Mild
- Moderate
- Severe
- Extreme
For each of the following activities please indicate the degree of difficulty you have experienced in the last week due to your knee.

<table>
<thead>
<tr>
<th>Activity</th>
<th>None</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Extreme</th>
</tr>
</thead>
<tbody>
<tr>
<td>A3. Rising from sitting</td>
<td></td>
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<tr>
<td>A4. Standing</td>
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<td>A5. Bending to floor/pick up an object</td>
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<td>A6. Walking on flat surface</td>
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<td>A7. Getting in/out of car</td>
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<td>A8. Going shopping</td>
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<tr>
<td>A9. Putting on socks/stockings</td>
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<td>A10. Rising from bed</td>
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<td>A11. Taking off socks/stockings</td>
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<td>A12. Lying in bed (turning over, maintaining knee position)</td>
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<tr>
<td>A13. Getting in/out of bath</td>
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<tr>
<td>A14. Sitting</td>
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<tr>
<td>A15. Getting on/off toilet</td>
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</tbody>
</table>
Knee injury and Osteoarthritis Outcome Score (KOOS), English version LK1.0

For each of the following activities please indicate the degree of difficulty you have experienced in the last week due to your knee.

A16. Heavy domestic duties (moving heavy boxes, scrubbing floors, etc)
- None
- Mild
- Moderate
- Severe
- Extreme

A17. Light domestic duties (cooking, dusting, etc)
- None
- Mild
- Moderate
- Severe
- Extreme

Function, sports and recreational activities
The following questions concern your physical function when being active on a higher level. The questions should be answered thinking of what degree of difficulty you have experienced during the last week due to your knee.

SP1. Squatting
- None
- Mild
- Moderate
- Severe
- Extreme

SP2. Running
- None
- Mild
- Moderate
- Severe
- Extreme

SP3. Jumping
- None
- Mild
- Moderate
- Severe
- Extreme

SP4. Twisting/pivoting on your injured knee
- None
- Mild
- Moderate
- Severe
- Extreme

SP5. Kneeling
- None
- Mild
- Moderate
- Severe
- Extreme

Quality of Life

Q1. How often are you aware of your knee problem?
- Never
- Monthly
- Weekly
- Daily
- Constantly

Q2. Have you modified your life style to avoid potentially damaging activities to your knee?
- Not at all
- Mildly
- Moderately
- Severely
- Totally

Q3. How much are you troubled with lack of confidence in your knee?
- Not at all
- Mildly
- Moderately
- Severely
- Extremely

Q4. In general, how much difficulty do you have with your knee?
- None
- Mild
- Moderate
- Severe
- Extreme
Appendix H: Borg’s Rating of Perceived Exertion

Instructions to the Borg-RPE-Scale®

During the work we want you to rate your perception of exertion, i.e. how heavy and strenuous the exercise feels to you and how tired you are. The perception of exertion is mainly felt as strain and fatigue in your muscles and as breathlessness or aches in the chest.

Use this scale from 6 to 20, where 6 means “No exertion at all” and 20 means “Maximal exertion.”

9 Very light. As for a healthy person taking a short walk at his or her own pace.

13 Somewhat hard. It still feels OK to continue.

15 It is hard and tiring, but continuing is not terribly difficult.

17 Very hard. It is very strenuous. You can still go on, but you really have to push yourself and you are very tired.

19 An extremely strenuous level. For most people this is the most strenuous exercise they have ever experienced.

Try to appraise your feeling of exertion and fatigue as spontaneously and as honestly as possible, without thinking about what the actual physical load is. Try not to underestimate, nor to overestimate. It is your own feeling of effort and exertion that is important, not how it compares to other people’s. Look at the scale and the expressions and then give a number. You can equally well use even as odd numbers.

Any questions?
6 No exertion at all
7 Extremely light
8 Very light
9 Light
10 Somewhat hard
11 Hard (heavy)
12 Very hard
13 Extremely hard
14 Maximal exertion