# HOW DO RUNNING AND BICYCLING AFFECT YOUR KNEES?

ANTHONY A. GATTI

# THE IN VIVO RESPONSE OF KNEE ARTICULAR CARTILAGE TO RUNNING AND BICYCLING

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## LAY ABSTRACT

Knee osteoarthritis is a degenerative joint disease that affects all knee tissues, particularly articular cartilage. This "wear and tear" condition reduces mobility and creates pain, collectively decreasing quality of life. Two important risk factors for knee osteoarthritis are age and obesity. While we cannot stop aging, exercise can have a positive impact on weight, particularly among adults with knee osteoarthritis. This thesis provides foundational information on how running and bicycling affects knee cartilage. First, we identified a useful method of measuring steps during running and pedal revolutions during bicycling. Second, we compared the effect of running and bicycling of equal cumulative load on knee cartilage, using MRI. The running activity was 1/3 the length of the bicycling activity but despite shorter exposure, running caused changes in cartilage shape and composition, while bicycling did not. These findings suggest that bicycling is a suitable aerobic activity that reduces loading at the knee.

ABSTRACT

**Background**

Knee osteoarthritis is a degenerative joint disease characterized by damaged cartilage, tendons, ligaments, synovium, and bone. Knee osteoarthritis causes joint pain, reduced joint function, and decreased quality of life and is the leading cause of chronic disability in older adults. Two of the major risk factors for knee osteoarthritis are increasing age and obesity. To decrease the occurrence of knee osteoarthritis in our aging population, it is important that we identify exercises that are safe for people with or at risk of knee osteoarthritis.

**Purpose**

The main purpose of this thesis was to compare the acute response of knee cartilage composition to two common aerobic activities, running and bicycling, of equal total load. To address the primary purpose, we first sought to determine the reliability and validity of measuring loading repetition during running (steps) and bicycling (pedal-revolutions) using accelerometry.

**Methods**

1) Twenty-two healthy adults completed running and bicycling activity bouts (five-minutes) while wearing six accelerometers: two at each the waist, thigh and shank. Accelerometer and video data were collected during each activity. 2) Fifteen healthy men completed running and bicycling activities of equal cumulative load that were preceded and followed by a series of magnetic resonance images.

**Results**

1) Excellent reliability (ICC≥.99; SEM≤1.0) and validity (Pearson≥.99) were found for step and pedal revolution measurements taken by an accelerometer placed at the shank. 2) Bicycling did not cause significant changes in cartilage composition ($p=0.274$); however, running did cause a change in cartilage composition ($p=0.002$).

**Conclusion**

Findings from this thesis suggest that to acquire reliable and valid step and pedal revolution measurement, accelerometers should be placed on the shank. Furthermore, bicycling causes no statistical changes in knee cartilage, while running does. Bicycling may therefore be used to combat obesity and maintain cardiovascular health in individuals with compromised joint health.

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LIST OF ABBREVIATIONS

| Abbreviation | Definition |
|---|---|
| (AC) | Articular Cartilage |
| (ANOVA) | Analysis of Variance |
| (BMI) | Body Mass Index |
| (dGEMRIC) | Delayed Gadolinium Enhanced Magnetic Resonance Imaging of Cartilage |
| (FOV) | Field of View |
| (FSE) | Fast Spin Echo |
| (FSPGR) | Fast Spoiled Gradient Recalled Echo |
| (ICC) | Intraclass Correlation |
| (IPAQ) | International Physical Activity Questionnaire |
| (LED) | Light Emitting Diode |
| (LEFS) | Lower Extremity Functional Scale |
| (LF) | Lateral Femur |
| (LT) | Lateral Tibia |
| (MESE) | Multi Echo Spin Echo |
| (MF) | Medial Femur |
| (MRI) | Magnetic Resonance Imaging |
| (MT) | Medial Tibia |
| (OA) | Osteoarthritis |
| (PAR-Q) | Physical Activity Readiness Questionnaire |
| (PD) | Proton Density |
| (PG) | Proteoglycan |

| | |
|---|---|
| ($R^2$) | Coefficient of Determination |
| (RPM) | Revolutions per Minutes |
| (SEM) | Standard Error of Measurement |
| (T1rho) | T1rho relaxation time |
| (T2) | T2 relaxation time |
| (TE) | Echo Time |
| (TR) | Repetition Time |
| (vGRF) | Vertical Ground Reaction Force |
| (vPRF) | Vertical Pedal Reaction Force |

## DECLARATION OF ACADEMIC ACHIEVEMENT

This thesis is the primary work of Master of Science candidate, Anthony A. Gatti. Anthony was responsible for the planning and execution of the following research study. Data enclosed in this thesis was collected during the 2014-2015 academic year. As the primary author, Anthony's contributions include: literature review, study designs, ethics applications, participant recruitment and consent, booking study visits, data collection, data analysis, and preparation of manuscripts. The second chapter of this thesis has been submitted for publication and the third chapter is intended for future publication.

Important contributors to this thesis include: Dr. Monica Maly, the thesis supervisor who funded this study, guided study design and interpretation of the results, and edited all submitted documents; Professor Paul Stratford, who provided expertise and guidance in study design and data analysis; Dr. Michael Noseworthy, who provided resources, guidance, and help for overall study design, and magnetic resonance imaging acquisition and analysis; Dr. Jack Callaghan who provided expertise in study design and biomechanics; and Elora Brenneman, who helped setup equipment, pilot test study protocols, and collect data necessary for both studies.

# CHAPTER 1
# INTRODUCTION

## Osteoarthritis

### Burden

Osteoarthritis (OA) is a degenerative joint disease that causes joint swelling, stiffness and pain; these factors reduce joint mobility (Badley & Glazier, 2004). In particular, OA decreases individuals' willingness and ability to ambulate. By decreasing mobility, OA reduces individuals' ability to complete activities of daily living and, importantly, restricts them from performing activities they enjoy (Badley & Glazier, 2004). Knee OA in particular is the leading cause of chronic disability in older adults (Guccione et al., 1994). Not only is the prevalence of OA high, but individuals with OA are at increased risk of mortality from other co-morbidities including cardiovascular disease, cancer, respiratory disease, gastrointestinal disease, and dementia (Nuesch et al., 2011).

Not only can OA be debilitating, it also affects many Canadians. It is estimated that more than half of people over 65 and approximately 80% of people over 75 have OA (Arden & Nevitt, 2006). The Arthritis Alliance of Canada estimated that in 2010, OA cost $10.2 billion dollars in direct costs (health care), and $17.3 billion in indirect costs, such as lost productivity, to the Canadian economy (Bombardier, Hawker, & Mosher, 2011). The economic burden of OA is projected to steadily increase in the foreseeable future, due to our aging and increasingly obese population (Bombardier et al., 2011; Felson et al., 2000).

### Pathology

Osteoarthritis is a degenerative joint disease that affects the whole joint (Felson et al., 2000; Goldring & Goldring, 2010). The hallmarks of OA include articular cartilage (AC) loss along with changes to the underlying bone, as well as cyst and osteophyte formation (Creamer & Hochberg, 1997; Felson, 2006). Not only are cartilaginous and bony structures affected, but degenerative changes to muscles, ligaments, and the synovium are also observed (Felson et al., 2000). Damage or disruption of healthy AC is hypothesized to be one of the earliest changes that leads to OA (Buckwalter, Mankin, & Grodzinsky, 2005). Articular cartilage is a specialized tissue that lines the ends of bones within joints and acts to attenuate and transmit forces from one bone to the next; therefore, damage to this structure may lead to abnormal joint biomechanics. These abnormal joint biomechanics accelerate degeneration of other joint tissues (Buckwalter et al., 2005; Lu & Mow, 2008). Furthermore, it has also been proposed that the loss of joint function observed in OA is directly caused by a loss of AC (Buckwalter et al., 2005).

## Physical Activity and Joint Health

The health benefits of physical activity are well documented (Blair & Brodney, 1999; Warburton, 2006). Physical activity decreases the risk of cardiovascular disease, cancer, osteoporosis, hypertension, diabetes, and depression; furthermore, physical activity decreases all-cause mortality (Lee & Skerrett, 2001; Warburton, 2006). Individuals with knee OA are often less active as a result of joint pain and decreased mobility. Approximately 40% of individuals with arthritis report that their physical activity is

limited due to pain from their disease (Badley & Glazier, 2004). Furthermore, a systematic review and meta-analysis reported that high quality evidence shows that only 13% of participants with OA complete the recommendation of >150 min/week of moderate to vigorous physical activity (Wallis, Webster, Levinger, & Taylor, 2013). Decreased activity suggests that individuals with knee OA are not benefiting from activities that would decrease their risk of numerous chronic diseases (Warburton, 2006).

A recent Cochrane review on 54 randomized control trials assessed the effect of land based exercise on knee OA concluding that individuals with knee OA benefit from physical activity (Fransen et al., 2015). The review found high quality evidence that physical activity reduces pain and improves quality of life; while moderate quality evidence suggests physical activity improves physical function. The positive effects on physical function and knee pain remained two to six months post treatment. While weight loss is a primary goal of exercise for individuals with knee OA, weight loss induced by exercise plus diet is better than either diet or exercise alone (Messier et al., 2013). The combination of diet and exercise caused greater weight loss, reduction in pain, and improvement in function compared to either alone.

Decreased physical activity in those with knee OA can be explained, in part, by pain, muscular strength (Holla et al., 2014) and obesity (Garver et al., 2014). Not only is muscular strength related to physical activity levels, but it is also positively correlated with physical functioning and inversely correlated with pain, two important variables in

quality of life (Johani et al., 2014). Furthermore, individuals with knee OA who are obese (BMI >30) participate in less physical activity than their normal or underweight counterparts (BMI<24.99) (Garver et al., 2014). Despite these findings, the direction of the relationship, that is, causation, between obesity, pain, and muscular strength with physical activity remains unclear in individuals with knee OA.

Furthermore it is unclear how physical activity affects cartilage health. It appears that too little or too much exposure to physical activity is detrimental to AC. When loading to healthy knee cartilage was limited for 7 weeks due to ankle injury, there were decreases in cartilage thickness (Hinterwimmer et al., 2004). Non-weight bearing also appears to change cartilage composition as measured using T1rho relaxation time (T1rho) and T2 relaxation time (T2); this composition change returns to baseline values after 4-weeks of full weight bearing (Richard B. Souza et al., 2012). Excessive loading is also detrimental. Large medial (relative to lateral) knee joint loads during one gait cycle predicted large decreases in medial tibial cartilage volume, over one year (Bennell et al., 2011). Despite individuals with knee OA having a lower step-count over the course of a day, they actually experience greater cumulative medial knee loading during walking over the day, compared to healthy controls (Maly, Robbins, Stratford, Birmingham, & Callaghan, 2013). This study highlights the complex relationship between joint loading that results from individual variations in anthropometrics, gait, and physical activity levels. These studies suggest that there is likely a “sweet spot” of mechanical loading, above or below which cartilage tissue may degrade. It is necessary that we expand upon these studies to

determine how various forms of physical activity affect cartilage health, including morphometric and compositional changes to cartilage.

An important gap in our understanding is how AC acutely responds to loading caused by physical activity, as well as how AC adapts, over time, as a result of physical activity. Such findings will provide the basis for physical activity recommendations that slow the progression of OA or decrease the risk of onset. Slowing the progression or decreasing the risk of OA will hopefully facilitate recommendations for sustained activity as one ages, decreasing individual risk of other chronic diseases (Warburton, 2006).

**Running and Bicycling**

Running is a popular form of physical activity, although it produces high impacts on lower extremity joints (Klein et al., 2007). Impact is defined as a high force being applied over a short period of time. In running, the collision between the foot and ground is greater than 1.8 times body mass (Bus, 2003) and occurs over 0.02-0.03 seconds (Clarke, Frederick, & Cooper, 1983). Clinicians commonly recommend bicycling as a "low-impact" alternative to running for people with knee OA (Kettunen & Kujala, 2004; Klein et al., 2007; Kutzner et al., 2012). Bicycling is low-impact because the foot is continually in contact with the bicycle pedal and there is no collision between the foot and pedal. Furthermore, during bicycling the bicycle seat off-loads body mass, decreasing loads exerted at the foot. Although bicycling is low-impact, it requires sustained load exposure during pedaling. The duration of loading on the lower extremity during bicycling is over

a longer period of time (~0.75s @ 80 revolutions per minute) than during the stance phase of running (~0.25s @ 4:45min/km pace and 80 steps/min) because a load is being applied to the foot throughout a pedal revolution (De Wit, De Clercq, & Aerts, 2000; Ericson & Nisell, 1987; Mornieux, Zameziati, Mutter, Bonnefoy, & Belli, 2006; Newmiller, Hull, & Zajac, 1988). Sustained load application allows for tissue creep to occur, causing the greatest amount of fluid movement and tissue deformation (Cohen, Foster, & Mow, 1998; Nordin & Frankel, 2012). A larger amount of tissue deformation leads to greater stress within the cartilage solid structure (Mow, Holmes, & Michael Lai, 1984). It is unclear how stress affects AC health and whether it promotes health by stimulating chondrocytes to produce collagen and proteoglycans; or if stress facilitates cartilage damage by overloading the tissue. It is likely a combination of stimulating collagen and proteoglycan development with some degradation (Bellucci & Seedhom, 2002; Seedhom, 2005; Smith et al., 2000). Due to the differing load characteristics between bicycling and running, it is likely that knee cartilage responds differently to each respective activity.

## Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) can determine the in vivo morphology (size and shape) and composition of knee AC (Choi & Gold, 2011). Specifically, the MRI technique of T2 relaxation measures how long a tissue takes to relax, in milliseconds (ms), after being excited by a magnetic field. T2 relaxation time is sensitive to water content, as well as the orientation of collagen fibrils, giving an indication of cartilage composition (Choi & Gold, 2011; T.J. Mosher, Liu, & Torok, 2010; Subburaj et al.,

2012). By taking two sets of MR images, one before and one after joint loading, we are able to observe how cartilage responds to loading by observing the change in T2 relaxation time (Liess, 2002; Timothy J. Mosher et al., 2005; T.J. Mosher et al., 2010; Subburaj et al., 2012).

**Magnetic Resonance Imaging Studies of Cartilage Loading**

Studies have documented that knee cartilage deforms 3-8% with exposure to activities ranging from 30 body-weight squats to 20-km runs (F. Eckstein, Lemberger, Stammberger, Englmeier, & Reiser, 2000; Kessler, 2005). Deformation patterns as well as the magnitude of deformation appears to be dependent on the type, frequency, and magnitude of loading (F Eckstein, 2005; Niehoff et al., 2011). Though, it is important to note that the total loading exposures of different activities were likely not equivalent in previous work.

Cartilage morphology recovers from this wide range of loading. Recovery of cartilage volume appears linear, requiring >90-minutes after 100 dynamic squats (Felix Eckstein, Tieschky, Faber, Englmeier, & Reiser, 1999; Kessler, Glaser, Tittel, Reiser, & Imhoff, 2008). The rate of recovery has been correlated ($r=0.87$ to $r=0.97$) with the amount of deformation that cartilage undergoes; it is hypothesized that greater deformation and faster recovery are indicative of unhealthy cartilage that is less able to resist water movement and deformation caused by loading (Choi & Gold, 2011; F Eckstein, 2005; Felix Eckstein et al., 1999). Despite these findings, studies of cartilage morphology were

unable to find differences in how healthy (n=11) and osteoarthritic (n=19) cartilage responds when 45 minutes of static loading equivalent to 50% of body mass is applied to one knee (Cotofana et al., 2011). Furthermore, previous participation in physical activity does not appear to influence the response of knee AC morphology. No differences in the response of patellar cartilage to squatting were found between sedentary controls (n=14), professional weight-lifters (n=7), and professional bobsleigh sprinters (n=7) (F Eckstein, 2005). The use of T2 relaxation and other MRI techniques that are sensitive to cartilage composition may further contribute to the knowledge gained through studies of cartilage morphology.

When T2 relaxation time is determined before and after loading, we can observe how water content and collagen fiber alignment change as a result of the respective load. Specifically, when running has been studied using T2 relaxation, the greatest change in T2 is observed in regions that typically bear the most load, and in superficial AC (Cha et al., 2012; T.J. Mosher et al., 2010; Subburaj et al., 2012). Typical changes in mean T2 caused by running are in the ranges of 1-4ms (T.J. Mosher et al., 2010) or 3-9% (Subburaj et al., 2012) depending on the region of interest. Not only does the greatest change occur superficially, but when comparing the changes in T2 caused by running 3.5 miles between older (>45 years of age) and younger (<20 years of age) individuals, there is a greater change in superficial T2 in the older group (Cha et al., 2012). The differing results of T2 relaxation between younger and older individuals indicates that aging may have an effect on the acute response of cartilage to load and therefore requires further

investigation. One study found similar changes in OA (n=44) versus healthy (n=93) cartilage T2 as a result of 10-minutes of static loading equivalent to 50% of body mass applied to the knee of interest while participants remained in the MRI scanner (R.B. Souza et al., 2014). In both healthy and OA knees, static loading caused a decrease in superficial weight-bearing T2; while T2 increased in non-weight-bearing and deep cartilage regions (R.B. Souza et al., 2014). These data suggest that fluid may flow from the superficial to deeper layer of cartilage under loading. These results are important in explaining how cartilage responds to high impact (running) and static loading; but further research that directly compares the response of cartilage between types of load and different activities is needed.

**Standardizing Load Exposure: Biomechanics**

Previous studies of the response of AC to loading have not quantified the joint biomechanics acting on and within the body that cause cartilage changes (Cotofana et al., 2011; F Eckstein, 2005; Felix Eckstein et al., 1999; F. Eckstein et al., 2000; Kessler, 2005; Kessler et al., 2008; Van Ginckel & Witvrouw, 2013). Changes to cartilage volume as a result of various activities, including knee bends, squatting, walking, running and bicycling, are different (F Eckstein, 2005; F. Eckstein et al., 2000). Although these studies have shown differing responses of cartilage to a variety of activities, it is unclear whether these differences are due to the nature of the activity or due to differences in the total load exposure caused by the different activities. Very few studies have attempted to

control for the total load exposure to determine whether the nature of the activity is responsible for unique changes to cartilage.

Boocock et al. (2009) performed a biomechanical analysis of running where the exposure to running was standardized to 5000 steps. The resulting changes to cartilage morphology were observed using MRI. This study found that the lateral compressive stress of the knee was significantly related to the percentage change in lateral femoral cartilage volume ($p<0.05$) (Boocock, McNair, Cicuttini, Stuart, & Sinclair, 2009). While normalizing to step-count does provide a means of comparing participants, differences in body mass, kinematics, and kinetics will likely lead to differences in total load exposure despite constant total step-count. More studies that characterize load exposure alongside MR imaging of AC are needed. It is particularly important to standardize load exposure when comparing the response of cartilage between different activities.

**Cumulative Load**

A measure of cumulative load can enable standardization of load exposure and therefore better comparisons of the effect of activity on AC between people. The sum of impulses (Ns) across one activity has been used to represent cumulative load (Stefanyshyn, Stergiou, Lun, Meeuwisse, & Worobets, 2006). Impulse is a product of force and the amount of time that the force is applied; impulse is represented by the area under a force vs. time graph (Stefanyshyn et al., 2006). By taking the area under a force versus time graph, it is possible to quantify the sum of the forces applied throughout an activity.

Cumulative load throughout a cycle of loading is just as important as peak forces, which are commonly reported but often reflect very short periods of time (Norman et al., 1998). The importance of cumulative load has been highlighted due to its ability to distinguish between healthy individuals and those with a pathology including patellofemoral pain and low back pain (Norman et al., 1998; Stefanyshyn et al., 2006). Accordingly, cumulative load, which provides a measure of total load exposure, may be useful in the study of the deformational behaviour of cartilage. Cumulative load will enable us to determine whether differences in the acute response of AC between different activities are the result of the nature of the activity, rather than total load exposure.

**Estimates of Cumulative Load**

The ideal cumulative load measurement would require direct measurement of joint contact forces inside the knee over the duration of an activity. Direct contact force measurement has been achieved in a very small sample of patients with a total knee replacement (Kutzner et al., 2012). Acquisition of such data is limited, and obviously has limitations as patients have an artificial knee joint, are typically of older age, and may have otherwise abnormal biomechanics that lead to the knee replacement. In order to determine forces acting at the knee in healthy adults the current gold standard is force measurement via force-platforms combined with three-dimensional motion capture. Kinetics obtained from force platforms and kinematics from motion capture can be combined to calculate forces and moments acting about each joint. Forces and moments can then be used to calculate the mean impulse of one movement, whether that is a step

during walk or running, a bending movement while working in a factory, or a pedal revolution during bicycling. Due to equipment limitations it is not currently feasible to directly measure forces and therefore to determine cumulative load of running or bicycling outside of the laboratory environment. Therefore, it is necessary that techniques are developed and tested to allow for estimation of cumulative load in a real world environment. Estimates of cumulative load are typically calculated as the product of laboratory derived impulse and loading repetition measured during a real-world activity.

**Cumulative Load Estimates during Gait and Running**

Estimates of cumulative load during gait have identified the impulse of one gait cycle using motion analyses in a laboratory and the repetition of gait during a typical day using accelerometry (Robbins, Birmingham, Jones, Callaghan, & Maly, 2009). The work by Robbins et al. showed that this method of impulse measurement in the laboratory and real world accelerometry can produce a reliable estimate of cumulative load (ICC 0.84-0.89). Impulse measurement during walking and running has been well documented in the literature with impulse being reported as the integral of force-time data collected using force platforms (Hanley & Mohan, 2014; Maly et al., 2013; Miller, Edwards, Brandon, Morton, & Deluzio, 2013; Munro, Miller, & Fuglevand, 1987; Nilsson & Thorstensson, 1989; Robbins et al., 2009; Wellenkotter, Kernozek, Meardon, & Suchomel, 2014). Accelerometers have been extensively used to measure step-count during walking and are highly valid and reliable at measuring step-count during fast gait speeds (>1.2 m/s) (Kelly et al., 2013; Rowlands, Stone, & Eston, 2007; Santos-Lozano et al., 2012). Though,

accelerometers provide poor measures of step-count during slow gait (Abel et al., 2011; Feito, Bassett, & Thompson, 2012; Ryan, 2006). The increased reliability and validity of measurements taken at high gait speeds indicates that accelerometers are likely a good tool to use for measuring step-counts during running. The location on the body in which accelerometers are placed, in order to measure loading repetition, influences the psychometric properties of the data recorded (Bouten, Sauren, Verduin, & Janssen, 1997; Lützner, Voigt, Roeder, Kirschner, & Lützner, 2014; Tudor-Locke, Barreira, & Schuna, 2014). Differences in reliability and validity between locations are likely due to differences in the accelerations occurring at various limb segments. For example, more distal limb-segments are likely to undergo greater accelerations than more proximal segments. Placement of accelerometers on the ankle yield better accuracy when measuring step-count compared to placement at the hip or lumbar spine (Korpan, Schafer, Wilson, & Webber, 2014).

**Cumulative Load Estimates during Bicycling**

Estimates of cumulative load during bicycling have not yet been attempted. To estimate cumulative load during bicycling, a reliable and valid means of measuring the impulse and load repetition is necessary. Force measurement at the bicycle pedal has been reported by a few groups (Rodrigo R. Bini, Hume, & Crofta, 2011; Boyd, Neptune, & Hull, 1997; M. L. Hull & Davis, 1981; M. L. Hull & Jorge, 1985; T. B. M. Hull & Wootten, 1996). Early studies were primarily concerned with designing a bicycle pedal capable of measuring force (M. L. Hull & Davis, 1981). Since the first pedals, others have

been developed and used to determine the effect of bicycle seat height on the effective pedal force (Rodrigo R. Bini et al., 2011), to compare effective forces produced by cyclists and triathletes (Candotti et al., 2007), and to determine the effect of the seats horizontal (fore/aft) position on knee joint forces (Rodrigo Rico Bini, Hume, Lanferdini, & Vaz, 2013). Current studies commonly measure forces in two directions (vertical and anterior/posterior) (Rodrigo R. Bini et al., 2011; Tamborindeguy & Rico Bini, 2011), break up force data into individual revolutions using electromagnetic switches (Rodrigo R. Bini et al., 2011), and use motion-analysis to determine angles at the bicycle pedal and crank arm as well as between various limb segments (Rodrigo Rico Bini et al., 2013; Candotti et al., 2007; Tamborindeguy & Rico Bini, 2011).

Similar to walking, accelerometers have been used to estimate energy expenditure during bicycling. Accelerometers placed on the low-back and hip during bicycling provides poor estimates of energy expenditure (de Groot & Nieuwenhuizen, 2013; Herman Hansen et al., 2014). Placement is likely the culprit in these poor results because the low back and hip are relatively stationary during bicycling. There has yet to be an investigation into the ability of accelerometers to measure pedal-revolution counts during bicycling. While bicycling does not have the same movement pattern as walking, the two activities do have similar vertical accelerations of the lower extremity. During bicycling and gait, accelerations of the thigh and shank are negative (downward) followed by positive (upward); this pattern repeats itself for each cycle. There is likely greater vertical displacement of the shank during bicycling as compared to walking.

## Gaps in the Literature

While it is clear that adequate physical activity is necessary to maintain joint health and cartilage integrity. Reviewing the literature reveals some gaps, which must be addressed to gain the knowledge necessary to develop exercise recommendations that promote the integrity of knee AC. Some of these gaps include the following:

1) Can accelerometers provide a reliable and valid measure of pedal and revolution count data during bicycling? If so, where is the best placement? Filling this gap is necessary in facilitating the estimation of cumulative load during bicycling to match the existing literature supporting use of accelerometry in estimations of cumulative load during running. Best placement of accelerometers is also of particular importance for the emerging popularity of "wearable" technology that is used to measures various aspects of physical activity.
2) How does knee AC acutely respond to two activities, both useful in promoting cardiovascular health and weight management, of equal cumulative load? Comparisons between activities using MRI have been performed in the past, but none have standardized the total load exposure during those activities.
3) How does knee AC composition, measured using T2 relaxation time, compare between different types of activity? T2 relaxation has been used to assess how knee AC responds to different types of load, though a direct comparison between different types of activity has yet to be performed.

4) Is there a relationship between how active an individual is and the response of their AC to activity? Previous research did not show activity history to condition the acute response of cartilage to activity. Though, only the acute response of cartilage to running, using T2, and to squatting, using morphometric measures, has been investigated.

## Purpose

This thesis is intended to address some of the outlined gaps in the literature. First, we required methods to measure cumulative load of running and bicycling activities. The purpose of the first study presented in this thesis was to determine the reliability and validity of step-count and pedal-revolution-count data produced by the GT3X+ accelerometer, when worn at different anatomic locations (waist, thigh, and shank). This study was performed to provide a basis for accurately measuring loading repetition during the common aerobic activities of running and bicycling.

Using methods developed in the first study, the purpose of the second study of this thesis was (1) to determine whether running or bicycling, of equal cumulative load, causes greater compositional changes in AC, and (2) to determine the relationship between self-reported physical activity history and changes in knee AC composition during running and bicycling. Laboratory measurements were used to measure the impulse of one running stride and one pedal revolution. As well, repetition of steps (running) and pedal revolutions (bicycling) were measured. These measurements were used to establish a

consistent cumulative load exposure to running and bicycling for each participant. Then, MRI was used to compare the effect of running and bicycling of equal cumulative load on knee AC composition and morphology.

This thesis advances the methodology around physical activity measurement. We tested the best anatomic placement of accelerometers to ensure measurements of step and pedal revolution count are both reliable and valid. As well, this thesis provides insight into how AC acutely responds to two common forms of aerobic exercise, running and bicycling. Understanding how AC responds to aerobic exercise is of particular importance in combatting obesity and decreasing the incidence of numerous other comorbidities in individuals with knee OA.

CHAPTER 2
ACCELEROMETER RELIABILITY & VALIDITY

# GT3X+ accelerometer placement affects the reliability of step-counts measured during running and pedal-revolution counts measured during bicycling

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## Introduction

Accelerometers are commonly used to quantify the physical activity that an individual performs (García-Ortiz et al., 2014; Loprinzi & Richart, 2014; Loprinzi, Sheffield, Tyo, & Fittipaldi-Wert, 2014; Maly, Robbins, Stratford, Birmingham, & Callaghan, 2013; Toftager et al., 2014; Vallance, Boyle, Courneya, & Lynch, 2014). Data produced by commercial accelerometers to track activity include activity counts and number of steps taken. An activity count is a measure of acceleration that is dependent on the device and algorithm used to analyze the collected acceleration data (Masse et al., 2005; Sirard, Forsyth, Oakes, & Schmitz, 2011). These algorithms are commonly proprietary.

Accelerometers produce activity count data that are sensitive and specific when distinguishing between standing, sitting, walking, running, and cycling in laboratory conditions (Skotte, Korshøj, Kristiansen, Hanisch, & Holtermann, 2014). While walking at normal gait speeds, energy expenditure estimates produced by the GT3X+ accelerometer (Actigraph, USA) were highly reliable (ICC 0.950-0.998) and valid when compared to oxygen consumption (r=.82, $P<0.01$), when worn at the waist (McMinn, Acharya, Rowe, Gray, & Allan, 2013; Santos-Lozano et al., 2012). As for step-count measurements, accelerometers produced highly valid and reliable data at fast gait speeds (>1.2 m/s), when worn at the waist (Kelly et al., 2013; Rowlands, Stone, & Eston, 2007; Santos-Lozano et al., 2012). However, step count data captured at the waist and thigh during slower gait speeds were less reliable (Abel et al., 2011; Feito, Bassett, & Thompson, 2012; Ryan, 2006), likely because accelerations fell below the device's

threshold to register a step (Johnson et al., 2014). It is possible that this underestimation of step counts is related to placing the accelerometers at the waist and thigh, which experience smaller accelerations than the shank.

The location of the accelerometer on the body has an impact on the data recorded due to differences in limb accelerations during movement (Bouten, Sauren, Verduin, & Janssen, 1997; Lützner, Voigt, Roeder, Kirschner, & Lützner, 2014; Tudor-Locke, Barreira, & Schuna, 2014). For example, during walking or running, placing a tri-axial accelerometer on the shank will expose the device to larger accelerations than if the accelerometer is placed on the trunk. This theory is supported by the finding that placement of the GT3X+ on the ankle in older adults yielded better accuracy as compared to placement on the hip or lumbar spine (Korpan, Schafer, Wilson, & Webber, 2014). Studies reporting step count validity during walking and/or jogging (<2.2m/s) have placed accelerometers in a variety of locations on the body, including the waist, wrist, ankle, shank, and lumbar spine (Korpan et al., 2014; Lützner et al., 2014; Tudor-Locke et al., 2014). Recently placement of accelerometers at the shank has been supported in the literature, though a comparison to the commonly recommended and used location of the waist has yet to be investigated (Lützner et al., 2014).

Data from accelerometers placed at the low back and hip significantly underestimated energy expenditure during bicycling (de Groot & Nieuwenhuizen, 2013; Herman Hansen et al., 2014). This underestimation is potentially due to placement, as these anatomic

locations are relatively stationary during cycling (low-back and hip). We are unaware of any investigations into the reliability and validity of pedal-revolution count data produced by accelerometers during cycling. Because the vertical accelerations during bicycling are likely similar to those during running, accelerometers may be useful in measuring pedal-revolution count during bicycling. Pedal-revolution count is typically measured using switches attached to the bicycle that are triggered upon each revolution. Switches are triggered photo-electrically, magnetically, or physically (Dotan & Bar-Or, 1983; Weltman, Stamford, & Fulco, 1979). These tools can only be used to measure pedal-revolution count and require specific fitting to the bicycle. The potential to measure both pedal-revolution count and step-count can broaden the application of accelerometers. This will allow for the measurement of both pedal-revolution count and step-count by one device during free-living conditions and continuous activities such as duathlons.

The purpose of this study was to estimate the extent to which the GT3X+ accelerometer (Actigraph, Fl, USA) produces reliable and valid data, when placed at different anatomic locations, for quantifying step-count during running and pedal-revolution count during bicycling. Inter-device and inter-segment reliability was determined from six accelerometers fitted at three anatomic locations (waist, thigh, and shank). Validity was determined by comparing data produced by the accelerometers with the gold standard, counts derived from videotape. Given existing literature, it was hypothesized that the GT3X+ would display excellent inter-device reliability and good inter-segment reliability

at all locations. It was also hypothesized that the GT3X+ would display excellent validity at the thigh during running and at the shank during bicycling.

## Materials & Methods

### Experimental Design and Protocol

This methodological study employed a cross-sectional design. Participants attended a single visit at a research laboratory. All participants performed warm-up and experimental bicycling and running bouts, each five minutes in duration. Therefore, each participant completed a total of four five minute bouts of activity. First, participants completed activity warm-ups to determine a self-selected moderate pace for running, and moderate self-selected power output for bicycling at a constant pedaling frequency of 80 revolutions per minute (RPM). A moderate pace and power was described to participants as something they could maintain for at least 20 minutes. Once the warm-up was finished, participants completed the experimental activity bout. Participants were provided with a 5-minute rest period between all activity bouts. The order of the activities (i.e., running versus bicycling) was randomized. During the experimental activity bouts, data were collected using six GT3X+ accelerometers (Actigraph, USA) and a T1i digital single lens reflex camera (Canon, Japan) capable of capturing video footage of the right leg. All participants wore shorts, a t-shirt and their own running shoes for this protocol. Participants provided their written informed consent. This study was approved by the Hamilton Integrated Research Ethics Board, Hamilton, Ontario, Canada.

**Participants**

Twenty-four participants between the ages of 18-35 years, who self-reported that they were healthy, were recruited from the McMaster community, using posters and social media. Participants were excluded if they self-reported recent injury to the lower extremity over the last 3-months, had self-reported degenerative joint disease, or were pregnant. Participants were also screened using the Physical Activity Readiness Questionnaire (PAR-Q) to ensure it was safe for them to participate in the exercise protocol (Canadian Society for Exercise Physiology, 2004).

**Outcome Measures**

Step-count during running and pedal-revolution count during cycling of only the right leg were the measures of interest. Running and cycling are cyclic activities, and both step-counts and pedal-revolutions must be identified from one event in the cycle. For running, step-count was defined using heel-strike for the right leg. Therefore, one step was defined as starting from heel-strike and ending just prior to the next heel-strike on the same foot. Similarly, the position to identify the start and end of one pedal-revolution was when the right bicycle crank arm was parallel to the ground (i.e., in the 3 o'clock position). These methods allowed for the measurement of steps and pedal revolutions of the right leg.

**Instrumentation**

**Activity Bouts.** Running was performed on a commercial treadmill (5.1AT, Advanced Fitness Group, USA). Participants self-selected a moderate running speed on the treadmill, which was determined during the warm-up. The speed was not altered throughout the five minute bout of activity. All participants ran at an incline of 0°.

The bicycling protocol was completed on an Excalibur Sport research grade cycle-ergometer (Lode, NL). Commercial road bike fitting guidelines created by an experienced bicycling fitter were modified for use during this application and allowed specific bicycle fit based on participant anthropometrics (Eric Bowen, 2011). To fit the bicycle to the participant, participant inseam length was measured and used to set the bicycle seat height (seat height from pedal spindle to top of seat= 1.11* inseam length). Once seat height was set, the seat forward and backward (fore/aft) position was set. The fore/aft position was set ensuring the most anterior aspect of the patella was within .5cm in front of and 1.5cm behind the pedal spindle. Lastly, the handlebar position was set based on participants' inseam length (distance from middle of bicycle seat to handlebars= [0.65*inseam length]+10cm). During all cycling bouts participants were instructed to pedal at 80 RPM. During the warm-up participants selected their desired moderate power-output, which was held constant throughout both bicycling bouts.

**Accelerometry.** Accelerometers were fitted prior to the activity bouts. A total of six accelerometers were attached to each participant's right leg and trunk. Two

accelerometers were affixed on the anterior midline of the shin, approximately 2 cm apart on the proximal-distal line at approximately the centre of mass. Two accelerometers were affixed to the thigh at the anterior midline of the thigh, approximately 2 cm apart on the proximal-distal line at approximately the centre of mass. The remaining two accelerometers were attached around the waist. The accelerometers worn at the waist were placed side-by-side, on the same belt, and were separated by approximately 1 cm. The midpoint between these two accelerometers was in line with the anterior superior iliac spine. All accelerometers were attached to participants using an elastic band and a buckle. Double-sided adhesive washers were also used to secure the thigh and shin accelerometers to the participants' skin. It should be noted that for the best measurement of step-counts the manufacturer recommends wearing the GT3X+ at the body's center-of-mass at the waist (Actigraph, 2013).

The GT3X+ accelerometers sampled accelerations in three axes (X, Y, and Z) at 100 Hz using a 12-bit analog to digital converter (Actigraph, 2013). The light emitting diode (LED) feature of the GT3X+ was programmed to flash at the commencement of data collection. The first flash was used to synchronize the accelerometers with the videotape. Actilife 6 software (Actigraph, USA) was used to initialize the GT3X+ and to analyze the collected data. Actilife has a built-in algorithm that uses a designated acceleration threshold in the vertical direction to trigger recording a step-count. In this study, step-count measurement was used to count both steps and pedal-revolutions. These counts

were determined for 1 s epochs. The sum of the steps taken over each of the first five minutes was calculated using epochs of 1 second (5 x 60-1s epochs).

**Videotape.** Step and pedal-revolution counts were manually identified from digital video recordings of each bout of activity as the gold standard measurements. Video recording was performed using a T1i digital single lens reflex camera (Canon, Japan). Video was recorded at 1080p resolution and 30 frames per second. During the participants' warm-up the video camera was setup on a tripod and focused to collect video in the sagittal plane. During the second five minute bout, while the accelerometers were collecting data, each participant was videotaped from the waist down. Video was recorded from 30 s prior to when the accelerometers began collecting data. During this 30 s period, participants were stationary within the camera field of view until the accelerometers began flashing. Once the LED flashes were observable, participants initiated their activity. Participants were videotaped until the end of their five minute activity.

The video recorded during each activity was analyzed using the video editing software VideoBlend (Mooii, Korea). VideoBlend was first used to synchronize the accelerometers and video by locating the frame in which the first LED flash appeared. The LED flash indicated that the accelerometers had started collecting data. Next, VideoBlend was used to cut the video into five, 1 min videos starting from the first LED flash.

Once the video was edited, Quicktime Player (Apple, USA) was used to play each, 1 min video at 15 frames per second (half speed). The number of steps or pedal revolutions was counted for each minute of video, on two separate occasions, by two separate raters. If there was a discrepancy between the two counts (occurred for 9 of 220 1-minute videos), counting was repeated for that video. Consensus was reached for all videos.

**Statistical Analysis**

To determine reliability, Type 2,1 intraclass correlations (ICC) and the standard error of measurement (SEM) were calculated. ICC provides a measure of relative agreement, while the SEM provides a measure of absolute reliability (Riddle & Stratford, 2013). Inter-device reliability, a comparison of two accelerometers placed at the same location, was calculated for accelerometers worn at the waist, thigh and shank. Inter-segment reliability, a comparison of accelerometers placed at different locations, was determined between all three locations (waist, thigh and shank) as well as, in pairs, between individual locations. Finally, Bland Altman plots were also generated to analyze absolute agreement for inter-device reliability.

Validity was determined by comparing the accelerometer count to the manual count from video using Pearson correlations. Pearson correlations provide a measure of relative agreement between the two measurement techniques. To comment on absolute agreement for validity purposes, Bland-Altman plots were generated.

A one-way analysis of variance (ANOVA) was used to test if differences existed between data obtained by accelerometry and video. Separate ANOVAs were conducted for each of step-counts and pedal-revolution counts. Both ANOVAs were performed using the measurements for the entire 5-minute activity. If differences were found, Bonferroni corrected comparisons were used to further examine the differences between individual measurements.

All ICC, SEM and Pearson Correlations were performed for each minute of the five collected minutes, as well as for the overall five minutes. This approach allowed for the observation of differences in reliability and validity due to changes in velocity, changes in step and pedal-revolution frequencies and slower speed of running or higher bicycling resistances during the first minute of each activity. Analyzing by each minute also allowed for the observation of any drift that may occur with the accelerometers throughout the collection period, resulting in error. All statistical analyses were performed using Stata 13.1 for Mac (StataCorp LP, TX, USA).

## Results

Twenty-four participants were recruited. Data from two participants were excluded thus data from 22 participants (8 women, 14 men) were included in these analyses. Data from two participants were excluded because the USB connection on one accelerometer malfunctioned for one participant (1.77 m; 59.3 kg; 18.95 kg/m$^2$) and a software error

occurred when downloading data in the other participant (1.86 m; 82.6 kg; 23.82 kg/m$^2$). The demographics for the remaining 22 participants in the sample are presented in **Table 2-1**.

**Table 2-1** also summarizes the data collected during running and bicycling activities among the entire sample and between women and men. During the collected trials there was a broad range of power outputs during bicycling (50-200 Watts) and running speeds (1.57-3.13 m/s). The mean steps per minute and pedal-revolutions per minute were similar in running and bicycling, differing by fewer than six per minute.

**Inter-device Reliability**

**Table 2-2** provides the ICC and SEM values for inter-device reliability during running, for each of the five minutes as well as over the whole five minutes. Data from two GT3X+ accelerometers placed at the same location demonstrated excellent inter-device reliability when placed at the waist and shank (ICCs ≥ .99 and SEM ≤ .92). The accelerometry data recorded at the thigh was less reliable (ICC .63–.87; SEM 3.34 – 7.71).

The ICC and SEM values for inter-device reliability calculated during bicycling are presented in **Table 2-3**. Similar to during running, data produced by the GT3X+ accelerometer placed at the shank during bicycling demonstrated excellent inter-device reliability (ICC ≥ .99; SEM ≤ .1.01). Placement at the thigh also provided excellent

inter-device reliability (ICC > .99; SEM ≤ .65). Two accelerometers placed at the waist provided poor inter-device reliability for pedal-revolution measurements (ICC .04-.25; SEM 10.8 – 75.9).

Bland Altman plots were also used to compare the measurements between accelerometers for reliability purposes. Plots compared measurements over the entire five minute activity protocol. Accelerometers placed at the waist and shank during running provided the best evidence of agreement. Accelerometers placed at the thigh and shank during bicycling provided the best evidence of agreement. One example of the Bland Altman plots is provided for reliability (**Figure 2-1**), while a table summarizing the other plots is provided (**Table 2-4**).

**Inter-segment Reliability**

To determine reliability between segments during running, the ICC and SEM values for inter-segment measurements are displayed in **Table 2-5**. During running, poor reliability was found between measurements taken at all three segments (ICC 0-.58; SEM ≥ 5.48). Poor inter-segment reliability was also found between measurements taken at the thigh and shank, and the waist and thigh (ICC < .54; SEM ≥ 6.56). Excellent agreement was found between measurements taken at the waist and shank (ICC >.92; SEM ≤ 1.60). Measurements from the thigh were different than measurements from the waist and shank ($p<.01$); but no differences were noted between the waist and shank ($p>.99$) (**Table 2-8**).

**Table 2-6** summarizes inter-segment reliability for bicycling. Similar to data produced during running, the inter-segment reliability for bicycling was poor for all but one combination. Measurements taken at the thigh and shank provided excellent inter-segment reliability (ICC >.99; SEM ≤ 1.00). There was poor inter-segment reliability between measurements taken at the waist and shank, the waist and thigh, and all three segments (ICC < .10; SEM > 3.37). Measurements from the waist were different than measurements from the thigh and shank ($p<.01$); but no differences were noted between the thigh and shank ($p>.999$) (**Table 2-8**).

**Validity**

When exploring validity during running, strong relationships were present between step-count measures produced by the GT3X+ and gold standard manual counts determined from video-tape when accelerometers were placed at the waist (r ≥.99; 95% confidence interval .98, >.99) and shank (r ≥.99; 95% confidence interval .98, >.99) (Table 7). No differences were noted between video-derived measurements and accelerometer measurements at the waist or shank ($p>.99$). Similarly, during bicycling strong relationships existed at the thigh (r ≥.99; 95% confidence interval .99, >.99) and shank (r ≥.99; 95% confidence interval .99, >.99). Again, no differences were observed between video and accelerometer measurements at the thigh or shank ($p>.99$). Poor validity was found for measurements of step-count taken at the thigh (r <.74; 95% confidence interval -.45, .85), and pedal-revolutions taken at the waist (r <.28; 95% confidence interval -.19, .53). Data yielded from video were different than, accelerometer derived, step-count

measurements taken at the thigh and pedal-revolution counts taken at the waist ($p<.01$). Bland Altman plots were also generated to assess agreement between data produced by the accelerometers and the gold standard measurement manual counts from videotape, for validity purposes (**Figure 2-2**; **Table 2-4**).

## Discussion

Findings indicate that the GT3X+ accelerometer produces data that can be used to measure step and pedal-revolution count in treadmill running and stationary bicycling. Reliability and validity were excellent for measurements taken at the waist and shank during running and at the thigh and shank during bicycling. These results expand on other studies that validated the ability of the GT3X+ to distinguish between running and bicycling, and that validated step-count during walking, and activity counts during running (Kelly et al., 2013; McMinn et al., 2013; Santos-Lozano et al., 2012; Skotte et al., 2014; Vanhelst, Baquet, Gottrand, & BéGhin, 2012)

If a single location is required to study both running and bicycling, only the shank appears useful for step-count measurement and pedal-revolution measurement. The shank placement provided excellent reliability and validity during both activities. Further data supporting the use of this placement comes from previous research that has shown that participants found accelerometer placement at the shank to be more comfortable, in comparison to placement at the thigh (Lützner et al., 2014). Increased comfort may lead

to improved compliance. It is recommended that shank placement be investigated for measurement of activity counts during laboratory conditions and activities of daily living. Comparisons of reliability, validity, comfort, and compliance should be made to other commonly used attachment locations: waist, wrist, and ankle (Ozemek, Kirschner, Wilkerson, Byun, & Kaminsky, 2014; Tudor-Locke et al., 2014).

The reliability and validity of data produced by accelerometers were tested during running and bicycling over a range of running speeds and bicycling power outputs. Although participants were asked to confine their pedaling frequency to 80 RPM, there was a wide range of pedaling frequencies recorded. This range covers that of preferred pedaling frequencies for trained cyclists, trained runners, and untrained individuals (69-96 RPM) when producing between 75 and 200 watts of power output (Marsh, Martin, & Foley, 2000). The power output observed in the present study covers the lower range of cyclist power outputs. In fact, the highest power observed was approximately 50W below that of trained triathlete's anaerobic threshold, an effort they could maintain during a typical race (≥ 1-hour) (Candotti et al., 2007). The running cadences cover the range of previously reported cadences (Paróczai & Kocsis, 2006). It is important to note that the running speeds observed in this study were slower than speeds completed by amateur male marathoners (Knechtle & Tanda, 2013). Therefore, data from the present study provide evidence that the GT3X+ accelerometer produces reliable and valid step and pedal-revolution counts over a range of commonly used cadences, and recreational running speeds and power outputs. Thus, the data in the current study support the use of

accelerometry-produced pedal and step-counts for recreational athletes, or adults working below typical race speeds.

The inter-device and inter-segment ICC and SEM indicate that measurements between accelerometers at the same location were more reliable than measurements between accelerometers at different locations. However, good agreement was present between segments that had good inter-device reliability and validity (waist and shank during running; thigh and shank during bicycling). These results support previous literature that measurements taken from different segments may not be comparable (Tudor-Locke et al., 2014). Therefore, when comparing the results of separate studies, readers and investigators should be cautious as to where the accelerometer was placed during data collection to allow for appropriate comparisons.

As well, reliability between measurements taken at the waist and shank during the first minute of running was lower than during the remaining four minutes of the activity bout. The first minute started from 0 m/s therefore this lower reliability could be due to greater error in measurement at slower speeds as was indicated in previous literature, or while running speed is changing (Abel et al., 2008; Feito, Bassett, Thompson, & Tyo, 2012).

As step-count frequencies increase during running, the accelerometer placed at the thigh produced data that over-estimated step-count. This over-estimation is observed in the positive slope of the Bland Altman plot (**Figure 2-2**). This error is potentially due to

differences in running gait that occur as step frequency changes, something that should be investigated in future research. It is also suggested that future research determine if this bias during high step frequencies exists during walking when accelerometers are worn on the thigh.

This study is not without limitations. Synchronization of accelerometer data and video recordings was not completed with an electronic trigger and therefore the observational technique could have led to small differences between measurement methods. The GT3X+ only uses accelerations in the vertical direction to measure step count. It is possible that incorporation of horizontal accelerations could have improved estimates of pedal revolution count as well as step-count, particularly the poor estimates produced for measurements taken at the thigh during running. This study was performed in a laboratory setting, and therefore does not represent measurements taken in free-living conditions. The range of step and pedal-revolution frequencies did cover the entire range of common frequencies, though relatively slow running speeds and low power outputs were selected by some participants. In the future, we would instead provide an anchor of perceived exertion on the Borg scale of "hard" to elicit greater paces from study participants. Future research should systematically test reliability and validity over a wide range of step and pedal-revolution frequencies and a wide range of speeds and power outputs. Running step and pedal-revolution counts should also be tested in free-living conditions.

## Conclusion

Based on the findings from this investigation, it is recommended that accelerometers be placed at the shank or waist when measuring step count during running, and be placed at the thigh or shank when measuring pedal revolutions during bicycling. If one location is necessary for both running and bicycling, data from the current study suggest the shank, due to the reliability, validity and previously reported increased comfort of this placement. It is important that future research test accelerometer placement under a wider range of conditions, including higher power outputs during cycling, faster running speeds, and a broader range of both running and bicycling cadences.

## References

Abel, M. G., Hannon, J. C., Sell, K., Lillie, T., Conlin, G., & Anderson, D. (2008). Validation of the Kenz Lifecorder EX and ActiGraph GT1M accelerometers for walking and running in adults. *Applied Physiology, Nutrition, and Metabolism = Physiologie Appliquée, Nutrition et Métabolisme*, *33*(6), 1155–1164. http://doi.org/10.1139/h08-103

Abel, M. G., Peritore, N., Shapiro, R., Mullineaux, D. R., Rodriguez, K., & Hannon, J. C. (2011). A comprehensive evaluation of motion sensor step-counting error. *Applied Physiology, Nutrition, and Metabolism*, *36*(1), 166–170. http://doi.org/10.1139/H10-095

Actigraph. (2013, May 13). GT3X+ and wGT3X+ device manual. Retrieved from http://dl.theactigraph.com/GT3Xp_wGT3Xp_Device_Manual.pdf

Bouten, C. V., Sauren, A. A., Verduin, M., & Janssen, J. D. (1997). Effects of placement and orientation of body-fixed accelerometers on the assessment of energy expenditure during walking. *Medical and Biological Engineering and Computing*, *35*(1), 50–56.

Canadian Society for Exercise Physiology. (2004). *Canadian physical activity, fitness & lifestyle approach: CSEP - health & fitness program's health-related appraisal & counselling strategy.* Ottawa, Ont.: Canadian Society for Exercise Physiology.

Candotti, C. T., Ribeiro, J., Soares, D. P., De Oliveira, áLvaro R., Loss, J. F., & GuimarãEs, A. C. S. (2007). Effective force and economy of triathletes and

cyclists. *Sports Biomechanics*, *6*(1), 31–43. http://doi.org/10.1080/14763140601058490

De Groot, S., & Nieuwenhuizen, M. G. (2013). Validity and reliability of measuring activities, movement intensity and energy expenditure with the DynaPort MoveMonitor. *Medical Engineering & Physics*, *35*(10), 1499–1505. http://doi.org/10.1016/j.medengphy.2013.04.004

Dotan, R., & Bar-Or, O. (1983). Load optimization for the Wingate anaerobic test. *European Journal of Applied Physiology and Occupational Physiology*, *51*(3), 409–417.

Eric Bowen. (2011, March 14). Road bikefitting guidelines: the essentials for proper fit. Velofit Revolution.

Feito, Y., Bassett, D. R., & Thompson, D. L. (2012). Evaluation of activity monitors in controlled and free-living environments: *Medicine & Science in Sports & Exercise*, *44*(4), 733–741. http://doi.org/10.1249/MSS.0b013e3182351913

Feito, Y., Bassett, D. R., Thompson, D. L., & Tyo, B. M. (2012). Effects of body mass index on step count accuracy of physical activity monitors. *Journal of Physical Activity & Health*, *9*(4), 594–600.

García-Ortiz, L., Recio-Rodríguez, J. I., Schmidt-Trucksäss, A., Puigdomenech-Puig, E., Martínez-Vizcaíno, V., Fernández-Alonso, C., … Gómez-Marcos, M. A. (2014). Relationship between objectively measured physical activity and cardiovascular aging in the general population – The EVIDENT trial. *Atherosclerosis*, *233*(2), 434–440. http://doi.org/10.1016/j.atherosclerosis.2014.01.021

Herman Hansen, B., Børtnes, I., Hildebrand, M., Holme, I., Kolle, E., & Anderssen, S. A. (2014). Validity of the ActiGraph GT1M during walking and cycling. *Journal of Sports Sciences*, *32*(6), 510–516. http://doi.org/10.1080/02640414.2013.844347

Johnson, M., Meltz, K., Hart, K., Schmudlach, M., Clarkson, L., & Borman, K. (2014). Validity of the Actical activity monitor for assessing steps and energy expenditure during walking. *Journal of Sports Sciences*, 1–8. http://doi.org/10.1080/02640414.2014.964747

Kelly, L. A., McMillan, D. G., Anderson, A., Fippinger, M., Fillerup, G., & Rider, J. (2013). Validity of actigraphs uniaxial and triaxial accelerometers for assessment of physical activity in adults in laboratory conditions. *BMC Medical Physics*, *13*(1), 5.

Knechtle, B., & Tanda, G. (2013). Marathon performance in relation to body fat percentage and training indices in recreational male runners. *Open Access Journal of Sports Medicine*, 141. http://doi.org/10.2147/OAJSM.S44945

Korpan, S. M., Schafer, J. L., Wilson, K. C., & Webber, S. C. (2014). Effect of ActiGraph GT3X+ Position and Algorithm Choice on Step Count Accuracy in Older Adults. *Journal of Aging and Physical Activity*. http://doi.org/10.1123/japa.2014-0033

Loprinzi, P. D., & Richart, S. M. (2014). White blood cell counts mediate the effects of physical activity on prostate-specific antigen levels. *Research Quarterly for Exercise and Sport*, *85*(3), 409–413. http://doi.org/10.1080/02701367.2014.930407

Loprinzi, P. D., Sheffield, J., Tyo, B. M., & Fittipaldi-Wert, J. (2014). Accelerometer-determined physical activity, mobility disability, and health. *Disability and Health Journal*, *7*(4), 419–425. http://doi.org/10.1016/j.dhjo.2014.05.005

Lützner, C., Voigt, H., Roeder, I., Kirschner, S., & Lützner, J. (2014). Placement makes a difference: Accuracy of an accelerometer in measuring step number and stair climbing. *Gait & Posture*, *39*(4), 1126–1132. http://doi.org/10.1016/j.gaitpost.2014.01.022

Maly, M. R., Robbins, S. M., Stratford, P. W., Birmingham, T. B., & Callaghan, J. P. (2013). Cumulative knee adductor load distinguishes between healthy and osteoarthritic knees–A proof of principle study. *Gait & Posture*, *37*(3), 397–401. http://doi.org/10.1016/j.gaitpost.2012.08.013

Marsh, A. P., Martin, P. E., & Foley, K. O. (2000). Effect of cadence, cycling experience, and aerobic power on delta efficiency during cycling. *Medicine and Science in Sports and Exercise*, *32*(9), 1630–1634.

Masse, L. C., Fuemmeler, B. F., Anderson, C. B., Matthews, C. E., Trost, S. G., Catellier, D. J., & Treuth, M. (2005). Accelerometer Data Reduction: A Comparison of Four Reduction Algorithms on Select Outcome Variables: *Medicine & Science in Sports & Exercise*, *37*(Supplement), S544–S554. http://doi.org/10.1249/01.mss.0000185674.09066.8a

McMinn, D., Acharya, R., Rowe, D. A., Gray, S. R., & Allan, J. L. (2013). Measuring activity energy expenditure: accuracy of the GT3X+ and actiheart monitors. *International Journal of Exercise Science*, *6*(3), 5.

Ozemek, C., Kirschner, M. M., Wilkerson, B. S., Byun, W., & Kaminsky, L. A. (2014). Intermonitor reliability of the GT3X+ accelerometer at hip, wrist and ankle sites during activities of daily living. *Physiological Measurement*, *35*(2), 129–138. http://doi.org/10.1088/0967-3334/35/2/129

Paróczai, R., & Kocsis, L. (2006). Analysis of human walking and running parameters as a function of speed. *Technology and Health Care: Official Journal of the European Society for Engineering and Medicine*, *14*(4-5), 251–260.

Riddle, D. L., & Stratford, P. W. (2013). *Is this change real?: interpreting patient outcomes in physical therapy*. Philadelphia, PA: F.A. Davis Co.

Rowlands, A. V., Stone, M. R., & Eston, R. G. (2007). Influence of speed and step frequency during walking and running on motion sensor output. *Medicine and Science in Sports and Exercise*, *39*(4), 716–727. http://doi.org/10.1249/mss.0b013e318031126c

Ryan, C. G. (2006). The validity and reliability of a novel activity monitor as a measure of walking. *British Journal of Sports Medicine*, *40*(9), 779–784. http://doi.org/10.1136/bjsm.2006.027276

Santos-Lozano, A., Torres-Luque, G., Marín, P., Ruiz, J., Lucia, A., & Garatachea, N. (2012). Intermonitor variability of GT3X accelerometer. *International Journal of Sports Medicine*, *33*(12), 994–999. http://doi.org/10.1055/s-0032-1312580

Sirard, J. R., Forsyth, A., Oakes, J. M., & Schmitz, K. H. (2011). Accelerometer test-retest reliability by data processing algorithms: results from the Twin Cities Walking Study. *Journal of Physical Activity & Health*, *8*(5), 668–674.

Skotte, J., Korshøj, M., Kristiansen, J., Hanisch, C., & Holtermann, A. (2014). Detection of physical activity types using triaxial accelerometers. *Journal of Physical Activity & Health*, *11*(1), 76–84. http://doi.org/10.1123/jpah.2011-0347

Toftager, M., Christiansen, L. B., Ersbøll, A. K., Kristensen, P. L., Due, P., & Troelsen, J. (2014). Intervention effects on adolescent physical activity in the multicomponent SPACE Study: a cluster randomized controlled trial. *PLoS ONE*, *9*(6), e99369. http://doi.org/10.1371/journal.pone.0099369

Tudor-Locke, C., Barreira, T. V., & Schuna, J. M. (2014). Comparison of step outputs for waist and wrist accelerometer attachment sites. *Medicine and Science in Sports and Exercise*. http://doi.org/10.1249/MSS.0000000000000476

Vallance, J. K., Boyle, T., Courneya, K. S., & Lynch, B. M. (2014). Associations of objectively assessed physical activity and sedentary time with health-related quality of life among colon cancer survivors: Objectively Assessed Physical Activity. *Cancer*, n/a–n/a. http://doi.org/10.1002/cncr.28779

Vanhelst, J., Baquet, G., Gottrand, F., & BéGhin, L. (2012). Comparative interinstrument reliability of uniaxial and triaxial accelerometers in free-living conditions. *Perceptual and Motor Skills*, *114*(2), 584–594. http://doi.org/10.2466/03.26.PMS.114.2.584-594

Weltman, A., Stamford, B. A., & Fulco, C. (1979). Recovery from maximal effort exercise: lactate disappearance and subsequent performance. *J Appl Physiol*, *47*(4), 677–682.

## Tables

**Table 2-1.** Means (standard deviations) of demographics of participants and running & bicycling activities in the total sample, as well as by sex.

| | Women (n=8) | Men (n=14) | Total | Minimum | Maximum |
|---|---|---|---|---|---|
| Demographics | | | | | |
| Age (y) | 24.13 (1.36) | 23.71 (2.23) | 23.86 (1.93) | 21 | 29 |
| Height (m) | 1.68 (0.09) | 1.80 (0.07) | 1.76 (0.09) | 1.50 | 1.95 |
| Body Mass (kg) | 62.90 (9.16) | 83.79 (13.05) | 76.19 (15.46) | 48.6 | 116 |
| Body Mass Index ($kg/m^2$) | 22.20 (1.90) | 25.83 (3.79) | 24.51 (3.64) | 19.02 | 36.82 |
| Running | | | | | |
| Speed (m/s) | 2.10 (.39) | 2.46 (.42) | 2.33 (0.44) | 1.56 | 3.13 |
| Steps minute 1 | 50.63 (6.93) | 56.88 (10.66) | 54.79 (9.89) | 22 | 69 |
| Steps minute 2-5 | 77.28 (4.67) | 78.66 (4.30) | 78.20 (4.38) | 71.5 | 86.25 |
| Bicycling | | | | | |
| Power (Watts) | 79.38 (16.13) | 114.29 (32.10) | 101.59 (31.94) | 50 | 200 |
| Pedal-revolutions minute 1 | 50.75 (24.08) | 60.19 (17.24) | 57.04 (19.77) | 7 | 85 |
| Pedal-revolutions minutes 2-5 | 84.00 (8.10) | 83.67 (5.97) | 83.78 (6.58) | 77.75 | 102.75 |

**Table 2-2.** Intra class correlations (ICCs) & standard error of measurement (SEM) examining inter-device reliability for step-count data captured during treadmill running. The two-sided 95% confidence interval is displayed in brackets.

| | **Minute 1** | **Minute 2** | **Minute 3** | **Minute 4** | **Minute 5** | **Whole 5 Minute Trial** |
|---|---|---|---|---|---|---|
| ICC | | | | | | |
| Waist | >.99 (>.99, >.99) | >.99 (.99, >.99) | .99 (.98, >.99) | >.99 (.99, >.99) | >.99 (.99, >.99) | >.99 (>.99, >.99) |
| Thigh | .87 (.22, .96) | .71 (0, .92) | .67 (0, .89) | .63 (0, .88) | .65 (.13, .86) | .65 (0, .89) |
| Shank | .99 (.98, >.99) | >.99 (>.99, >.99) | .99 (.98, >.99) | >.99 (.99, >.99) | >.99 (.99, >.99) | >.99 (>.99, >.99) |
| SEM | | | | | | |
| Waist | .52 (.40, .74) | .24 (.19, .35) | .41 (.32, .59) | .23 (.18, .34) | .30 (.23, .42) | .97 (.75, 1.39) |
| Thigh | 3.34 (2.57, 4.77) | 5.05 (3.89, 7.22) | 6.75 (5.19, 9.64) | 6.50 (5.00, 9.30) | 7.71 (5.93, 11.01) | 24.57 (18.90, 35.11) |
| Shank | .92 (.71, 1.31) | .30 (.23, .43) | .42 (.32, .59) | .30 (.23, .43) | .34 (.26, .49) | .91 (.70, 1.31) |

**Table 2-3.** Intra class correlations (ICC) & standard error of measurement (SEM) examining inter-device reliability for pedal-revolution count data captured during stationary bicycling. The two-sided 95% confidence interval is displayed in brackets.

| | **Minute 1** | **Minute 2** | **Minute 3** | **Minute 4** | **Minute 5** | **Whole Trial** |
|---|---|---|---|---|---|---|
| ICC | | | | | | |
| Waist | .04 (0, .45) | .13 (0, .51) | .11 (0, .49) | .23 (0, .58) | .25 (0, .60) | .15 (0, .52) |
| Thigh | >.99 (>.99, >.99) | >.99 (.99, >.99) | >.99 (.99, >.99) | >.99 (.99, >.99) | >.99 (.99, >.99) | >.99 (>.99, >.99) |
| Shank | >.99 (>.99, >.99) | >.99 (.99, >.99) | >.99 (.99, >.99) | >.99 (.99, >.99) | >.99 (.99, >.99) | .99 (>.99, >.99) |
| SEM | | | | | | |
| Waist | 10.77 (8.29, 15.39) | 15.56 (11.97 22.24) | 16.94 (13.04, 24.21) | 16.62 (12.79, 23.75) | 16.48 (12.68, 23.55) | 75.89 (58.38, 108.45) |
| Thigh | .55 (.42, .78) | .48 (.37, .69) | .45 (.35, .65) | .51 (.39, .73) | .41 (.31, .58) | .65 (.50, .94) |
| Shank | .81 (.62, 1.15) | .43 (.33, .62) | .35(.27, .51) | .33 (.25, .47) | .40 (.30, .57) | 1.01 (.78, 1.45) |

**Table 2-4.** Bland Altman plots, the mean measurement error & +/- 2 standard deviations for step & pedal-revolution count between accelerometers (reliability) & between accelerometers & videotape (validity).

| **Running** | **Mean** | **Mean – 2SD** | **Mean +2SD** | **Bicycling** | **Mean** | **Mean – 2SD** | **Mean +2SD** |
|---|---|---|---|---|---|---|---|
| Reliability | | | | Reliability | | | |
| Waist | .39 | -2.34 | 3.16 | Waist | -28.45 | -243.10 | 186.19 |
| Thigh | 49.20 | -20.28 | 118.69 | Thigh | 0.00 | -1.85 | 1.85 |
| Shank | -.27 | -2.90 | 2.36 | Shank | 0.73 | -2.05 | 3.50 |
| Validity | | | | Validity | | | |
| Waist | -2.69 | -6.92 | 1.53 | Waist | -363.92 | -527.08 | -200.75 |
| Thigh | 68.18 | -77.10 | 213.46 | Thigh | 1.15 | -2.50 | 4.79 |
| Shank | 1.44 | -2.04 | 4.91 | Shank | 1.06 | -3.05 | 5.18 |

**Table 2-5.** Intra class correlations (ICC) & standard error of measurement (SEM) examining inter-segment reliability for step-count data captured during treadmill running. The two-sided 95% confidence interval is displayed in brackets.

| | **Minute 1** | **Minute 2** | **Minute 3** | **Minute 4** | **Minute 5** | **Whole Trial** |
|---|---|---|---|---|---|---|
| ICC | | | | | | |
| All Segments | .58 (.12, .83) | .03 (0, .20) | .02 (0, .17) | 0 (0, 1.39) | .03 (0, .17) | 0 (0, .13) |
| Thigh-Shank | .54 (0, .82) | 0 (0, .24) | 0 (0, .22) | 0 (0, .19) | 0 (0, .20) | 0 (0, .18) |
| Waist-Shank | .93 (.10, .98) | .99 (.99, >.99) | .99 (.99, >.99) | .99 (.99, >.99) | >.99 (>.99, >.99) | .98 (.41, >.99) |
| Waist-Thigh | .46 (0, .79) | 0 (0, .24) | 0 (0, .21) | 0 (0, .19) | 0 (0, .20) | 0 (0, .17) |
| SEM | | | | | | |
| All Segments | 5.48 (4.52, 6.96) | 9.68 (7.98, 12.30) | 10.14 (8.36, 12.90) | 9.87 (8.14, 12.54) | 9.08 (7.49, 11.55) | 41.31 (34.06, 52.51) |
| Thigh-Shank | 6.56 (5.05, 9.38) | 11.85 (9.12, 16.94) | 12.40 (9.54, 17.72) | 12.10 (9.31, 17.29) | 11.15 (8.58, 15.93) | 50.32 (38.71, 71.91) |
| Waist-Shank | 1.51 (1.16, 2.15) | .30 (.23, .43) | .32 (.24, .45) | .33 (.25, .47) | .17 (.13, .24) | 1.60 (1.23, 2.29) |
| Waist-Thigh | 6.68 (5.14, 9.55) | 11.84 (9.11, 16.93) | 12.44 (9.57, 17.78) | 12.06 (9.28, 17.24) | 11.10 (8.54, 15.87) | 50.84 (39.12, 72.66) |

**Table 2-6.** Intra class correlations (ICC) & standard error of measurement (SEM) examining inter-segment reliability for pedal-revolution count data captured during stationary bicycling. The two-sided 95% confidence interval is displayed in brackets.

| | **Minute 1** | **Minute 2** | **Minute 3** | **Minute 4** | **Minute 5** | **Whole Trial** |
|---|---|---|---|---|---|---|
| ICC | | | | | | |
| All Segments | .10 (0, .32) | .01 (0, .05) | .01 (0, .04) | .02 (0, .07) | .02 (0, .09) | .02 (0, .07) |
| Thigh-Shank | >.99 (.99, >.99) | >.99 (.99, >.99) | >.99 (>.99, >.99) | >.99 (.99, >.99) | >.99 (>.99, >.99) | >.99 (>.99, >.99) |
| Waist-Shank | 0 (0, .08) | 0 (0, .03) | 0 (0, .02) | .01 (0, .06) | .01 (0, .08) | .01 (0, .04) |
| Waist-Thigh | 0 (0, .08) | .01 (0, .03) | 0 (0, .02) | .01 (0, .05) | .01 (0, .08) | .01(0, .04) |
| SEM | | | | | | |
| All Segments | 11.14 (9.19, 14.16) | 3.37 (2.78, 4.28) | 3.89 (3.21, 4.95) | 4.16 (3.43, 5.29) | 4.05 (3.34, 5.15) | 19.37 (15.97, 24.62) |
| Thigh-Shank | .98 (.76, 1.41) | .43 (.33, .62) | .30 (.23, .43) | .43 (.33, .62) | .34 (.26, .49) | 1.00 (0.77, 1.44) |
| Waist-Shank | 13.44 (10.34, 19.1) | 4.12 (3.17, 5.88) | 4.75 (3.65, 6.78) | 5.08 (3.91, 7.26) | 4.95 (3.80, 7.07) | 23.66 (18.20, 33.81) |
| Waist-Thigh | 13.82 (10.63, 19.74) | 4.11(3.17, 5.88) | 4.77 (3.67, 6.82) | 5.10 (3.92, 7.28) | 4.97 (3.83, 7.11) | 23.76 (18.28, 33.95) |

**Table 2-7.** Pearson correlation coefficients between step and pedal-revolution counts measured by accelerometers and the gold standard measurement of counts derived from video. The two-sided 95% confidence interval is displayed in brackets.

| | **Minute 1** | **Minute 2** | **Minute 3** | **Minute 4** | **Minute 5** | **Whole Trial** |
|---|---|---|---|---|---|---|
| Running | | | | | | |
| Waist | .99 (.98, .99) | .99 (.99, >.99) | .99 (.98, >.99) | .99 (.99, >.99) | .99 (.98, .99) | >.99 (.99, >.99) |
| Thigh | .74 (.58, .85) | -.05 (-.33, .24) | -.11 (-.39, .18) | -.11 (-.38, .19) | -.10 (-.38, .19) | -.18 (-.45, .11) |
| Shank | .99 (.99, >.99) | .99 (.98, >.99) | .99 (.98, >.99) | .99 (.99, >.99) | .99 (.98, .99) | >.99 (>.99, >.99) |
| Bicycling | | | | | | |
| Waist | .10 (-.19, .38) | .16 (-.14, .42) | .13 (-.17, .40) | .23 (-.06, .49) | .28 (-.01, .53) | .18 (-.11, .45) |
| Thigh | >.99 (>.99, >.99) | >.99 (.99, >.99) | >.99 (.99, >.99) | >.99 (.99, >.99) | .99 (.99, >.99) | >.99 (>.99, >.99) |
| Shank | >.99 (.99, >.99) | >.99 (.99, >.99) | >.99 (.99, >.99) | >.99 (.99, >.99) | .99 (.99, >.99) | >.99 (>.99, >.99) |

**Table 2-8.** Bonferroni corrected multiple comparisons between measurements yielded from video and accelerometry-based step and pedal-revolution count. Note that the waist, thigh, and shank measurements were obtained with the GTX3+ accelerometer.

| | Video | Waist | Thigh |
|---|---|---|---|
| Running | | | |
| Waist | >0.99 | | |
| Thigh | <0.01 | <0.01 | |
| Shank | >0.99 | >0.99 | <0.01 |
| Bicycling | | | |
| Waist | <0.01 | | |
| Thigh | >0.99 | <0.01 | |
| Shank | >0.99 | <0.01 | >0.99 |

## Figures

**Figure 2-1.** Bland-Altman plot of inter-device reliability at the thigh during stationary bicycling. Mean pedal-revolution count produced by two accelerometers located at the thigh versus the difference between the two measurements. The mean (solid line) and +/- 2 standard deviations of the mean (dashed lines) are shown.

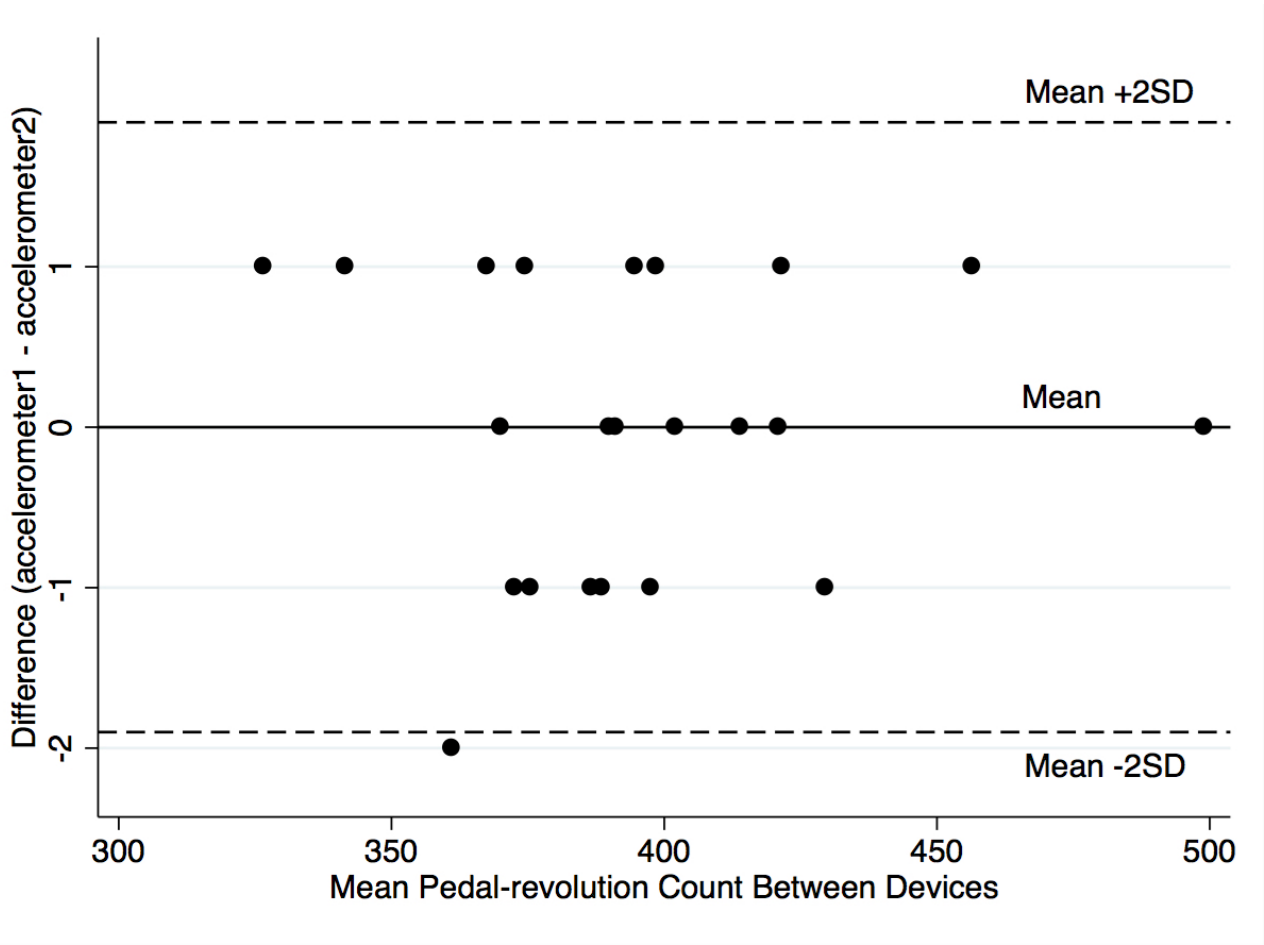
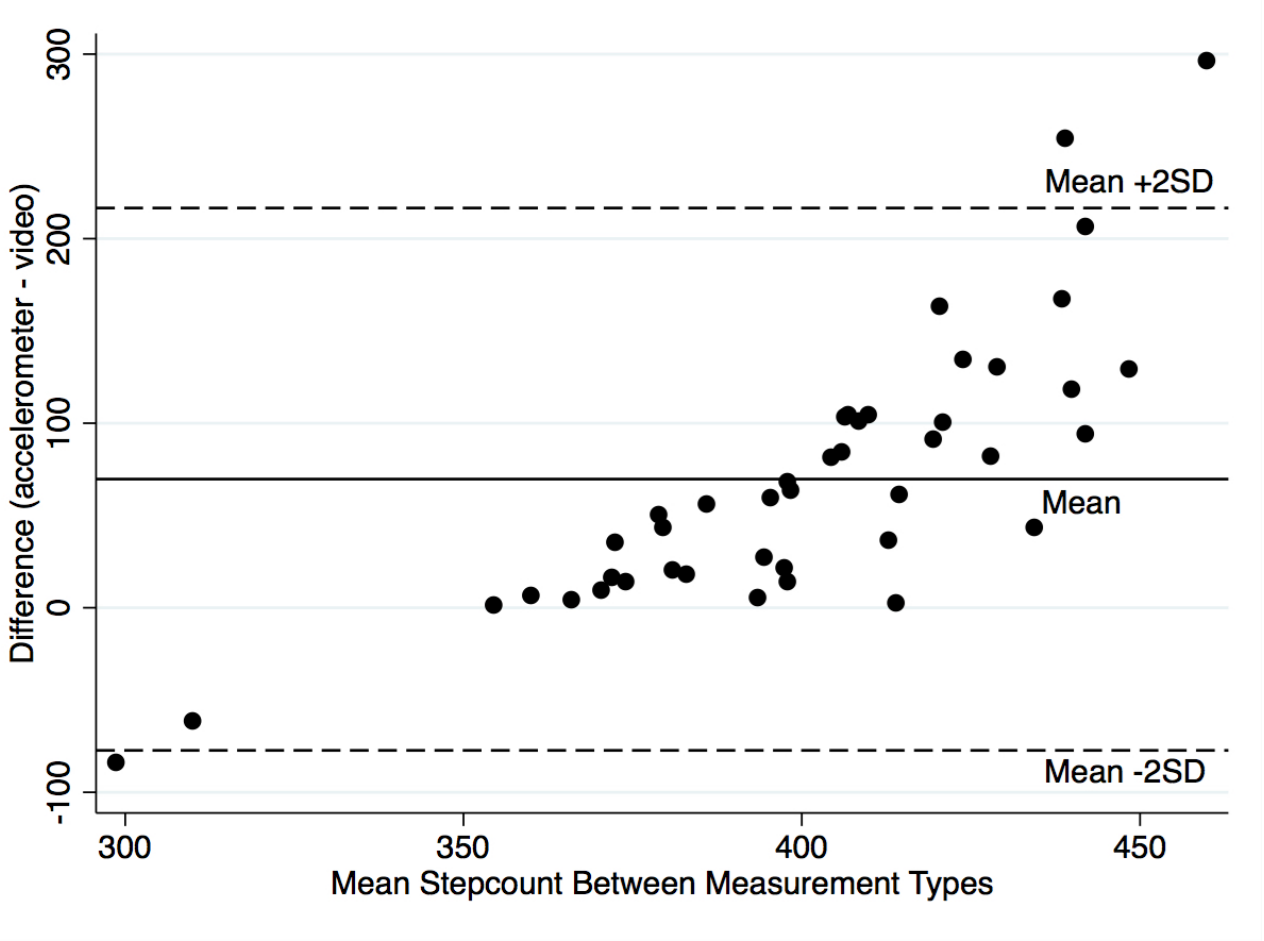


**Figure 2-2.** Bland-Altman plot of accelerometer measured step-count validity at the thigh during treadmill running. Mean step-count produced by the accelerometers located at the thigh and the video derived step-count versus the difference between the two measurements. The mean (solid line) and +/- 2 standard deviations of the mean (dashed lines) are shown.



CHAPTER 3
RESPONSE OF CARTILAGE TO BICYCLING AND RUNNING

**Running but not Bicycling Causes Compositional Changes in Knee Articular Cartilage**

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## Introduction

Mechanical loading is necessary to promote articular cartilage (AC) health; though, the amount and type of loading that is optimal is not well understood (Bennell et al., 2011; Hinterwimmer et al., 2004; Urquhart et al., 2011; Van Ginckel et al., 2010). We must understand how various types and durations of load affect AC to prevent the onset of degenerative AC changes that lead to osteoarthritis (OA) at the knee, hip and other joints. For example, a major risk factor for knee OA is obesity (Anderson & Felson, 1988; David T. Felson, Anderson, Naimark, Walker, & Meenan, 1988). The relationship between obesity and knee OA is, at least in part, driven by large mechanical loads on the lower-extremity caused by excess body mass. To combat obesity, and hopefully the signs and symptoms of knee OA, physical activity is critical (D. T. Felson, Zhang, Anthony, Naimark, & Anderson, 1992; Urquhart et al., 2011). To ensure we are not worsening an OA joint during physical activity, we must improve our understanding of the in vivo response of AC to loading.

Magnetic resonance imaging (MRI) is useful when studying acute changes in AC morphology (volume and thickness) in response to load. Studies of AC morphology have investigated the effect of knee bends, dynamic versus static loading, running, squatting, walking, and bicycling on knee articular cartilage (Boocock, McNair, Cicuttini, Stuart, & Sinclair, 2009; Cotofana et al., 2011; F Eckstein, 2005; Felix Eckstein, Tieschky, Faber, Englmeier, & Reiser, 1999; F. Eckstein, Lemberger, Stammberger, Englmeier, & Reiser, 2000; Kessler, 2005; Kessler, Glaser, Tittel, Reiser, & Imhoff, 2008). Knee AC volume

and thickness are reduced when exposed to physical activities, ranging from as little loading as 30 body-weight squats (F Eckstein, 2005) to loads incurred during 20-km runs (Kessler, 2005). Type of loading is important, with a 20s static wall squat causing greater changes in patellar AC thickness compared to 30 dynamic squats (-4.9% vs. -2.8% $p<0.05$). Interestingly the single sustained squat caused smaller changes in AC volume than 30 dynamic squats (-4.9% vs. -5.9%; $p<0.05$). It is very important to note, though, that it is unclear whether the load induced on patellar cartilage from 20s of static squatting was equivalent and therefore comparable to 30 dynamic squats.

While useful for characterizing acute AC responses, morphology provides little insight into the mechanisms by which these cartilage responses occur. Differences in AC composition likely explain the differences in knee AC deformation observed between individuals (Lu & Mow, 2008; Mow & Guo, 2002). Studies are necessary to examine the impact of composition on AC deformation. Of particular importance is proteoglycan (PG) concentration, as the attraction between negatively charged PGs and cations present in the fluid phase of AC resists ion and therefore fluid flow. This resistance to fluid flow controls the amount and rate of AC deformation under mechanical loads (Lu & Mow, 2008).

MRI techniques sensitive to AC composition, including T2 relaxation time (T2) and T1rho relaxation time (T1rho) have been used to explore these mechanisms underlying cartilage deformation (Choi & Gold, 2011). T2 is positively correlated with water

concentration and influenced by collagen fiber alignment; and T1rho is negatively correlated to PG concentration (Choi & Gold, 2011). AC deformation is caused by a local decrease in water volume, reflected by a decrease in T2 and T1rho (Liess, 2002) signaling a decrease in water content and therefore increase in PG concentration (Souza et al., 2010). As such, fluid recovery 45 minutes after 60 knee-bends is detectable using T2 (change of 2.6% $p<0.05$) (Liess, 2002). T2 and T1rho showed that running causes greater changes in superficial AC compared to other subregions (Cha et al., 2012; Timothy J. Mosher et al., 2005; T.J. Mosher, Liu, & Torok, 2010; Subburaj et al., 2012), with greater changes observed in older as compared to younger individuals (Cha et al., 2012). When stratifying 20 healthy individuals into two groups based on activity history, Subburaj and colleagues found no change in AC T2 (4.5% vs. 3.9% $p=0.382$) or T1rho (9.8% vs. 7.5% $p=0.113$) after running in the low-activity group (Subburaj et al., 2012). Finally, static loading created greater changes in AC T1rho and T2 relaxation times in individuals with knee OA compared to healthy controls (Souza et al., 2014).

Missing in the literature is a comparison of the compositional changes in knee AC in response to different activities. In addition, there is a lack of documentation of the cumulative load exposures of these activities, confounding existing comparisons of acute change in cartilage morphology and composition between activities. The only study that standardized loading exposure (5000 running strides) found that the maximum lateral compressive stress while running related to the percentage change in lateral femoral cartilage volume (Boocock et al., 2009). Without characterization of mechanical loads,

we are unable to compare physical activities, or identify the ideal types of activity to promote cartilage health.

To directly address these gaps, the purpose of this study was three-fold: (1) to determine whether running and bicycling cause changes in weight-bearing knee AC composition, as measured using T2, (2) to determine whether there are differences in the compositional change in AC, as measured using T2 relaxation, between running and bicycling of equal cumulative load, and (3) to determine the relationship between self-reported physical activity history and changes in knee AC composition during running and bicycling. In a secondary analysis, we explored which specific weight-bearing regions [medial tibia (M.T.), lateral tibia (L.T.), medial femur (M.F.), and lateral femur (L.F.)] of AC experience changes in T2 and cartilage morphometry in response to loading. We hypothesized that (1) both running and bicycling will cause significant decreases in T2; (2) despite exposure to the same cumulative load, sustained loads during bicycling will cause greater changes in T2 relaxation than the high impact loads during running; and (3) there to be an inverse relationship between activity history and the change in T2 relaxation caused by running and bicycling. This work will show how AC acutely responds to two different types of aerobic exercise: running and bicycling. These findings are a fundamental step toward designing aerobic exercise to promote cartilage integrity in addition to combatting obesity, one of the major risk factors for OA (Wilson, Zakkak, & Lanier, 2009).

# Methods

## Experimental Design and Protocol

The study used an experimental, cross-sectional design. Participants attended one visit to McMaster University for biomechanical analyses and attended two separate visits to the St. Joseph's Imaging Research Center to obtain MRIs preceding and following two different activity protocols (**Figure 3-1**). These MRI visits were arranged in the morning to minimize exposure to activity before each visit. The activity protocols were running and bicycling, participants were arbitrarily assigned to perform their running or bicycling activity first. Truly random assignment was not feasible due to scheduling conflicts and individual participant changes in scheduling throughout the study. Five out of 15 participants performed the running visit first; 10 performed the bicycling visit first.

## Participants

Sixteen healthy men between 18-35 years were recruited from the McMaster community using posters and social media. Potential participants were excluded for the following reasons: self-reported injury to the lower extremity within the past 3-months; history of orthopedic surgery; signs and symptoms consistent with the clinical criteria for knee OA according to the American College of Rheumatology (Altman et al., 1986); Lower Extremity Functional Scale (LEFS) score <74 (Stratford, Kennedy, & Hanna, 2004; Y.-C. Wang, Hart, Stratford, & Mioduski, 2009); answering "Yes" to a question on the Physical Activity Readiness Questionnaire (PAR-Q) (Canadian Society for Exercise Physiology, 2004); or a body mass > 200 lbs. The last exclusion criterion ensured all participants

could be accommodated in the MRI scanner. As well, participants were carefully screened for contraindications to MRI, including having any implanted medical devices, cardiac stints, or heart operations, brain aneurysm clip(s), cochlear implants, a hearing aid, or embedded shrapnel or bullets in the body.

**Biomechanics Data Collection**

Biomechanics data were collected to determine the cumulative exposures to the vertical reaction force; that is, the sum of the vertical ground/pedal reaction impulses during running and bicycling.

**Running.** Force measurements were collected during running to calculate the vertical ground reaction force (vGRF) impulse of one running stride. Participants completed a warm-up run at a self-selected speed for 5-minutes on a commercial treadmill (5.1AT, Advanced Fitness Group, USA). This warm-up was used to determine their self-selected moderate running speed (described as a speed participants were comfortable maintaining for at least 20-minutes), and to determine their mean step-count per minute, using an accelerometer (GTX3, Actigraph, Fl, USA). Then, participants performed at least 5 practice trials of over-ground running along a laboratory runway (11.9m). Running speed was measured using photoelectric gates to ensure collected trials were within +/- 5% of the participants self-selected moderate running speed (Brower Timing Systems, Utah, USA). The runway was equipped with three embedded force platforms (OR6-7, AMTI, MA, USA) sampling at 1000Hz. After practice, participants

completed trials until they completed at least 5 successful trials. A successful trial was defined by two criteria: the right foot was planted on a single force platform for the entire stance phase, from heel strike to toe off; and a running speed equivalent to +/- 5% of self-selected moderate.

The vGRF signals from successful trials were filtered using a dual-pass second order low-pass Butterworth filter at 20Hz. The filter cut-off was determined using residual analysis (Winter, 2005) (Matlab, Math-works, Inc, El Segundo, California). The impulse of the vGRF of the step was calculated using the trapezoidal method (Maly, Robbins, Stratford, Birmingham, & Callaghan, 2013). The mean step vGRF impulse was determined by averaging the impulses of the 5 trials. Steps-per-minute was calculated from the accelerometer data.

**Bicycling.** Force measurements were collected during bicycling to calculate the vertical pedal reaction force (vPRF) impulse of a bicycle pedal revolution. Bicycling was performed on a Lode Excalibur cycle ergometer (Lode, NL). The pedal reaction forces were collected using a bicycle pedal fitted with a bi-axial load-measuring device (Novatech, UK). Force data during bicycling were collected in two directions (vertical, anterior/posterior) and were sampled at 1000 Hz. Furthermore, an electromagnetic switch was used to measure pedaling frequency. A revolution started when the right bicycle pedal crank arm passed the electromagnetic switch at the 9 o'clock position. The

revolution ended and the next revolution started when the crank arm returned back to the 9 o'clock position.

All participants were fitted to the cycle-ergometer using commercial road bicycle fitting guidelines and individual anthropometrics (Eric Bowen, 2011). To fit the bicycle to the participant, participant inseam length was measured and used to set the bicycle seat height (seat height from pedal spindle to top of seat= 1.11* inseam length). Once seat height was set, the seat forward and backward (fore/aft) position was set. The fore/aft position was set ensuring the most anterior aspect of the patella was within .5cm in front of and 1.5cm behind the pedal spindle. Lastly, the handlebar position was set based on participants' inseam length (distance from middle of bicycle seat to handlebars= [0.65*inseam length]+10cm). After the bicycle was setup, participants completed a 5-minute warm-up. During the warm-up, participants self-selected a moderate power output when pedaling at 80 revolutions per minute (RPM). After the warm-up, participants completed a 5-minute collected trial at 80 RPM and their self-selected moderate power.

The vPRF signals were filtered using a dual-pass second order low-pass Butterworth filter at 10Hz. The filter cut-off was determined using residual analysis (Winter, 2005) (Matlab, Math-works, Inc, El Segundo, California). The bicycling vPRF data were then divided into individual revolutions using the electromagnetic switch. The first 25 revolutions were removed from the analysis because these revolutions accelerated the pedal from a velocity of zero rad/s and were therefore not representative of the

revolutions throughout the rest of the activity (Gatti, Brenneman, & Maly, 2015). The vPRF impulses of the remaining revolutions were determined using the trapezoidal method (Maly et al., 2013). The mean of the vPRF impulses analyzed was then calculated. The mean pedal frequency of the entire activity was determined using data collected from the electromagnetic switch.

**Establishing Equivalent Cumulative Loads.**

Force data from the running and bicycling bouts were used to ensure the MRI activity bouts were of equivalent cumulative load. If the first visit was running, the participant performed a 15-minute running bout at their self-selected running speed.

If the first visit was bicycling, the length of the bicycling bout was calculated to elicit an equivalent cumulative load to that which the participant would experience during a 15-minute run. In this instance, the mean step frequency and mean vGRF impulse-per-step were used to estimate the cumulative load of the 15-minute run using equation (1). The estimated cumulative load of the running activity was then used along with the mean vPRF impulse-per-pedal-revolution and the set pedaling frequency to determine the length of the bicycling activity using equation (2)

**Equation (1)** [(cycles/min) * (impulse/cycle)= (impulse/min); (impulse/min) * (min)= cumulative load]

**Equation (2)** [(cumulative load / (impulse/cycle)= total cycles; total cycles/ (cycles/min)= total minutes].

Cycles= revolutions for bicycling and steps for running, impulse and cumulative load were measured in N*s.

In all instances, the vPRF was collected for the entire bicycling activity; and the number of steps during running was measured using a commercial accelerometer (Actigraph, USA). Data collected during the first visit (run or bike) were used to calculate the cumulative load of that activity. The cumulative load of the first visit was then used to refine the length of the second visit (run or bike) necessary to elicit an equivalent cumulative load using equation (2). This method allowed for total load exposure between the two activities to be as close as possible for each participant, while allowing for comparisons between participants by using a common running duration.

**Magnetic Resonance Imaging Data Acquisition**

MR images were acquired using a 3-Tesla GE Discovery 750, with a dedicated transmit and 8-channel receive knee coil array (Invivo Corp.). On one of the two MRI visits, three clinical scans were acquired for each study participant to ensure the knee joint was healthy. These scans were reviewed by an experienced radiologist (ST) to confirm health of the knee. ***(1) A sagittal proton density***: TR=2200ms, TE=29.28ms, FOV=16cm, frequency=127.78, matrix=320x224, pixels=0.3125mm x 0.3125mm, slice thickness=4mm, slice spacing=0.4mm, echo-train length=9, pixel band-width=162.77, number of excitations=1, flip angle=142°. ***(2) A coronal proton density***: TR=3000ms, TE=39.55ms, FOV=16cm, frequency=127.78, matrix=320x256, pixels=0.3125mm x

0.3125mm, slice thickness=4mm, slice spacing=0.4mm, echo-train length=8, pixel band-width=122.07, number of excitations=1, flip angle=142°. ***(3) An axial fat saturated T2***: TR=3583ms, TE=82.456ms, FOV=14cm, frequency=127.78, matrix=320x224, pixels=0.2734mm x 0.2734mm, slice thickness=4mm, slice spacing=1mm, echo-train length=14, pixel band-width=162.77, number of excitations=1.5, flip angle= 142°.

The primary images of interest were obtained pre and post activity at each of two MRI visits. To decrease the effect of previous activity on the first set of images, all imaging occurred in the morning (T.J. Mosher et al., 2010) and the first set of images was taken after the participant lay supine for 30-minutes (Subburaj et al., 2012). To quantitatively answer the primary research question, two imaging sequences were used. (1) Sagittal fast spin echo multi-echo images were acquired in order to calculate, pixel-wise, T2 relaxation time, PD, and the corresponding coefficient of determination ($R^2$). For segmentation purposes a 3D fat-saturated sagittal fast spoiled gradient recalled (FSPGR) sequence was used. ***T2Map, PD Map and $R^2$ Map***: TR=2450ms, TE=6.312ms, 12.624ms, 18.936ms, 25.248ms, 31.56ms, 37.872ms, 44.184ms, 50.496ms, FOV=16cm, frequency=127.78, matrix=256 x 256, pixels=0.625mm x 0.625mm, slice thickness=3mm, slice spacing=1mm, echo-train length=1, pixel band-width=488.28, number of excitations=1, flip angle=90°. ***3D FSPGR FS***: TR=17.388ms, TE=5.832ms, FOV=16cm, frequency=127.78, matrix=512x512, pixels=0.3125mm x 0.3125mm, slice thickness=1mm, slice spacing=1mm, echo-train length=1, pixel band-width=122.07, number of excitations=1, flip angle=18°.

**Magnetic Resonance Image Analysis**

T2 and PD maps were constructed from the multi-echo fast spin echo (FSE) images using a custom-written Matlab program (Math-works, Inc, El Segundo, California). The program fitted the pixel intensity collected from each of the 8-echos to the following equation: $S(TE)=PD \exp(-TE/T2)$ using a Levenberg-Marquardt fitting algorithm (Subburaj et al., 2012). In the equation, S(TE) is equal to the signal intensity for a given TE, PD is the signal intensity when TE= 0, and T2 is the time it takes for the signal intensity to decay 63% (Blumenkrantz & Majumdar, 2007). To minimize error associated with partial volume effects, voxels with T2 >100ms were excluded (Kumar et al., 2014, 2015; Souza et al., 2014; Subburaj et al., 2012). To further reduce the effect of error, any voxels with $R^2<0.7$ were excluded. $R^2$ of 0.7 was on average 2.5 standard deviations from the image mean, therefore pixels with the lowest 0.6% $R^2$, from the entire image, were excluded.

The 3D FSPGR images were segmented using a semi-automated, atlas-based, method (QMetrics, NY, USA). Images were segmented, as previously described (Tamez-Pena et al., 2012), into bone, cartilage, and cartilage sub-regions using five atlases. This approach produced 5 separate segmentations that were compared on a voxel-by-voxel basis to create one segmentation map. Cartilage segmentations were obtained for the medial weight bearing and lateral weight bearing regions of the femur, and medial and lateral tibial cartilage (Tamez-Pena et al., 2012). Cartilage segmentation maps were used to

determine the volume ($mm^3$) and mean thickness (mm) of each region of interest. This method yielded test-retest precision of cartilage thickness values between 0.014mm (0.6%) at the femur to 0.038mm (1.6%) at the femoral trochlea in images obtained with a 3.0T MRI (Tamez-Pena et al. 2012). T2 images and maps were manually registered to the 3D FSPGR images and coinciding segmentations using 3D Slicer (Fedorov et al., 2012). Once registered, segmented weight-bearing regions of cartilage were overlaid onto T2 maps and mean T2 values calculated for each weight-bearing region (3D Slicer).

**Self-reported Physical Activity**

To represent physical activity, the International Physical Activity Questionnaire (IPAQ) was used (Hagströmer, Oja, & Sjöström, 2006; IPAQ Research Committee, 2005). The IPAQ is a self-report questionnaire used to compare physical activity levels between individuals. The IPAQ includes items that assess physical activity performed during work, transportation, domestic activities, and leisure time sports. The IPAQ yields a score in MET-minutes/week. A MET is the metabolic energy required to perform an activity, with one MET being equivalent to resting metabolic rate. METs increase with increasing activity intensity and higher MET-minutes/week reflect higher activity levels. MET-minutes are calculated by multiplying the MET score of an activity by the number of minutes that activity is performed. The MET-minutes for all activities performed during a week are summed to yield the MET-minutes/week.

The IPAQ has been tested on a range of ages from 15 to 69 years (Terwee, Bouwmeester, van Elsland, de Vet, & Dekker, 2011). Data from the IPAQ show good test-retest reliability (Spearman's correlation ~0.8) (Craig et al., 2003; van Poppel, Chinapaw, Mokkink, van Mechelen, & Terwee, 2010). Criterion validity for the IPAQ in comparison to accelerometry has yielded Spearman's correlation from 0.3 to 0.55 with better validity for vigorous (0.63, $p<0.001$) as compared to moderate physical activity (0.12, $p>0.05$) (Craig et al., 2003; Hagströmer et al., 2006).

**Statistical Analysis**

Descriptive statistics were calculated. All data was tested for normality. Paired t-tests were used to determine if the duration and cumulative load of the running and bicycling activities were significantly different. Two analyses of variance (ANOVA) were used to determine if there was a main effect of loading on T2; one ANOVA was used for each of running and bicycling. To answer the second and third research questions, the change in T2 was determined for each region of interest (T2 change = post - pre). For question two, an ANOVA was used to determine whether the change in T2 was different between running and bicycling. For question 3, the change in T2 was used as the dependent variable in a regression, with MET-minutes/week used as the potential predictor.

In a secondary analysis, an ANOVA was performed for each region of interest to determine whether there was a main effect of loading, or activity, or an interaction effect of load#activity on T2, cartilage volume, or thickness. The results of this ANOVA

identified if T2, volume or thickness changed pre to post loading (loading), whether there is an effect of activity on T2, volume or thickness when pre and post data are combined (activity); and whether there is a difference in the change in T2, volume, or thickness between the two activities (loading#activity). Lastly, t-tests were performed for each activity and region of interest to determine whether bicycling or running caused a change in T2, thickness, or volume. To account for multiple comparisons, t-tests were evaluated at a p-value of 0.0021 (p=0.05/24) to allow for Bonferroni correction.

A convenience sample of 16 was recruited. This sample size was calculated for a medium and a large effect size. The sample size was calculated assuming $\alpha$=0.05; power=0.8, that a strong correlation of 0.8 existed between repeated measures that a moderate effect size is equal to 0.15 and that a large effect size is equal to 0.35 (J. Cohen, 1992). The sample size necessary to answer questions 1 and 2 and perform their respective ANOVAs with a large effect size was determined to be n=10, and with a moderate effect size was determine to be n=38.

## Results

### Participant Demographics

Sixteen men were recruited, 15 of which completed the study and were included in these analyses. The demographics of the participants are presented in **Table 3-1**. Due to equipment failure, one participant had only half of the bicycling biomechanics data from the MRI visit, and one participant had no bicycling biomechanics data from the MRI visit.

For the participant with half of the bicycling data, the partial data was used to estimate cumulative load of the entire activity. For the participant with no bicycling data, the laboratory-derived estimate of cumulative load was used.

**Table 3-2** summarizes the data collected during running and bicycling activities at the biomechanics visit to McMaster University. Bicycling power outputs ranged from 85 to 200 W and running speeds ranged from 7.9 to 13.2 km/h. Running and bicycling cadences were similar (mean 77.0 versus 80.2). Due to the difference in the impulse produced by each activity, the duration of running and bicycling activities performed at the MRI were different ($p<0.01$) (**Table 3-3**). Despite the difference in activity durations, there was < 1% difference between the mean cumulative load of the running and bicycling activities with cumulative loads of 338.42 KN*s and 340.44KN*s, respectively. The cumulative loads of the running and bicycling activities were not different ($p=0.54$).

**Comparison of Change in T2 caused by Running & Bicycling**

Bicycling did not cause a change in T2 from pre to post loading ($p=0.274$); however, running did cause a change in T2 ($p=0.002$) (**Table 3-5**). The change in T2 between running and bicycling was approaching but did not reach significance ($p=0.052$) (**Table 3-6**). Activity history measured using the IPAQ predicted the change in tibial T2 ($\beta=0.0003$; $p=0.006$) (**Table 3-7**; **Figure 3-3**). Activity history was not a predictor for femoral T2 or collated data from the tibia and femur.

**Regional Analyses of Change in T2, Thickness and Volume caused by Activity**

Secondary analysis showed that there was an effect of loading on T2 in all regions except for the medial femur (M.T. $p<0.001$; L.T. $p<0.001$; L.F. $p=0.030$) (**Table 3-8**). There was no effect of activity or interaction effect of loading#activity in any regions (**Table 3-8**). Mean thickness had a main loading effect in the medial tibia ($p=0.030$) and lateral tibia ($p<0.001$), and an interaction effect of loading#activity in the lateral tibia ($p=0.037$) and lateral femur ($p=0.007$) (**Table 3-8**). There was an effect of loading on volume in all regions (M.T. $p=0.011$; L.T. $p=0.001$; M.F. $p=0.010$; L.F. $p=0.010$), and there was an interaction effect of loading#activity on volume in the lateral femur ($p=0.002$) (**Table 3-8**), this interaction can be observed in **Figure 3-2**.

After bicycling, no change in T2 was noted in any subregion (**Figure 3-2**). After running, regional decreases in T2 were observed in the tibia (M.T. -6.11% $p=0.001$; L.T. -5.60% $p<0.001$) but not in the femur (**Figure 3-2**).

For morphometry, bicycling only caused a reduction in mean thickness of lateral tibial cartilage (-1.44% $p<0.001$). All other thickness and volume measurements remained unchanged after bicycling. Running caused a reduction in mean thickness of both medial and lateral regions of the tibia (M.T. -2.45% $p=0.002$; L.T -3.13%. $p<0.001$) but not the femur. As well, running caused a reduction in both the medial and lateral tibial volume (M.T. -4.57% $p<0.001$; L.T. -3.44% $p=0.001$); as well as a reduction in medial femoral cartilage volume (M.F. -2.71% $p<0.001$).

## Discussion

These analyses provided insight into the acute response of knee AC to running and bicycling. While bicycling did not cause a change in weight-bearing AC T2, similar to previous findings, running changed tibiofemoral cartilage T2 (Cha et al., 2012; Timothy J. Mosher et al., 2005; T.J. Mosher et al., 2010; Subburaj et al., 2012). Interestingly there was no statistically significant difference in T2 change between the activities; however a trend towards significance may indicate our sample size was too small to detect the changes in T2 after bicycling and the difference between the two activities. Contrary to our original hypothesis, this trend suggests running may cause a greater decrease in T2 than bicycling. Future work could explore whether the magnitude of forces associated with running, rather than the durations of sustained loading, are responsible for greater changes in cartilage composition after running in comparison to bicycling. Lastly, it was found that previous activity history influences the effect of loading on tibial cartilage T2. Those with high levels of activity exposures experienced less cartilage change in response to loading.

It is interesting that running changed T2 of tibiofemoral AC (5-10%), of a magnitude consistent with previous findings (3-9%; Subburaj 2012), while exposure to an equivalent cumulative load during bicycling did not. It is possible that no changes occurred after bicycling due to the relatively low peak forces acting at the tibiofemoral joint during bicycling (131% body mass @ 120 W and 60 RPM), which are less than those during walking (250% body mass) (Kutzner et al., 2012). While not significant, the trend

towards greater decreases in T2 caused by running was contrary to our original hypothesis. We hypothesized greater cartilage changes would result after bicycling because static, sustained loads cause tissue creep (N. P. Cohen, Foster, & Mow, 1998; Nordin & Frankel, 2012). In this study, it is likely that another aspect of loading, such as greater peak forces or greater loading rates during running, drove the greater changes in T2 compared to bicycling. This rationale is consistent with previous findings that high impact loading (40cm jumps) caused changes in tibiofemoral cartilage volume (6.1% medial tibia; 7.2% lateral tibia) whereas static loading (200% body mass while standing on one leg) did not (F Eckstein, 2005).

Previous activity exposure may condition tibial but not femoral AC. This finding may be due to differences in load distribution between the tibia and femur. Modeling of the tibiofemoral joint using fluoroscopy and MRI indicated that the contact points on the tibia does not significantly change with knee flexion angles ranging from 0° to 90° of knee flexion (Li, 2005). Meanwhile, the contact points on the femur do significantly change from 0° to 30°, 30° to 60°, and 60° to 90° degrees of knee flexion (Li, 2005). The relatively constant loading of the tibia may allow it to undergo greater conditioning than the femur; this phenomenon is similar to conditioning of the patella and ankle that has been previously described (Seedhom, 2005). Previous research has indicated that just 10 weeks of running can improve cartilage composition (that is, increase in proteoglycan content) as measured using delayed Gadolinium Enhanced Magnetic Resonance Imaging of Cartilage (dGEMRIC) (Van Ginckel et al., 2010). In this previous work, analyses of

changes in cartilage composition were only performed on the medial femoral cartilage overlying the posterior horn of the meniscus. Results of the current study indicate that even greater changes may have occurred to tibial cartilage as compared to femoral.

The changes in cartilage composition during running and bicycling appear to be consistent with, but not identical to, the changes observed in cartilage morphometry. For example, in subregion analyses, running caused a reduction in composition (T2) and morphometry (thickness, and volume) in medial and lateral tibial cartilage. Though, in two instances (lateral tibia after bicycling and medial femur after running) only cartilage morphometry changed, and composition did not. T2 is often associated to water content, which we assume decreases with cartilage compression therefore producing the decrease in T2 that we observe post activity. These differences between morphometric and compositional changes indicate that the change in AC composition is likely not entirely driven or related to morphometric changes, and therefore may not be entirely related to water content. It is important to note that changes in T2 may also be explained by changes in the collagen structure (Choi & Gold, 2011; Timothy J. Mosher et al., 2005). For instance, cartilage T2 is highly influenced by the angle of collagen fibers with respect to the external magnetic field (L. Wang & Regatte, 2015).

An important note is that to establish an equivalent cumulative load, the bicycling activity was on average >3 times the length of the running activity. As these are two common forms of aerobic activity potentially used to combat obesity, it is of interest to determine

how they compare metabolically. An investigation of energy expenditure using pulmonary gas-exchange showed that, in men, bicycling expended 14.77 kJ/(kg*h) and jogging expended 30.45 kJ/(kg*h) (Gao et al., 2012). If these values of energy expenditure were extrapolated to the activity durations from the current study it would indicate that our study participants on average expended 11.46 kJ/kg during bicycling and 7.60 kJ/kg during running. The current study suggests that bicycling is more metabolically active than running, while having minimal effect on tibiofemoral AC, in comparison to running. These findings are particularly important due to the necessity of aerobic exercise to combat obesity in individuals with knee OA. Future research is needed to directly compare energy expenditure and the response of knee AC to various activities among people with knee OA.

This study is not without limitations. Due to funding limitations, we present data from a relatively small sample. It is possible that results trending towards significance and subregion analyses would be improved by an increased sample size. It is recommended that future research comparing the response of knee AC between activities is conducted but with greater sample sizes. Furthermore, during the MRI visit, cumulative load during running was estimated. Measurement of the running impulse in the laboratory was overground, while the running protocol performed at the MRI was on a treadmill. It is not clear whether overground and treadmill running are equivalent (Fellin, Manal, & Davis, 2010; Riley et al., 2008; Willy & Davis, 2008). Impulses of the external ground/pedal reaction forces, and measurement of repetition, were used to normalize the cumulative

load between activities. This method improves upon previous studies; however, this study could be further enhanced by normalizing activity durations based on direct measurement of knee reaction forces, or estimated knee joint loading calculated using inverse dynamics. Lastly, some recovery of tissue after the activity protocol is likely. Recovery was minimized by locating exercise equipment directly outside of the MRI room and by performing imaging necessary to calculate T2 maps as the first acquired sequence.

While there has been some work on the acute response of knee AC in OA (Souza et al., 2014) future research must expand this work to determine how varying types and durations of load affects osteoarthritic AC as compared to healthy AC. Furthermore, due to the ability for activity history to predict changes in T2 in the tibia it is important that future research continue to investigate the protective effect that activity may have on knee AC.

## Conclusion

Running causes changes in weight-bearing knee AC T2, while bicycling of an equivalent cumulative load did not affect knee AC T2. A corresponding trend indicated that running likely causes a greater decrease in T2 than bicycling. Lastly, activity history modulated the acute response of tibial AC to loading but did not affect the response of weight-bearing femoral cartilage to loading.

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**Author Contributions**

Anthony Gatti designed the study, collected data, performed the analysis, and prepared the manuscript; Michael Noseworthy aided in study design, data analysis and preparation of the manuscript; Paul Stratford aided in study design, data analysis, and preparation of the manuscript; Elora Brenneman aided in study design and data collection; Saara Totterman aided in study design and data analysis; José Tamez-Peña aided in study design and data analysis; Monica Maly designed the study, guided analysis and prepared the manuscript.

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## Conflict of Interest

Saara Totterman and José Tamez-Peña are employed by QMetrics Technologies.

## References

Altman, R., Asch, E., Bloch, D., Bole, G., Borenstein, D., Brandt, K., … others. (1986). Development of criteria for the classification and reporting of osteoarthritis: classification of osteoarthritis of the knee. *Arthritis & Rheumatism*, *29*(8), 1039–1049.

Anderson, J. J., & Felson, D. T. (1988). Factors associated with osteoarthritis of the knee in the first national Health and Nutrition Examination Survey (HANES I) evidence for an association with overweight, race, and physical demands of work. *American Journal of Epidemiology*, *128*(1), 179–189.

Bennell, K. L., Bowles, K.-A., Wang, Y., Cicuttini, F., Davies-Tuck, M., & Hinman, R. S. (2011). Higher dynamic medial knee load predicts greater cartilage loss over 12 months in medial knee osteoarthritis. *Annals of the Rheumatic Diseases*, *70*(10), 1770–1774. http://doi.org/10.1136/ard.2010.147082

Blumenkrantz, G., & Majumdar, S. (2007). Quantitative magnetic resonance imaging of articular cartilage in osteoarthritis. *Eur Cell Mater*, *13*, 76–86.

Boocock, M., McNair, P., Cicuttini, F., Stuart, A., & Sinclair, T. (2009). The short-term effects of running on the deformation of knee articular cartilage and its relationship to biomechanical loads at the knee. *Osteoarthritis and Cartilage*, *17*(7), 883–890. http://doi.org/10.1016/j.joca.2008.12.010

Canadian Society for Exercise Physiology. (2004). *Canadian physical activity, fitness & lifestyle approach: CSEP - health & fitness program's health-related appraisal & counselling strategy.* Ottawa, Ont.: Canadian Society for Exercise Physiology.

Cha, J. G., Lee, J. C., Kim, H. J., Han, J. K., Lee, E. H., Kim, Y. D., & Jeon, C. H. (2012). Comparison of MRI T2 Relaxation Changes of Knee Articular Cartilage before and after Running between Young and Old Amateur Athletes. *Korean Journal of Radiology*, *13*(5), 594. http://doi.org/10.3348/kjr.2012.13.5.594

Choi, J.-A., & Gold, G. E. (2011). MR Imaging of Articular Cartilage Physiology. *Magnetic Resonance Imaging Clinics of North America*, *19*(2), 249–282. http://doi.org/10.1016/j.mric.2011.02.010

Cohen, J. (1992). A power primer. *Psychological Bulletin*, *112*(1), 155.

Cohen, N. P., Foster, R. J., & Mow, V. C. (1998). Composition and dynamics of articular cartilage: structure, function, and maintaining healthy state. *Journal of Orthopaedic & Sports Physical Therapy*, *28*(4), 203–215.

Cotofana, S., Eckstein, F., Wirth, W., Souza, R. B., Li, X., Wyman, B., … Majumdar, S. (2011). In vivo measures of cartilage deformation: patterns in healthy and osteoarthritic female knees using 3T MR imaging. *European Radiology*, *21*(6), 1127–1135. http://doi.org/10.1007/s00330-011-2057-y

Craig, C. L., Marshall, A. L., Sj??Str??M, M., Bauman, A. E., Booth, M. L., Ainsworth, B. E., … Oja, P. (2003). International Physical Activity Questionnaire: 12-Country Reliability and Validity: *Medicine & Science in Sports & Exercise*, *35*(8), 1381–1395. http://doi.org/10.1249/01.MSS.0000078924.61453.FB

Eckstein, F. (2005). In vivo cartilage deformation after different types of activity and its dependence on physical training status. *Annals of the Rheumatic Diseases*, *64*(2), 291–295. http://doi.org/10.1136/ard.2004.022400

Eckstein, F., Lemberger, B., Stammberger, T., Englmeier, K. H., & Reiser, M. (2000). Patellar cartilage deformation in vivo after static versus dynamic loading. *Journal of Biomechanics*, *33*(7), 819–825.

Eckstein, F., Tieschky, M., Faber, S., Englmeier, K.-H., & Reiser, M. (1999). Functional analysis of articular cartilage deformation, recovery, and fluid flow following dynamic exercise in vivo. *Anatomy and Embryology*, *200*(4), 419–424.

Eric Bowen. (2011, March 14). Road bikefitting guidelines: the essentials for proper fit. Velofit Revolution.

Fedorov, A., Beichel, R., Kalpathy-Cramer, J., Finet, J., Fillion-Robin, J.-C., Pujol, S., … Kikinis, R. (2012). 3D Slicer as an image computing platform for the Quantitative Imaging Network. *Magnetic Resonance Imaging*, *30*(9), 1323–1341. http://doi.org/10.1016/j.mri.2012.05.001

Fellin, R. E., Manal, K., & Davis, I. S. (2010). Comparison of lower extremity kinematic curves during overground and treadmill running. *Journal of Applied Biomechanics*, *26*(4), 407.

Felson, D. T., Anderson, J. J., Naimark, A., Walker, A. M., & Meenan, R. F. (1988). Obesity and knee osteoarthritis: the Framingham Study. *Annals of Internal Medicine*, *109*(1), 18–24.

Felson, D. T., Zhang, Y., Anthony, J. M., Naimark, A., & Anderson, J. J. (1992). Weight loss reduces the risk for symptomatic knee osteoarthritis in women. The Framingham Study. *Annals of Internal Medicine*, *116*(7), 535–539.

Gao, Z., Wang, X., Zhuo, Q., Wang, J., Hu, F., Piao, J., … Cao, H. (2012). [Energy expenditure on different physical activities of rural adults in North China]. *Wei Sheng Yan Jiu = Journal of Hygiene Research*, *41*(1), 75–79.

Gatti, A., Brenneman, E., & Maly, M. R. (2015). Estimating Cumulative Load from Impulse Measurements during Bicycling. Presented at the 12th Annual Ontario Biomechanics Conference, Ontario.

Green, S. B. (1991). How Many Subjects Does It Take To Do A Regression Analysis. *Multivariate Behavioral Research*, *26*(3), 499–510. http://doi.org/10.1207/s15327906mbr2603_7

Hagströmer, M., Oja, P., & Sjöström, M. (2006). The International Physical Activity Questionnaire (IPAQ): a study of concurrent and construct validity. *Public Health Nutrition*, *9*(06). http://doi.org/10.1079/PHN2005898

Hinterwimmer, S., Krammer, M., Krotz, M., Glaser, C., Baumgart, R., Reiser, M., & Eckstein, F. (2004). Cartilage atrophy in the knees of patients after seven weeks of partial load bearing. *Arthritis & Rheumatism*, *50*(8), 2516–2520. http://doi.org/10.1002/art.20378

IPAQ Research Committee. (2005). Guidelines for Data Processing and Analysis of the International Physical Activity Questionnaire (IPAQ).

Kessler, M. A. (2005). Volume Changes in the Menisci and Articular Cartilage of Runners: An In Vivo Investigation Based on 3-D Magnetic Resonance Imaging. *American Journal of Sports Medicine*, *34*(5), 832–836. http://doi.org/10.1177/0363546505282622

Kessler, M. A., Glaser, C., Tittel, S., Reiser, M., & Imhoff, A. B. (2008). Recovery of the Menisci and Articular Cartilage of Runners After Cessation of Exercise: Additional Aspects of In Vivo Investigation Based on 3-Dimensional Magnetic Resonance Imaging. *The American Journal of Sports Medicine*, *36*(5), 966–970. http://doi.org/10.1177/0363546507313093

Kumar, D., Souza, R. B., Singh, J., Calixto, N. E., Nardo, L., Link, T. M., … Majumdar, S. (2014). Physical Activity and Spatial Differences in Medial Knee T1rho and T2 Relaxation Times in Knee Osteoarthritis. *Journal of Orthopaedic & Sports Physical Therapy*, *44*(12), 964–972. http://doi.org/10.2519/jospt.2014.5523

Kumar, D., Souza, R. B., Subburaj, K., MacLeod, T. D., Singh, J., Calixto, N. E., … Majumdar, S. (2015). Are There Sex Differences in Knee Cartilage Composition and Walking Mechanics in Healthy and Osteoarthritis Populations? *Clinical Orthopaedics and Related Research®*. http://doi.org/10.1007/s11999-015-4212-2

Kutzner, I., Heinlein, B., Graichen, F., Rohlmann, A., Halder, A. M., Beier, A., & Bergmann, G. (2012). Loading of the Knee Joint During Ergometer Cycling: Telemetric In Vivo Data. *Journal of Orthopaedic & Sports Physical Therapy*, *42*(12), 1032–1038. http://doi.org/10.2519/jospt.2012.4001

Liess, C. (2002). Detection of changes in cartilage water content using MRI T2-mapping in vivo. *Osteoarthritis and Cartilage*, *10*(12), 907–913. http://doi.org/10.1053/joca.2002.0847

Li, G. (2005). In Vivo Articular Cartilage Contact Kinematics of the Knee: An Investigation Using Dual-Orthogonal Fluoroscopy and Magnetic Resonance

Image-Based Computer Models. *American Journal of Sports Medicine*, *33*(1), 102–107. http://doi.org/10.1177/0363546504265577

Lu, X. L., & Mow, V. C. (2008). Biomechanics of Articular Cartilage and Determination of Material Properties: *Medicine & Science in Sports & Exercise*, *40*(2), 193–199. http://doi.org/10.1249/mss.0b013e31815cb1fc

Maly, M. R., Robbins, S. M., Stratford, P. W., Birmingham, T. B., & Callaghan, J. P. (2013). Cumulative knee adductor load distinguishes between healthy and osteoarthritic knees–A proof of principle study. *Gait & Posture*, *37*(3), 397–401. http://doi.org/10.1016/j.gaitpost.2012.08.013

Mosher, T. J., Liu, Y., & Torok, C. M. (2010). Functional cartilage MRI T2 mapping: evaluating the effect of age and training on knee cartilage response to running. *Osteoarthritis and Cartilage*, *18*(3), 358–364. http://doi.org/10.1016/j.joca.2009.11.011

Mosher, T. J., Smith, H. E., Collins, C., Liu, Y., Hancy, J., Dardzinski, B. J., & Smith, M. B. (2005). Change in Knee Cartilage T2 at MR Imaging after Running: A Feasibility Study1. *Radiology*, *234*(1), 245–249. http://doi.org/10.1148/radiol.2341040041

Mow, V. C., & Guo, X. E. (2002). M ECHANO -E LECTROCHEMICAL P ROPERTIES OF A RTICULAR C ARTILAGE : Their Inhomogeneities and Anisotropies. *Annual Review of Biomedical Engineering*, *4*(1), 175–209. http://doi.org/10.1146/annurev.bioeng.4.110701.120309

Nordin, M., & Frankel, V. H. (Eds.). (2012). *Basic biomechanics of the musculoskeletal system* (4th ed). Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins.

Riley, P. O., Dicharry, J., Franz, J., Croce, U. D., Wilder, R. P., & Kerrigan, D. C. (2008). A Kinematics and Kinetic Comparison of Overground and Treadmill Running: *Medicine & Science in Sports & Exercise*, *40*(6), 1093–1100. http://doi.org/10.1249/MSS.0b013e3181677530

Seedhom, B. B. (2005). Conditioning of cartilage during normal activities is an important factor in the development of osteoarthritis. *Rheumatology*, *45*(2), 146–149. http://doi.org/10.1093/rheumatology/kei197

Souza, R. B., Kumar, D., Calixto, N., Singh, J., Schooler, J., Subburaj, K., … Majumdar, S. (2014). Response of knee cartilage T1rho and T2 relaxation times to in vivo mechanical loading in individuals with and without knee osteoarthritis. *Osteoarthritis and Cartilage*. http://doi.org/10.1016/j.joca.2014.04.017

Souza, R. B., Stehling, C., Wyman, B. T., Hellio Le Graverand, M.-P., Li, X., Link, T. M., & Majumdar, S. (2010). The effects of acute loading on T1rho and T2 relaxation times of tibiofemoral articular cartilage. *Osteoarthritis and Cartilage*, *18*(12), 1557–1563. http://doi.org/10.1016/j.joca.2010.10.001

Stratford, P. W., Kennedy, D. M., & Hanna, S. E. (2004). Condition-specific Western Ontario McMaster Osteoarthritis Index was not superior to region-specific Lower Extremity Functional Scale at detecting change. *Journal of Clinical Epidemiology*, *57*(10), 1025–1032. http://doi.org/10.1016/j.jclinepi.2004.03.008

Subburaj, K., Kumar, D., Souza, R. B., Alizai, H., Li, X., Link, T. M., & Majumdar, S. (2012). The Acute Effect of Running on Knee Articular Cartilage and Meniscus Magnetic Resonance Relaxation Times in Young Healthy Adults. *The American Journal of Sports Medicine*, *40*(9), 2134–2141. http://doi.org/10.1177/0363546512449816

Tamez-Pena, J. G., Farber, J., Gonzalez, P. C., Schreyer, E., Schneider, E., & Totterman, S. (2012). Unsupervised Segmentation and Quantification of Anatomical Knee Features: Data From the Osteoarthritis Initiative. *IEEE Transactions on Biomedical Engineering*, *59*(4), 1177–1186. http://doi.org/10.1109/TBME.2012.2186612

Terwee, C. B., Bouwmeester, W., van Elsland, S. L., de Vet, H. C. W., & Dekker, J. (2011). Instruments to assess physical activity in patients with osteoarthritis of the hip or knee: a systematic review of measurement properties. *Osteoarthritis and Cartilage*, *19*(6), 620–633. http://doi.org/10.1016/j.joca.2011.01.002

Urquhart, D. M., Tobing, J. F. L., Hanna, F. S., Berry, P., Wluka, A. E., Ding, C., & Cicuttini, F. M. (2011). What Is the Effect of Physical Activity on the Knee Joint? A Systematic Review: *Medicine & Science in Sports & Exercise*, *43*(3), 432–442. http://doi.org/10.1249/MSS.0b013e3181ef5bf8

Van Ginckel, A., Baelde, N., Almqvist, K. F., Roosen, P., McNair, P., & Witvrouw, E. (2010). Functional adaptation of knee cartilage in asymptomatic female novice runners compared to sedentary controls. A longitudinal analysis using delayed Gadolinium Enhanced Magnetic Resonance Imaging of Cartilage (dGEMRIC).

*Osteoarthritis and Cartilage*, *18*(12), 1564–1569. http://doi.org/10.1016/j.joca.2010.10.007

van Poppel, M. N. M., Chinapaw, M. J. M., Mokkink, L. B., van Mechelen, W., & Terwee, C. B. (2010). Physical activity questionnaires for adults: a systematic review of measurement properties. *Sports Medicine (Auckland, N.Z.)*, *40*(7), 565–600. http://doi.org/10.2165/11531930-000000000-00000

Wang, L., & Regatte, R. R. (2015). Investigation of Regional Influence of Magic-Angle Effect on T2 in Human Articular Cartilage with Osteoarthritis at 3 T. *Academic Radiology*, *22*(1), 87–92. http://doi.org/10.1016/j.acra.2014.07.015

Wang, Y.-C., Hart, D. L., Stratford, P. W., & Mioduski, J. E. (2009). Clinical interpretation of a lower-extremity functional scale–derived computerized adaptive test. *Physical Therapy*, *89*(9), 957–968.

Willy, R., & Davis, I. S. (2008). Instrumented comparison of overground and treadmill running in healthy individuals: 632: May 28 4: 45 PM-5: 00 PM. In *Proceedings of the 2008 Annual Meeting of the American College of Sports Medicine* (Vol. 40, pp. S27–S28). Indianapolis, IN.

Wilson, D. B., Zakkak, J. M., & Lanier, J. O. (2009). Peer Reviewed: The Association Between Body Mass Index and Arthritis Among US Adults: CDC's Surveillance Case Definition. *Preventing Chronic Disease*, *6*(2). Retrieved from http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2687862/

Winter, D. A. (2005). *Biomechanics and motor control of human movement* (3rd ed). Hoboken, New Jersey: John Wiley & Sons.

**Table 3-1.** Mean, standard deviation (SD), minimum, and maximum values of demographics of participants including age, height, body mass, body mass index, activity history measured using the International Physical Activity Questionnaire (IPAQ), and lower extremity function measured using the Lower Extremity Functional Scale (LEFS).

| | Mean | SD | Min | Max |
|---|---|---|---|---|
| Age (y) | 25.8 | 4.2 | 20 | 33 |
| Height (m) | 1.79 | 0.06 | 1.70 | 1.89 |
| Body Mass (kg) | 75.8 | 9.7 | 59.5 | 93.5 |
| Body Mass Index ($kg/m^2$) | 23.71 | 2.62 | 18.53 | 27.16 |
| Activity History (Metabolic mins/week) | 6570.6 | 4158.7 | 924 | 17287.5 |
| Lower Extremity Functional Scale (/80) | 79.8 | 0.6 | 78 | 80 |

**Table 3-2.** Mean, standard deviation (SD), minimum, and maximum values for running and bicycling biomechanics data collected at visit one to McMaster University.

| | Mean | SD | Min | Max |
|---|---|---|---|---|
| Running | | | | |
| Speed (km/hr) | 10.0 | 1.3 | 7.9 | 13.2 |
| Impulse/step (N*s) | 282.0 | 39.0 | 213.0 | 348.6 |
| Steps/min | 77.0 | 2.6 | 75.0 | 83.0 |
| Impulse/min (N*s/min) | 21940.9 | 2773.7 | 17518.6 | 26232.0 |
| Bicycling | | | | |
| Power (W) | 125.3 | 32.1 | 85.0 | 200.0 |
| Impulse/rev (N*s) | 91.3 | 16.5 | 69.0 | 114.6 |
| Revs/min | 80.2 | 0.7 | 78.5 | 81.3 |
| Impulse/min (N*s/min) | 7320.5 | 1319.4 | 5539.4 | 9262.3 |

**Table 3-3.** Mean, standard deviation (SD), minimum, and maximum values for running and bicycling activities collected at visits two and three to St. Joseph's Imaging Research Centre. Cumulative load is the measured total vertical pedal reaction force impulse (bicycling); and the product of step count and total vertical ground reaction force impulse (running).

| | Mean | SD | Min | Max |
|---|---|---|---|---|
| Running | | | | |
| Total Steps | 1193.6 | 98.2 | 1043 | 1400 |
| Cumulative Load (N*s) | 338420.7 | 52208.0 | 264962.2 | 415674.6 |
| Run Time (min:s) | 14:58 | 1:05 | 13:37 | 17:44 |
| Bicycling | | | | |
| Total Revolutions | 3749.9 | 529.9 | 2946 | 4755 |
| Cumulative Load (N*s) | 340444.3 | 47934.8 | 273736.6 | 421041.9 |
| Bike Time (min:s) | 46:32 | 6:37 | 36:27 | 59:06 |

**Table 3-4.** Mean, standard deviation (SD), minimum and maximum values for T2 relaxation, mean thickness, and volume of tibiofemoral articular cartilage pre and post running and bicycling, for each region of interest. T2 relaxation is the mean T2(ms) for the region of interest. Mean thickness is the mean cartilage thickness for the region of interest.

| | Pre | | | | Post | | | |
|---|---|---|---|---|---|---|---|---|
| | **Mean** | **SD** | **Min** | **Max** | **Mean** | **SD** | **Min** | **Max** |
| **Running** | | | | | | | | |
| Mean Thickness (mm) | | | | | | | | |
| Medial Tibia | 2.08 | 0.18 | 1.74 | 2.32 | 2.03 | 0.18 | 1.74 | 2.32 |
| Lateral Tibia | 2.66 | 0.24 | 2.26 | 3.18 | 2.58 | 0.23 | 2.23 | 3.05 |
| Medial Femur | 2.06 | 0.22 | 1.71 | 2.48 | 2.04 | 0.23 | 1.63 | 2.46 |
| Lateral Femur | 2.04 | 0.18 | 1.56 | 2.35 | 1.99 | 0.17 | 1.45 | 2.18 |
| Volume ($mm^{3)}$ | | | | | | | | |
| Medial Tibia | 2306.76 | 359.54 | 1836.33 | 3030.08 | 2203.39 | 370.02 | 1753.13 | 2930.18 |
| Lateral Tibia | 3066.73 | 492.82 | 2303.32 | 4423.74 | 2957.76 | 448.93 | 2244.83 | 4074.90 |
| Medial Femur | 2331.73 | 377.28 | 1736.14 | 2996.88 | 2269.55 | 373.67 | 1588.87 | 2952.85 |
| Lateral Femur | 2223.14 | 275.84 | 1567.78 | 2630.97 | 2135.52 | 294.83 | 1329.69 | 2543.56 |
| Mean T2 (ms) | | | | | | | | |
| Medial Tibia | 36.605 | 2.853 | 31.926 | 42.008 | 34.349 | 3.160 | 28.302 | 39.061 |
| Lateral Tibia | 31.669 | 2.958 | 27.920 | 37.285 | 29.860 | 2.675 | 24.282 | 34.715 |
| Medial Femur | 32.535 | 5.367 | 21.516 | 41.090 | 28.491 | 3.177 | 23.426 | 34.022 |
| Lateral Femur | 36.268 | 5.538 | 27.366 | 48.710 | 34.562 | 4.782 | 26.885 | 43.033 |
| **Bicycling** | | | | | | | | |
| Mean Thickness (mm) | | | | | | | | |
| Medial Tibia | 2.06 | 0.15 | 1.87 | 2.32 | 2.06 | 0.18 | 1.77 | 2.41 |
| Lateral Tibia | 2.64 | 0.23 | 2.38 | 3.22 | 2.61 | 0.24 | 2.27 | 3.20 |
| Medial Femur | 2.09 | 0.18 | 1.79 | 2.42 | 2.08 | 0.17 | 1.77 | 2.36 |
| Lateral Femur | 2.06 | 0.10 | 1.88 | 2.23 | 2.07 | 0.10 | 1.91 | 2.26 |
| Volume ($mm^3$) | | | | | | | | |
| Medial Tibia | 2304.85 | 285.19 | 1973.44 | 3023.54 | 2270.53 | 309.83 | 1838.18 | 3042.09 |
| Lateral Tibia | 3080.36 | 470.48 | 2450.39 | 4438.18 | 3026.26 | 514.76 | 2329.69 | 4527.93 |
| Medial Femur | 2365.38 | 296.40 | 2004.11 | 2929.85 | 2348.73 | 279.38 | 1959.86 | 2801.76 |
| Lateral Femur | 2242.36 | 199.83 | 1964.16 | 2604.68 | 2251.45 | 187.02 | 1925.29 | 2584.75 |
| Mean T2 (ms) | | | | | | | | |
| Medial Tibia | 35.807 | 2.890 | 31.474 | 40.208 | 34.450 | 2.479 | 29.920 | 38.534 |
| Lateral Tibia | 30.322 | 3.395 | 26.389 | 36.230 | 29.636 | 2.605 | 25.163 | 35.220 |
| Medial Femur | 29.819 | 3.672 | 25.800 | 38.962 | 30.272 | 4.953 | 22.321 | 36.033 |
| Lateral Femur | 37.247 | 3.682 | 29.829 | 44.037 | 35.354 | 4.645 | 24.266 | 42.255 |

**Table 3-5.** Analyses of variance (ANOVA) to determine the main effects of loading (pre to post activity) on T2 relaxation time of weightbearing tibiofemoral articular cartilage. Separate ANOVAs were run for each of running and bicycling. Effect size is reported as Cohen's f statistic and bold font indicates significance ($p<0.05$).

| Activity | Loading | Participant | $R^2$ |
|---|---|---|---|
| Running | **p=0.002** | **p<0.001** | 0.384 |
| Effect size (Cohen's f) | 0.255 | 0.551 | |
| Bicycling | p=0.274 | **p=0.002** | 0.277 |
| Effect size (Cohen's f) | 0.040 | 0.452 | |

**Table 3-6.** Analysis of variance (ANOVA) to determine the main effect of activity type (bicycling or running) on the change in T2 relaxation time of weight-bearing tibiofemoral articular cartilage. Effect size is reported as Cohen's f statistic.

| | Activity | Participant | $R^2$ |
|---|---|---|---|
| Change in T2 (ms) | p=0.052 | p=0.579 | 0.148 |
| Effect size (Cohen's f) | 0.161 | 0.000 | |

**Table 3-7.** Summary of results for regressions used to determine whether activity history, as measured using the International Physical Activity Questionnaire (IPAQ), can predict the change in T2 in tibial, femoral and all weight-bearing articular cartilage. One outlier was removed from the analysis due to an extremely high activity level. Bold font indicates significance ($p<0.05$).

| Region | Coefficient | Significance | $R^2$ |
|---|---|---|---|
| Tibia | | | 0.1436 |
| Activity history (metabolic min/week) | 0.0003 | **0.006** | |
| Constant | -3.1800 | **<0.001** | |
| Femur | | | 0.0003 |
| Activity history (metabolic min/week) | 0.0000 | 0.906 | |
| Constant | -1.9830 | 0.288 | |
| Whole weight bearing region | | | 0.0112 |
| Activity history (metabolic min/week) | 0.0002 | 0.286 | |
| Constant | -2.5815 | **0.001** | |

**Table 3-8.** Analyses of variance (ANOVA) to determine the main effects of loading (pre to post activity), activity type (running or bicycling) and the interaction effect of loading*activity type on mean thickness, volume, and T2 relaxation time of weight-bearing tibiofemoral articular cartilage. One ANOVA was run for each region of interest (medial tibia, lateral tibia, medial femur, lateral femur). Effect size is reported for each variable as Cohen's f statistic and bold font indicates significance ($p<0.05$).

| Measurement | Activity | Loading | Activity | Loading*Activity | Participant | $R^2$ |
|---|---|---|---|---|---|---|
| Mean Thickness (mm) | Medial Tibia | **p=0.030** | p=0.810 | p=0.081 | **p<0.001** | 0.947 |
| | Effect size (Cohen's f) | 0.076 | 0.000 | 0.056 | 3.271 | |
| | Lateral Tibia | **p<0.001** | p=0.298 | **p=0.037** | **p<0.001** | 0.978 |
| | Effect size (Cohen's f) | 0.132 | 0.008 | 0.046 | 4.324 | |
| | Medial Femur | p=0.098 | p=0.785 | p=0.499 | **p<0.001** | 0.976 |
| | Effect size (Cohen's f) | 0.035 | 0.000 | 0.000 | 4.685 | |
| | Lateral Femur | p=0.069 | p=0.540 | **p=0.007** | **p<0.001** | 0.944 |
| | Effect size (Cohen's f) | 0.061 | 0.000 | 0.104 | 2.700 | |
| Volume ($mm^3$) | Medial Tibia | **p=0.011** | p=0.456 | p=0.187 | **p<0.001** | 0.940 |
| | Effect size (Cohen's f) | 0.099 | 0.000 | 0.036 | 2.998 | |
| | Lateral Tibia | **p=0.001** | p=0.086 | p=0.244 | **p<0.001** | 0.977 |
| | Effect size (Cohen's f) | 0.084 | 0.036 | 0.016 | 4.722 | |
| | Medial Femur | **p=0.010** | p=0.879 | p=0.124 | **p<0.001** | 0.981 |
| | Effect size (Cohen's f) | 0.057 | 0.000 | 0.027 | 4.972 | |
| | Lateral Femur | **p=0.010** | p=0.336 | **p=0.002** | **p<0.001** | 0.966 |
| | Effect size (Cohen's f) | 0.076 | 0.000 | 0.097 | 3.288 | |
| Mean T2(ms) | Medial Tibia | **p<0.001** | p<0.308 | p<0.214 | **p<0.001** | 0.843 |
| | Effect size (Cohen's f) | 0.322 | 0.016 | 0.049 | 1.431 | |
| | Lateral Tibia | **p<0.001** | p=0.189 | p=0.090 | **p<0.001** | 0.048 |
| | Effect size (Cohen's f) | 0.202 | 0.045 | 0.073 | 2.076 | |
| | Medial Femur | p=0.132 | p=0.753 | p=0.058 | p=0.114 | 0.427 |
| | Effect size (Cohen's f) | 0.142 | 0.000 | 0.207 | 0.383 | |
| | Lateral Femur | **p=0.030** | p=0.523 | p=0.898 | **p<0.001** | 0.712 |
| | Effect size (Cohen's f) | 0.175 | 0.0 | 0.0 | 1.119 | |

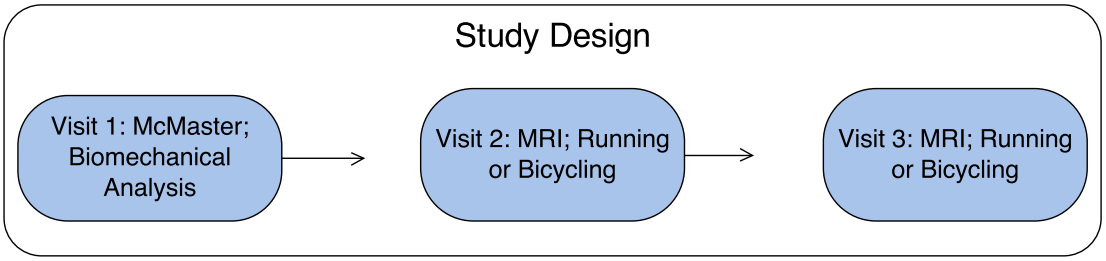


**Figure 3-1.** Schematic describing the order of study visits. Participants first visited McMaster University for biomechanical analysis. Participants then made two visits to St. Joseph's Imaging Research Centre to obtain MRIs preceding and following two different activity protocols (running and bicycling).

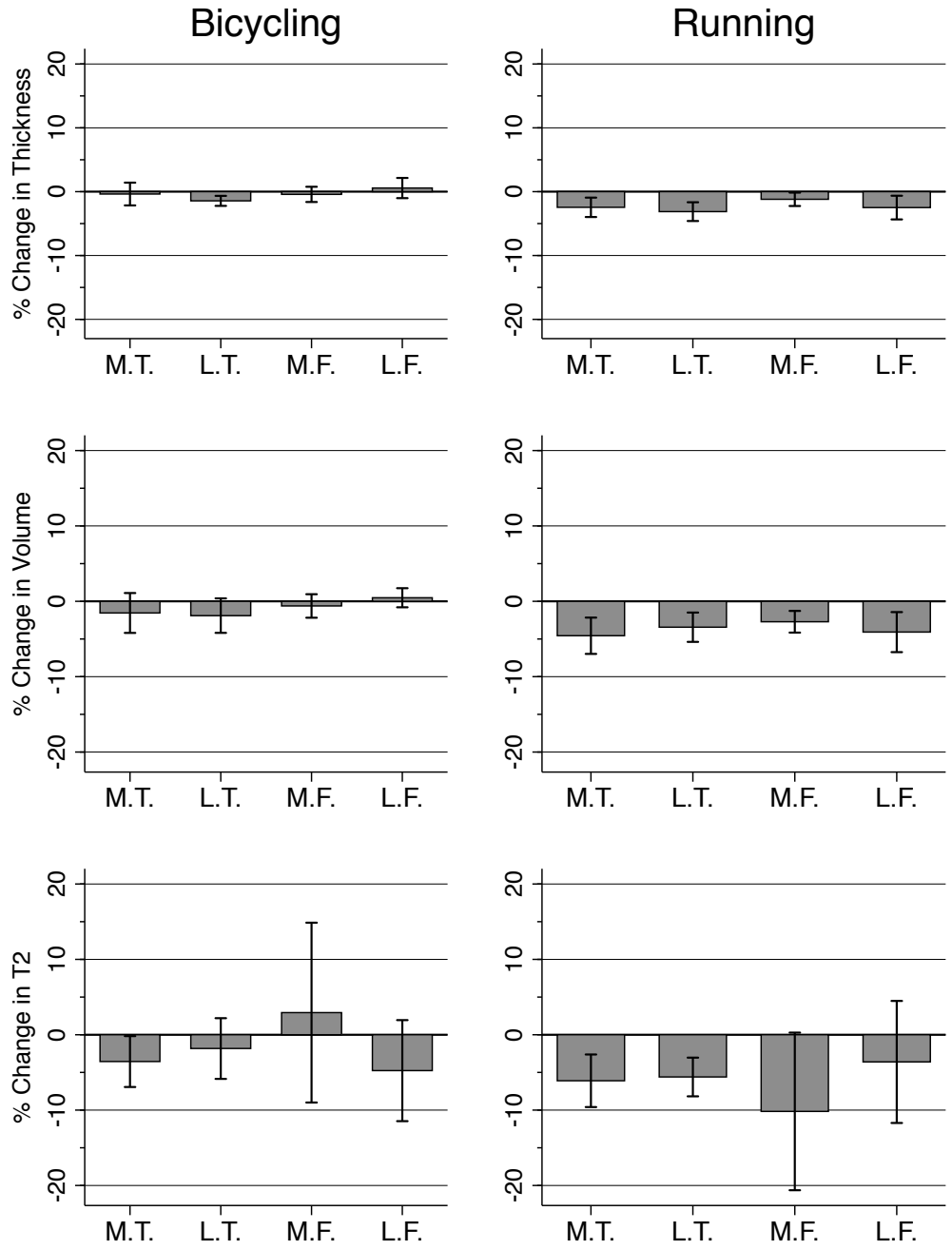


**Figure 3-2.** The mean and 95% confidence interval for the percent change in articular cartilage thickness, volume, and T2 of the medial tibia (M.T.), lateral tibia (L.T.), medial femur (M.F.), and lateral femur (L.F.) caused by running and bicycling.

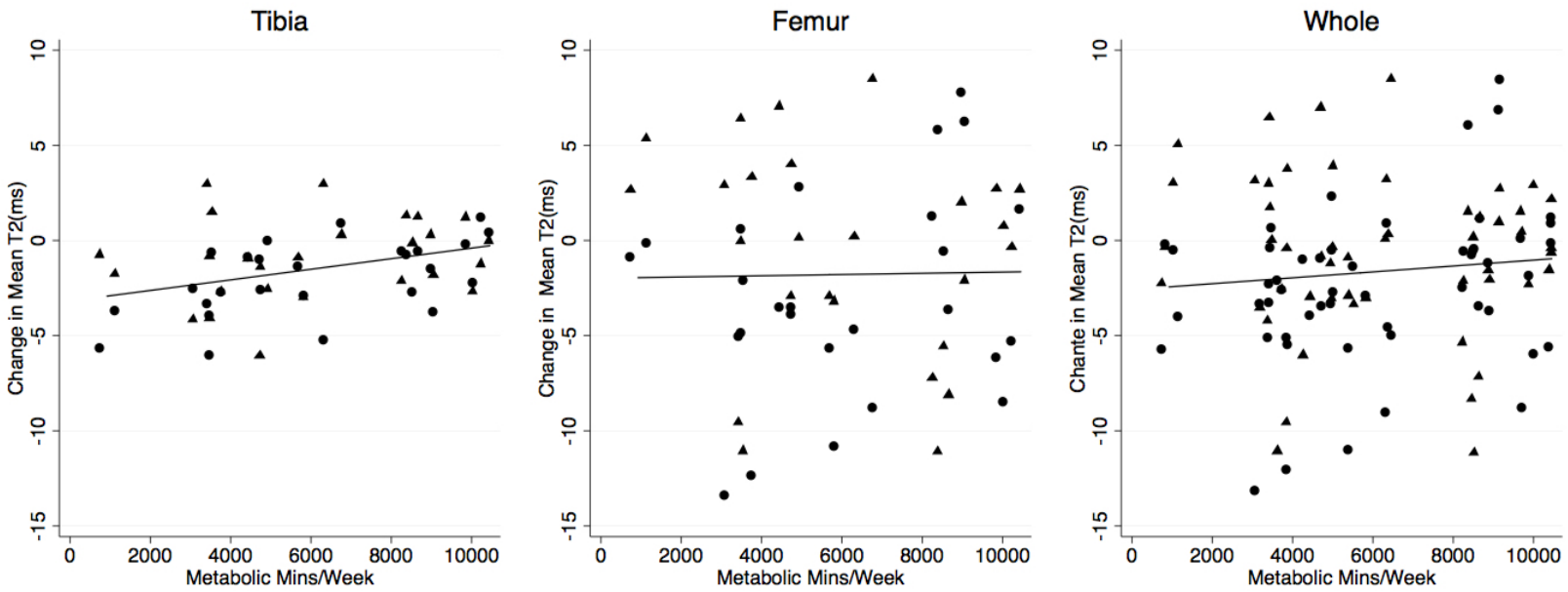


**Figure 3-3.** The change in mean T2(ms) in weight-bearing Tibia, Femur, and all Tibiofemoral cartilage plotted against self-reported participant activity history measured in metabolic minutes per week using the International Physical Activity Questionnaire (IPAQ). Changes in T2 resulting from running are plotted with circles, and changes resulting from bicycling are plotted with triangles.

# CHAPTER 4
# DISCUSSION

The results of these studies add to the current body of knowledge pertaining to the quantification of aerobic exercise and to our understanding of the in vivo response of knee AC to running and bicycling. In the first study we determined that placement of an accelerometer at the shank provides excellent reliability (ICC ≥0.99) and validity (Pearson correlation ≥0.99) of step and pedal revolution count. These findings support previous work that accelerometer placement at the shank during walking and stair climbing was deemed to be more reliable than ankle and thigh placement (Lützner, Voigt, Roeder, Kirschner, & Lützner, 2014); and demonstrated for the first time that shank placement yielded reliable data during bicycling.

The primary goal of this thesis was the comparison of in vivo knee AC response to running and bicycling. The results of the first study within this thesis enabled for standardization of cumulative load between the two activities. This knowledge was used to 1) determine each participant's mean step-frequency while running at their self-selected pace at the first visit, and 2) to measure loading repetition (steps) during the MRI running protocol (Maly, Robbins, Stratford, Birmingham, & Callaghan, 2013).

The investigation into the acute response of knee AC T2 to activity found significant changes after running in only the tibia (medial, and lateral tibia), but no changes after bicycling. The changes observed after running (5.6-6.1%) were similar to what has been

previously reported (3-9%) (Subburaj et al., 2012). An insignificant change in the medial tibia induced by bicycling (3.5%) was lower than previously reported changes after running. The comparison of bicycling to running using equivalent loads would not have been possible without the methods developed in the first study.

## Outcome Measurement

The results of any research study are only as good as the methods used to collect and analyze the data. In this thesis, we formally tested the reliability and validity of the GT3X+ accelerometer to provide confidence in measurements of loading repetition necessary for our investigation into the acute response of knee AC to bicycling and running. During the preparation and analysis of the second study, informal testing, and refinement of other measurement techniques were necessary. We created a means of measuring force data during bicycling, and of measuring the outcome of interest, mean T2 relaxation time.

### Bicycling Forces

Force measurement during bicycling has been achieved by a number of groups (Candotti et al., 2007; M. L. Hull & Davis, 1981; M. L. Hull & Jorge, 1985; T. B. M. Hull & Wootten, 1996; Leirdal & Ettema, 2011). In planning for this thesis, we searched the literature for possible designs and methods of creating a load-measuring pedal. Through this search we sourced a manufacturer of load cells, Novatech (UK), which had previously produced a bicycle pedal capable of measuring force. The previous pedal

utilized a clip-in system. We collaborated with them to change the design creating a system that did not rely on clip-ins but instead could be outfitted with clip-ins in the future. The pedal is capable of measuring force in two directions, the vertical (Y) and anterior/posterior (X) directions (Wu & Cavanagh, 1995). The pedal was outfitted with two amplifiers, one for each channel (each force direction). The amplifiers increased the signals that were being produced by the pedal. The amplified signals were then inputted into an analog to digital converter to allow the signal to be read, displayed, and recorded on a desktop computer. An electromagnetic switch was also setup on the right side of the bicycle. The electromagnetic switch was used to signal the start and end of a pedal revolution and the resulting signal was also inputted into the analog to digital converter to be synchronized with force measurements.

After the pedal was setup, we manually calibrated the pedal using known weights. We first loaded the Y (vertical or superior-inferior) direction with increasing mass, noting the voltage outputted by the pedal for each known mass. Similarly, we noted the voltage output for each mass as we unloaded the pedal, to explore hysteresis. These measurements were plotted and a regression run to determine the intercept (1.08 N), slope (320.41 N/V) and fit (>0.99) of the line (**Figure 4-2**) (M. L. Hull & Davis, 1981; T. B. M. Hull & Wootten, 1996). To calibrate forces in the X (anterior-posterior) direction, a rig was created (**Figure 4-4**). The X direction was tested in both the positive and negative direction, and again a regression was run to determine the intercept (0.41 N), slope (102.40 N/V), and fit (>0.99) of the line (**Figure 4-3**). These methods were necessary to

facilitate the valid measurement of force during bicycling in two directions. An example of forces, in the Y direction, measured during bicycling is provided, **Figure 4-5**. For comparison, an example of running force data is also provided, **Figure 4-6**.

**Mean T2 Relaxation**

To tackle the second obstacle, determining T2, we had to 1) segment cartilage into regions of interest and 2) generate T2 maps. Cartilage segmentation was achieved through collaboration with QMetrics, a world leader in highly-automated cartilage segmentation. Collaboration with QMetrics allowed for rapid, reliable, and valid segmentation of cartilage (Tamez-Pena et al., 2012) (**Figure 4-7**). Cartilage segmentation was used to determine morphometric characteristics of each participant including volume, and thickness. More importantly it was used in the calculation of mean T2 relaxation time for each region of interest.

In order to calculate T2 maps, a number of avenues were available and were tested. Commercially available software associated with the MRI scanner could produce T2 maps. In addition, there are also various other programs (ImageJ, Osirix, and independent programs) available that produce T2maps. All of these available options were somewhat of a "blackbox" as we were not entirely privy to how T2 was calculated. These programs also lacked additional information that we desired, including proton density and coefficient of determination ($R^2$) maps. To navigate around these obstacles, we wrote a custom program (Matlab). With the extensive aid of Dr. Michael Noseworthy,

a program was written to calculate T2, PD, and Rsq using the equation S(TE)=PD exp(-TE/T2) fitted to each pixel of collected MR data, using a Levenberg-Marquardt fitting algorithm, as previously reported (Li et al., 2007; Matzat, McWalter, Kogan, Chen, & Gold, 2014; Souza et al., 2013; Subburaj et al., 2012) . This approach took extensive compute time, though it ensured all variables of interest were calculated. One significant advantage was that we were entirely certain as to how T2 data were obtained. Once the cartilage was segmented and T2 maps generated, it was necessary to develop a workflow, to ensure all participants were analyzed in the same manner. An overview of the imaging analysis workflow is attached in **Figure 4-9**.

## New Insights

### Cumulative Load

The results of our first study allow for accurate measurement of loading repetition and therefore better estimation of cumulative load. Using these methods, we were the first to standardize cumulative loads between different activities to enable reasonable comparisons of the acute responses of AC. When participants self-selected a moderate running speed and moderate power output during bicycling, the duration of bicycling was 3 times that of running. The only previous research to compare running and bicycling had participants run 200m (1min 12seconds; assuming a running speed of 10km/hr equivalent to the mean of the current study) and bicycling for 10 minutes (Eckstein, 2005). To elicit equal loads between running and bicycling, the current study suggests that the study by Eckstein and colleagues should have increased running distance by 3 times, to 600m, to

induce a running duration ~ 1/3 that of the bicycling activity (3min 20seconds). While other research has compared different types of loading, the comparability of these loads is questionable, as no standardization of loading was performed (Eckstein, Lemberger, Stammberger, Englmeier, & Reiser, 2000).

**Cartilage, Activity, and Health.**

Decreases in joint function are directly related to a reduction in AC (Buckwalter, Mankin, & Grodzinsky, 2005). Further, physical activity is beneficial for overall health, particularly in individuals with degenerative changes in the knee joint (Fransen et al., 2015; Messier et al., 2013). Thus, it is particularly important that we identify safe activities, and activity levels that minimize the risk of AC damage. For example, while physical activity protected against cartilage loss in healthy adults with greater cartilage volume at baseline, exposure to repetitious physical activity (i.e., walking >10,000 steps/day) increased cartilage loss over 2.7 years in those with low cartilage volume at baseline ($p=0.046$) (Dore et al., 2013).

To directly address the need to identify physical activities that produce a minimal risk to knee AC, the current study adds valuable insight into the acute effect of running and bicycling on knee AC composition and morphology. Contrary to our hypothesis, bicycling did not cause a significant change in cartilage T2 and caused minimal changes in cartilage morphometry. Meanwhile, running did cause changes in T2 and extensive changes in cartilage morphometry. These results support previous studies which suggest

bicycling as a suitable activity for individuals with knee OA and joint pathology (Kutzner et al., 2012). This finding is important, as bicycling may be used to combat obesity and numerous comorbidities including cardiovascular disease, cancer, respiratory disease, and gastrointestinal disease that are often associated with decreased activity, among those at risk for, or with established knee OA (Garver et al., 2014; Nuesch et al., 2011).

## Limitations

This investigation was not without limitations. First, although we were the first to standardize cumulative load when comparing two activities using MRI, our methods could be improved. We measured cumulative load at the foot and were primarily interested in loading at the knee. In future work, estimates of knee loads could be derived using inverse dynamics from lower limb kinematics and kinetics. The measurement of forces localized to the joint of interest will minimize the effect of differences between participants in terms of joint kinematics that may affect joint and therefore cartilage loading. Not only will joint measurement reduce differences between participants, but it will also account for differences in how external kinetics are transferred to the joint of interest between activities, again caused by differences in kinematics.

The remainder of our limitations lie primarily around the acquisition and analysis of MR images. First, we had to devise a plan to allow for imaging participants immediately pre and post exercise. The major challenges associated with this acquisition were MRI time, MRI cost, and scheduling. To measure the change in knee AC, a set of scans are required

before and after the activity. This requires booking MRI time for the pre and post scans as well as for the time in-between, while the participant is exercising. To minimizing the overall cost in this study, participants were scanned in tandem so that when one participant was exercising the next participant was undergoing their pre-exercise scans. Tandem scanning did decrease the overall cost. Though, it required relatively complex scheduling to ensure participants were booked in pairs. Scheduling conflicts made it impractical to truly randomize participants to which activity they performed first, running or bicycling. It is therefore possible that some bias has been introduced therefore affecting the comparison between running and bicycling.

As for the images themselves, to obtain T2 values it was necessary that we use an imaging pulse sequence from which the calculation of T2 is possible. There are numerous options available that can be used to calculate T2, including but not limited to multi-echo spin-echo (MESE), fast spin echo (FSE), and magnetization-prepared spoiled gradient echo images. Although, a recent methodological study by Matzat and colleagues found differences in T2 calculated using these different pulse sequences (Matzat et al., 2014). We used a widely available FSE pulse sequence (GE Cartigram, USA) that was deemed to have amongst the best fits as compared to the reference standard (Matzat et al., 2014). There is limited ability to compare T2 values obtained via this sequence and others. Furthermore, investigations into the effect of different processing methods (Raya et al., 2009), and the use of different MRI scanners (Balamoody et al., 2013) found differences in the measurement of T2. These studies highlight the potential variability in T2

measurement between different research groups. It is therefore ill-advised that absolute T2 values are directly compared between studies. Nonetheless, it provides some confidence that our study did show a similar percent decrease (5-10%) to previous studies (3-9%) (Subburaj et al., 2012), indicating that relative change values from various studies could be comparable.

Lastly, the second study of this thesis is limited as we only determined T2 for each region of interest and did not provide a depth-wise evaluation of T2. Many studies have found a depth dependent response of knee AC to running (Cha et al., 2012; Timothy J. Mosher et al., 2005; T.J. Mosher, Liu, & Torok, 2010; Subburaj et al., 2012). It is possible that upon evaluation by depth that new findings and differences between bicycling and running will emerge. Future work will include the development of methods necessary to determine depth-wise T2. However, results from depth-wise analysis should be treated with caution. T2 maps commonly have pixel resolution in the range of 0.3-0.5mm (Cha et al., 2012; T.J. Mosher et al., 2010; Subburaj et al., 2012) while cartilage from the present study was in the range of 2mm thick. Therefore, T2 maps likely contain, on average, between 4 and 6 pixels across. Depth-wise segmentation reported in the literature that divides cartilage into halves (Subburaj et al., 2012), thirds (T.J. Mosher et al., 2010), or makes continuous comparisons (Cha et al., 2012; Timothy J. Mosher et al., 2005) should be interpreted in light of this knowledge.

## Future Directions

This work has provided novel information about the impact of two common aerobic activities, bicycling and running, on knee articular cartilage deformation and composition. These results indicate that bicycling may hold much promise as an aerobic activity that is of particular benefit for individuals with signs or symptoms of knee joint degeneration. However, before physical activity recommendations can be made to people with degenerative changes in knee articular cartilage, more work is necessary. First, work is needed at determining the optimal bicycle setup and optimal work rate (power output, and cadence) for individuals at risk of or with knee OA. This is highlighted by the fact that differences in bicycle setup can increase knee shear forces by upwards up 26% (Bini, Hume, Lanferdini, & Vaz, 2013). To address this gap, future research should start with motion analysis to systematically test a variety of bicycle setups, power outputs, and cadences and their effect on forces acting at the knee. On a separate but related path, we must continue to develop our understanding of the in vivo response of cartilage to activity. In particular, a direct comparison of the response of healthy and OA cartilage to common aerobic activities, bicycling in particular, are needed.

After testing and development of optimal bicycle setup and of the acute response of OA cartilage to bicycling a long-term analysis of the effect of bicycling in individuals with knee OA is needed. An intervention study should be run that gradually increases intensity and/or duration of bicycling in individuals with knee OA. An intervention study of this

type will test the effect of a bicycling program on self-reported knee pain, mobility, biomechanics, and on knee AC health (composition and morphometry) using MRI.

# REFERENCES

Abel, M. G., Peritore, N., Shapiro, R., Mullineaux, D. R., Rodriguez, K., & Hannon, J. C. (2011). A comprehensive evaluation of motion sensor step-counting error. *Applied Physiology, Nutrition, and Metabolism*, *36*(1), 166–170. http://doi.org/10.1139/H10-095

Arden, N., & Nevitt, M. (2006). Osteoarthritis: Epidemiology. *Best Practice & Research Clinical Rheumatology*, *20*(1), 3–25. http://doi.org/10.1016/j.berh.2005.09.007

Badley, E. M., & Glazier, R. H. (2004). *Arthritis and related conditions in Ontario ICES research atlas*. Toronto, Ont.: Institute for Clinical Evaluative Sciences. Retrieved from http://site.ebrary.com/id/10170210

Balamoody, S., Williams, T. G., Wolstenholme, C., Waterton, J. C., Bowes, M., Hodgson, R., … Hutchinson, C. E. (2013). Magnetic resonance transverse relaxation time T2 of knee cartilage in osteoarthritis at 3-T: a cross-sectional multicentre, multivendor reproducibility study. *Skeletal Radiology*, *42*(4), 511–520. http://doi.org/10.1007/s00256-012-1511-5

Bellucci, G., & Seedhom, B. B. (2002). Tensile fatigue behaviour of articular cartilage. *Biorheology*, *39*(1), 193–199.

Bennell, K. L., Bowles, K.-A., Wang, Y., Cicuttini, F., Davies-Tuck, M., & Hinman, R. S. (2011). Higher dynamic medial knee load predicts greater cartilage loss over 12 months in medial knee osteoarthritis. *Annals of the Rheumatic Diseases*, *70*(10), 1770–1774. http://doi.org/10.1136/ard.2010.147082

Bini, R. R., Hume, P. A., & Crofta, J. L. (2011). Effects of saddle height on pedal force effectiveness. *Procedia Engineering*, *13*, 51–55. http://doi.org/10.1016/j.proeng.2011.05.050

Bini, R. R., Hume, P. A., Lanferdini, F. J., & Vaz, M. A. (2013). Effects of moving forward or backward on the saddle on knee joint forces during cycling. *Physical Therapy in Sport*, *14*(1), 23–27. http://doi.org/10.1016/j.ptsp.2012.02.003

Blair, S. N., & Brodney, S. (1999). Effects of physical inactivity and obesity on morbidity and mortality: current evidence and research issues. *Medicine and Science in Sports and Exercise*, *31*, S646–S662.

Bombardier, C., Hawker, G., & Mosher, D. (2011, October 27). The Impact of Arthritis in Canada: Today and Over the Next 30 Years. Arthritis Alliance of Canada.

Boocock, M., McNair, P., Cicuttini, F., Stuart, A., & Sinclair, T. (2009). The short-term effects of running on the deformation of knee articular cartilage and its relationship to biomechanical loads at the knee. *Osteoarthritis and Cartilage*, *17*(7), 883–890. http://doi.org/10.1016/j.joca.2008.12.010

Bouten, C. V., Sauren, A. A., Verduin, M., & Janssen, J. D. (1997). Effects of placement and orientation of body-fixed accelerometers on the assessment of energy expenditure during walking. *Medical and Biological Engineering and Computing*, *35*(1), 50–56.

Boyd, T. F., Neptune, R. R., & Hull, M. L. (1997). Pedal and knee loads using a multi-degree-of-freedom pedal platform in cycling. *Journal of Biomechanics*, *30*(5), 505–511.

Buckwalter, J. A., Mankin, H. J., & Grodzinsky, A. J. (2005). Articular cartilage and osteoarthritis. *Instructional Course Lectures*, *54*, 465–480.

Bus, S. A. (2003). Ground Reaction Forces and Kinematics in Distance Running in Older-Aged Men: *Medicine & Science in Sports & Exercise*, *35*(7), 1167–1175. http://doi.org/10.1249/01.MSS.0000074441.55707.D1

Candotti, C. T., Ribeiro, J., Soares, D. P., De Oliveira, áLvaro R., Loss, J. F., & GuimarãEs, A. C. S. (2007). Effective force and economy of triathletes and cyclists. *Sports Biomechanics*, *6*(1), 31–43. http://doi.org/10.1080/14763140601058490

Cha, J. G., Lee, J. C., Kim, H. J., Han, J. K., Lee, E. H., Kim, Y. D., & Jeon, C. H. (2012). Comparison of MRI T2 Relaxation Changes of Knee Articular Cartilage before and after Running between Young and Old Amateur Athletes. *Korean Journal of Radiology*, *13*(5), 594. http://doi.org/10.3348/kjr.2012.13.5.594

Choi, J.-A., & Gold, G. E. (2011). MR Imaging of Articular Cartilage Physiology. *Magnetic Resonance Imaging Clinics of North America*, *19*(2), 249–282. http://doi.org/10.1016/j.mric.2011.02.010

Clarke, T. E., Frederick, E. C., & Cooper, L. B. (1983). Effects of shoe cushioning upon ground reaction forces in running. *International Journal of Sports Medicine*, *4*(4), 247–251. http://doi.org/10.1055/s-2008-1026043

Cohen, N. P., Foster, R. J., & Mow, V. C. (1998). Composition and dynamics of articular cartilage: structure, function, and maintaining healthy state. *Journal of Orthopaedic & Sports Physical Therapy*, *28*(4), 203–215.

Cotofana, S., Eckstein, F., Wirth, W., Souza, R. B., Li, X., Wyman, B., … Majumdar, S. (2011). In vivo measures of cartilage deformation: patterns in healthy and osteoarthritic female knees using 3T MR imaging. *European Radiology*, *21*(6), 1127–1135. http://doi.org/10.1007/s00330-011-2057-y

Creamer, P., & Hochberg, M. C. (1997). Osteoarthritis. *Lancet*, *350*(9076), 503–508. http://doi.org/10.1016/S0140-6736(97)07226-7

de Groot, S., & Nieuwenhuizen, M. G. (2013). Validity and reliability of measuring activities, movement intensity and energy expenditure with the DynaPort MoveMonitor. *Medical Engineering & Physics*, *35*(10), 1499–1505. http://doi.org/10.1016/j.medengphy.2013.04.004

De Wit, B., De Clercq, D., & Aerts, P. (2000). Biomechanical analysis of the stance phase during barefoot and shod running. *Journal of Biomechanics*, *33*(3), 269–278.

Dore, D. A., Winzenberg, T. M., Ding, C., Otahal, P., Pelletier, J.-P., Martel-Pelletier, J., … Jones, G. (2013). The association between objectively measured physical activity and knee structural change using MRI. *Annals of the Rheumatic Diseases*, *72*(7), 1170–1175. http://doi.org/10.1136/annrheumdis-2012-201691

Eckstein, F. (2005). In vivo cartilage deformation after different types of activity and its dependence on physical training status. *Annals of the Rheumatic Diseases*, *64*(2), 291–295. http://doi.org/10.1136/ard.2004.022400

Eckstein, F., Lemberger, B., Stammberger, T., Englmeier, K. H., & Reiser, M. (2000). Patellar cartilage deformation in vivo after static versus dynamic loading. *Journal of Biomechanics*, *33*(7), 819–825.

Eckstein, F., Tieschky, M., Faber, S., Englmeier, K.-H., & Reiser, M. (1999). Functional analysis of articular cartilage deformation, recovery, and fluid flow following dynamic exercise in vivo. *Anatomy and Embryology*, *200*(4), 419–424.

Ericson, M. O., & Nisell, R. (1987). Patellofemoral joint forces during ergometric cycling. *Physical Therapy*, *67*(9), 1365–1369.

Feito, Y., Bassett, D. R., & Thompson, D. L. (2012). Evaluation of activity monitors in controlled and free-living environments: *Medicine & Science in Sports & Exercise*, *44*(4), 733–741. http://doi.org/10.1249/MSS.0b013e3182351913

Felson, D. T. (2006). Osteoarthritis of the knee. *New England Journal of Medicine*, *354*(8), 841–848.

Felson, D. T., Lawrence, R. C., Dieppe, P. A., Hirsch, R., Helmick, C. G., Jordan, J. M., … Zhang, Y. (2000). Osteoarthritis: new insights. Part 1: the disease and its risk factors. *Annals of Internal Medicine*, *133*(8), 635–646.

Fransen, M., McConnell, S., Harmer, A. R., Van der Esch, M., Simic, M., & Bennell, K. L. (2015). Exercise for osteoarthritis of the knee. In The Cochrane Collaboration (Ed.), *Cochrane Database of Systematic Reviews*. Chichester, UK: John Wiley & Sons, Ltd. Retrieved from http://doi.wiley.com/10.1002/14651858.CD004376.pub3

Garver, M. J., Focht, B. C., Dials, J., Rose, M., Lucas, A. R., Devor, S. T., … Rejeski, W. J. (2014). Weight Status and Differences in Mobility Performance, Pain Symptoms, and Physical Activity in Older, Knee Osteoarthritis Patients. *Arthritis*, *2014*, 1–7. http://doi.org/10.1155/2014/375909

Goldring, M. B., & Goldring, S. R. (2010). Articular cartilage and subchondral bone in the pathogenesis of osteoarthritis: Articular cartilage and subchondral bone. *Annals of the New York Academy of Sciences*, *1192*(1), 230–237. http://doi.org/10.1111/j.1749-6632.2009.05240.x

Guccione, A. A., Felson, D. T., Anderson, J. J., Anthony, J. M., Zhang, Y., Wilson, P. W., … Kannel, W. B. (1994). The effects of specific medical conditions on the functional limitations of elders in the Framingham Study. *American Journal of Public Health*, *84*(3), 351–358.

Hanley, B., & Mohan, A. K. (2014). Changes in Gait During Constant Pace Treadmill Running. *The Journal of Strength & Conditioning Research*, *28*(5), 1219–1225.

Herman Hansen, B., Børtnes, I., Hildebrand, M., Holme, I., Kolle, E., & Anderssen, S. A. (2014). Validity of the ActiGraph GT1M during walking and cycling. *Journal of Sports Sciences*, *32*(6), 510–516. http://doi.org/10.1080/02640414.2013.844347

Hinterwimmer, S., Krammer, M., Krotz, M., Glaser, C., Baumgart, R., Reiser, M., & Eckstein, F. (2004). Cartilage atrophy in the knees of patients after seven weeks of partial load bearing. *Arthritis & Rheumatism*, *50*(8), 2516–2520. http://doi.org/10.1002/art.20378

Holla, J. F. M., Sanchez-Ramirez, D. C., van der Leeden, M., Ket, J. C. F., Roorda, L. D., Lems, W. F., … Dekker, J. (2014). The avoidance model in knee and hip osteoarthritis: a systematic review of the evidence. *Journal of Behavioral Medicine*. http://doi.org/10.1007/s10865-014-9571-8

Hull, M. L., & Davis, R. R. (1981). Measurment of pedal loading in bicycling: I. Instrumentation. *Journal of Biomechanics*, *14*(12), 843–855.

Hull, M. L., & Jorge, M. (1985). A method for biomechanical analysis of bicycle pedalling. *Journal of Biomechanics*, *18*(9), 631–644.

Hull, T. B. M., & Wootten, D. (1996). An improved accuracy six-load component pedal dynamometer for cycling. *Journal of Biomechanics*, *29*(8), 1105–1110.

Johani, A. H. Al-, Kachanathu, S. J., Hafez, A. R., Ahaideb, A. Al-, Algarni, A. D., Alroumi, A. M., & Alanezi, A. M. (2014). Comparative Study of Hamstring and Quadriceps Strengthening Treatments in the Management of Knee Osteoarthritis. *Journal of Physical Therapy Science*, *26*(6), 817.

Kelly, L. A., McMillan, D. G., Anderson, A., Fippinger, M., Fillerup, G., & Rider, J. (2013). Validity of actigraphs uniaxial and triaxial accelerometers for assessment of physical activity in adults in laboratory conditions. *BMC Medical Physics*, *13*(1), 5.

Kessler, M. A. (2005). Volume Changes in the Menisci and Articular Cartilage of Runners: An In Vivo Investigation Based on 3-D Magnetic Resonance Imaging. *American Journal of Sports Medicine*, *34*(5), 832–836. http://doi.org/10.1177/0363546505282622

Kessler, M. A., Glaser, C., Tittel, S., Reiser, M., & Imhoff, A. B. (2008). Recovery of the Menisci and Articular Cartilage of Runners After Cessation of Exercise: Additional Aspects of In Vivo Investigation Based on 3-Dimensional Magnetic

Resonance Imaging. *The American Journal of Sports Medicine*, *36*(5), 966–970. http://doi.org/10.1177/0363546507313093

Kettunen, J. A., & Kujala, U. M. (2004). Exercise therapy for people with rheumatoid arthritis and osteoarthritis. *Scandinavian Journal of Medicine and Science in Sports*, *14*(3), 138–142. http://doi.org/10.1111/j.1600-0838.2004.00396.x

Klein, G. R., Levine, B. R., Hozack, W. J., Strauss, E. J., Antonio, J. A. D', Macaulay, W., & Di Cesare, P. E. (2007). Return to Athletic Activity after Total Hip Arthroplasty. *The Journal of Arthroplasty*, *22*(2), 171–175. http://doi.org/10.1016/j.arth.2006.09.001

Korpan, S. M., Schafer, J. L., Wilson, K. C., & Webber, S. C. (2014). Effect of ActiGraph GT3X+ Position and Algorithm Choice on Step Count Accuracy in Older Adults. *Journal of Aging and Physical Activity*. http://doi.org/10.1123/japa.2014-0033

Kutzner, I., Heinlein, B., Graichen, F., Rohlmann, A., Halder, A. M., Beier, A., & Bergmann, G. (2012). Loading of the Knee Joint During Ergometer Cycling: Telemetric In Vivo Data. *Journal of Orthopaedic & Sports Physical Therapy*, *42*(12), 1032–1038. http://doi.org/10.2519/jospt.2012.4001

Lee, I.-M., & Skerrett, P. J. (2001). Physical activity and all-cause mortality: what is the dose-response relation? *Medicine and Science in Sports and Exercise*, *33*(6; SUPP), S459–S471.

Leirdal, S., & Ettema, G. (2011). Pedaling Technique and Energy Cost in Cycling: *Medicine & Science in Sports & Exercise*, *43*(4), 701–705. http://doi.org/10.1249/MSS.0b013e3181f6b7ea

Liess, C. (2002). Detection of changes in cartilage water content using MRI T2-mapping in vivo. *Osteoarthritis and Cartilage*, *10*(12), 907–913. http://doi.org/10.1053/joca.2002.0847

Li, X., Benjamin Ma, C., Link, T. M., Castillo, D.-D., Blumenkrantz, G., Lozano, J., … Majumdar, S. (2007). In vivo T1ρ and T2 mapping of articular cartilage in osteoarthritis of the knee using 3T MRI. *Osteoarthritis and Cartilage*, *15*(7), 789–797. http://doi.org/10.1016/j.joca.2007.01.011

Lützner, C., Voigt, H., Roeder, I., Kirschner, S., & Lützner, J. (2014). Placement makes a difference: Accuracy of an accelerometer in measuring step number and stair climbing. *Gait & Posture*, *39*(4), 1126–1132. http://doi.org/10.1016/j.gaitpost.2014.01.022

Lu, X. L., & Mow, V. C. (2008). Biomechanics of Articular Cartilage and Determination of Material Properties: *Medicine & Science in Sports & Exercise*, *40*(2), 193–199. http://doi.org/10.1249/mss.0b013e31815cb1fc

Maly, M. R., Robbins, S. M., Stratford, P. W., Birmingham, T. B., & Callaghan, J. P. (2013). Cumulative knee adductor load distinguishes between healthy and osteoarthritic knees–A proof of principle study. *Gait & Posture*, *37*(3), 397–401. http://doi.org/10.1016/j.gaitpost.2012.08.013

Matzat, S. J., McWalter, E. J., Kogan, F., Chen, W., & Gold, G. E. (2014). $T_2$ Relaxation time quantitation differs between pulse sequences in articular cartilage: $T_2$ Relaxation Time Sequence Comparison. *Journal of Magnetic Resonance Imaging*, n/a–n/a. http://doi.org/10.1002/jmri.24757

Messier, S. P., Mihalko, S. L., Legault, C., Miller, G. D., Nicklas, B. J., DeVita, P., … Loeser, R. F. (2013). Effects of Intensive Diet and Exercise on Knee Joint Loads, Inflammation, and Clinical Outcomes Among Overweight and Obese Adults With Knee Osteoarthritis: The IDEA Randomized Clinical Trial. *JAMA*, *310*(12), 1263. http://doi.org/10.1001/jama.2013.277669

Miller, R. H., Edwards, W. B., Brandon, S. C. E., Morton, A. M., & Deluzio, K. J. (2013). Why Don't Most Runners Get Knee Osteoarthritis? A Case for Per-Unit-Distance Loads: *Medicine & Science in Sports & Exercise*, 1. http://doi.org/10.1249/MSS.0000000000000135

Mornieux, G., Zameziati, K., Mutter, E., Bonnefoy, R., & Belli, A. (2006). A cycle ergometer mounted on a standard force platform for three-dimensional pedal forces measurement during cycling. *Journal of Biomechanics*, *39*(7), 1296–1303. http://doi.org/10.1016/j.jbiomech.2005.03.020

Mosher, T. J., Liu, Y., & Torok, C. M. (2010). Functional cartilage MRI T2 mapping: evaluating the effect of age and training on knee cartilage response to running. *Osteoarthritis and Cartilage*, *18*(3), 358–364. http://doi.org/10.1016/j.joca.2009.11.011

Mosher, T. J., Smith, H. E., Collins, C., Liu, Y., Hancy, J., Dardzinski, B. J., & Smith, M. B. (2005). Change in Knee Cartilage T2 at MR Imaging after Running: A Feasibility Study1. *Radiology*, *234*(1), 245–249. http://doi.org/10.1148/radiol.2341040041

Mow, V. C., Holmes, M. H., & Michael Lai, W. (1984). Fluid transport and mechanical properties of articular cartilage: a review. *Journal of Biomechanics*, *17*(5), 377–394.

Munro, C. F., Miller, D. I., & Fuglevand, A. J. (1987). Ground reaction forces in running: a reexamination. *Journal of Biomechanics*, *20*(2), 147–155.

Newmiller, J., Hull, M. L., & Zajac, F. E. (1988). A mechanically decoupled two force component bicycle pedal dynamometer. *Journal of Biomechanics*, *21*(5), 375–386.

Niehoff, A., Müller, M., Brüggemann, L., Savage, T., Zaucke, F., Eckstein, F., … Brüggemann, G.-P. (2011). Deformational behaviour of knee cartilage and changes in serum cartilage oligomeric matrix protein (COMP) after running and drop landing. *Osteoarthritis and Cartilage*, *19*(8), 1003–1010. http://doi.org/10.1016/j.joca.2011.04.012

Nilsson, J., & Thorstensson, A. (1989). Ground reaction forces at different speeds of human walking and running. *Acta Physiologica Scandinavica*, *136*(2), 217–227. http://doi.org/10.1111/j.1748-1716.1989.tb08655.x

Nordin, M., & Frankel, V. H. (Eds.). (2012). *Basic biomechanics of the musculoskeletal system* (4th ed). Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins.

Norman, R., Wells, R., Neumann, P., Frank, J., Shannon, H., & Kerr, M. (1998). A comparison of peak vs cumulative physical work exposure risk factors for the

reporting of low back pain in the automotive industry. *Clinical Biomechanics*, *13*(8), 561–573. http://doi.org/10.1016/S0268-0033(98)00020-5

Nuesch, E., Dieppe, P., Reichenbach, S., Williams, S., Iff, S., & Juni, P. (2011). All cause and disease specific mortality in patients with knee or hip osteoarthritis: population based cohort study. *BMJ*, *342*(mar08 2), d1165–d1165. http://doi.org/10.1136/bmj.d1165

Raya, J. G., Dietrich, O., Horng, A., Weber, J., Reiser, M. F., & Glaser, C. (2009). $T_2$ measurement in articular cartilage: Impact of the fitting method on accuracy and precision at low SNR. *Magnetic Resonance in Medicine*, NA–NA. http://doi.org/10.1002/mrm.22178

Robbins, S. M. K., Birmingham, T. B., Jones, G. R., Callaghan, J. P., & Maly, M. R. (2009). Developing an estimate of daily cumulative loading for the knee: Examining test–retest reliability. *Gait & Posture*, *30*(4), 497–501. http://doi.org/10.1016/j.gaitpost.2009.07.118

Rowlands, A. V., Stone, M. R., & Eston, R. G. (2007). Influence of speed and step frequency during walking and running on motion sensor output. *Medicine and Science in Sports and Exercise*, *39*(4), 716–727. http://doi.org/10.1249/mss.0b013e318031126c

Ryan, C. G. (2006). The validity and reliability of a novel activity monitor as a measure of walking. *British Journal of Sports Medicine*, *40*(9), 779–784. http://doi.org/10.1136/bjsm.2006.027276

Santos-Lozano, A., Torres-Luque, G., Marín, P., Ruiz, J., Lucia, A., & Garatachea, N. (2012). Intermonitor variability of GT3X accelerometer. *International Journal of Sports Medicine*, *33*(12), 994–999. http://doi.org/10.1055/s-0032-1312580

Seedhom, B. B. (2005). Conditioning of cartilage during normal activities is an important factor in the development of osteoarthritis. *Rheumatology*, *45*(2), 146–149. http://doi.org/10.1093/rheumatology/kei197

Smith, R. L., Trindade, M. C. D., Ikenoue, T., Mohtai, M., Das, P., Carter, D. R., … Schurman, D. J. (2000). Effects of shear stress on articular chondrocyte metabolism. *Biorheology*, *37*(1), 95–107.

Souza, R. B., Baum, T., Wu, S., Feeley, B. T., Kadel, N., Li, X., … Majumdar, S. (2012). Effects of Unloading on Knee Articular Cartilage T1rho and T2 Magnetic Resonance Imaging Relaxation Times: A Case Series. *Journal of Orthopaedic & Sports Physical Therapy*, *42*(6), 511–520. http://doi.org/10.2519/jospt.2012.3975

Souza, R. B., Feeley, B. T., Zarins, Z. A., Link, T. M., Li, X., & Majumdar, S. (2013). T1rho MRI relaxation in knee OA subjects with varying sizes of cartilage lesions. *The Knee*, *20*(2), 113–119. http://doi.org/10.1016/j.knee.2012.10.018

Souza, R. B., Kumar, D., Calixto, N., Singh, J., Schooler, J., Subburaj, K., … Majumdar, S. (2014). Response of knee cartilage T1rho and T2 relaxation times to in vivo mechanical loading in individuals with and without knee osteoarthritis. *Osteoarthritis and Cartilage*. http://doi.org/10.1016/j.joca.2014.04.017

Stefanyshyn, D. J., Stergiou, P., Lun, V. M. Y., Meeuwisse, W. H., & Worobets, J. T. (2006). Knee Angular Impulse as a Predictor of Patellofemoral Pain in Runners.

*American Journal of Sports Medicine*, *34*(11), 1844–1851. http://doi.org/10.1177/0363546506288753

Subburaj, K., Kumar, D., Souza, R. B., Alizai, H., Li, X., Link, T. M., & Majumdar, S. (2012). The Acute Effect of Running on Knee Articular Cartilage and Meniscus Magnetic Resonance Relaxation Times in Young Healthy Adults. *The American Journal of Sports Medicine*, *40*(9), 2134–2141. http://doi.org/10.1177/0363546512449816

Tamborindeguy, A. C., & Rico Bini, R. (2011). Does saddle height affect patellofemoral and tibiofemoral forces during bicycling for rehabilitation? *Journal of Bodywork and Movement Therapies*, *15*(2), 186–191. http://doi.org/10.1016/j.jbmt.2009.07.009

Tamez-Pena, J. G., Farber, J., Gonzalez, P. C., Schreyer, E., Schneider, E., & Totterman, S. (2012). Unsupervised Segmentation and Quantification of Anatomical Knee Features: Data From the Osteoarthritis Initiative. *IEEE Transactions on Biomedical Engineering*, *59*(4), 1177–1186. http://doi.org/10.1109/TBME.2012.2186612

Tudor-Locke, C., Barreira, T. V., & Schuna, J. M. (2014). Comparison of step outputs for waist and wrist accelerometer attachment sites. *Medicine and Science in Sports and Exercise*. http://doi.org/10.1249/MSS.0000000000000476

Van Ginckel, A., & Witvrouw, E. (2013). Acute Cartilage Loading Responses After an In Vivo Squatting Exercise in People With Doubtful to Mild Knee Osteoarthritis: A

Case-Control Study. *Physical Therapy*, *93*(8), 1049–1060. http://doi.org/10.2522/ptj.20120491

Wallis, J. A., Webster, K. E., Levinger, P., & Taylor, N. F. (2013). What proportion of people with hip and knee osteoarthritis meet physical activity guidelines? A systematic review and meta-analysis. *Osteoarthritis and Cartilage*, *21*(11), 1648–1659. http://doi.org/10.1016/j.joca.2013.08.003

Warburton, D. E. R. (2006). Health benefits of physical activity: the evidence. *Canadian Medical Association Journal*, *174*(6), 801–809. http://doi.org/10.1503/cmaj.051351

Wellenkotter, J., Kernozek, T., Meardon, S., & Suchomel, T. (2014). The Effects of Running Cadence Manipulation on Plantar Loading in Healthy Runners. *International Journal of Sports Medicine*, *35*(09), 779–784. http://doi.org/10.1055/s-0033-1363236

Wu, G., & Cavanagh, P. R. (1995). ISB recommendations for standardization in the reporting of kinematic data. *Journal of Biomechanics*, *28*(10), 1257–1261.

FIGURES

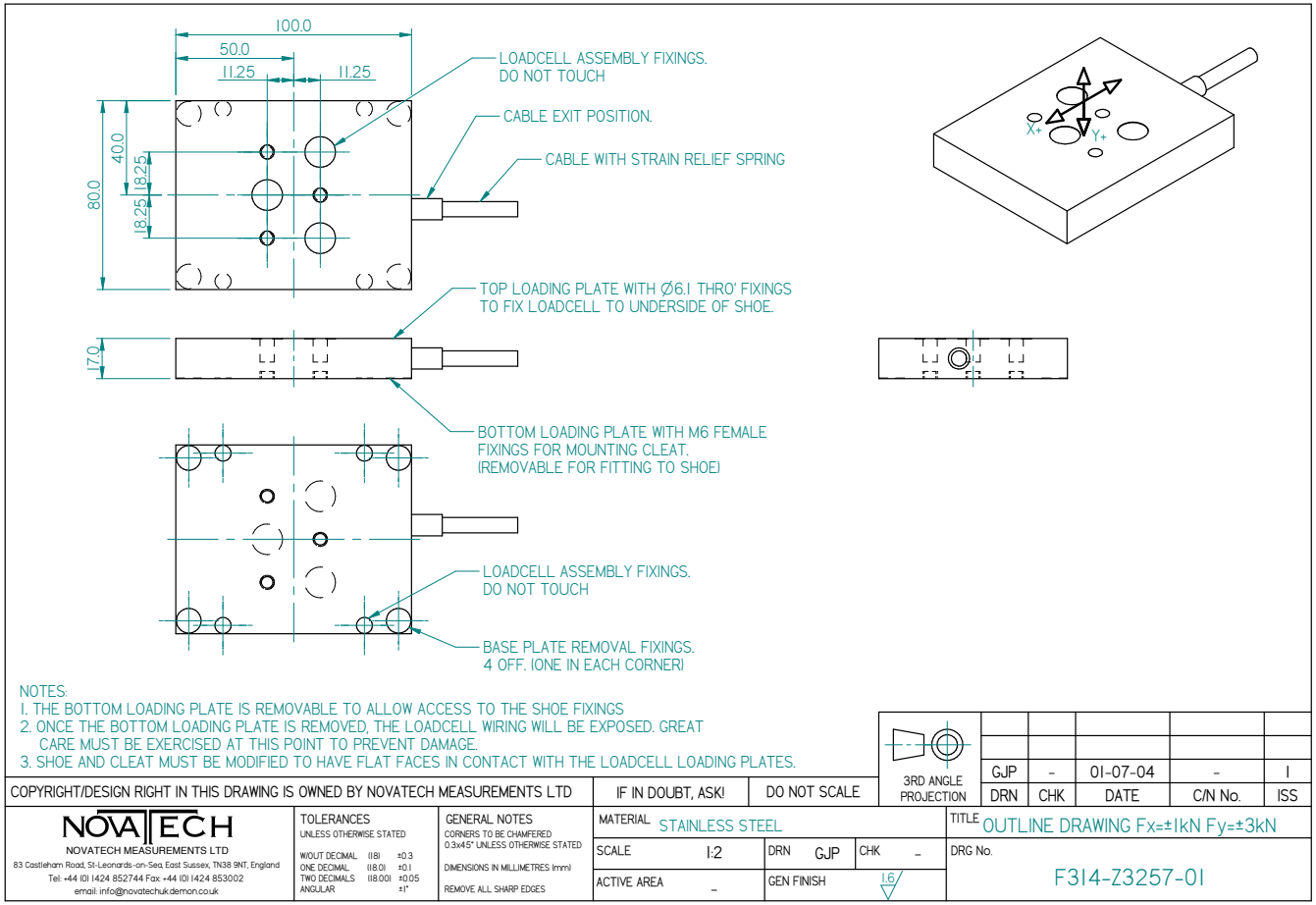


**Figure 4-1.** Design of the load cell used to measure pedal reaction forces (Fy 0-3k N; Fx 0-1k N). The load cell was attached to the right bicycle pedal. Not displayed in this drawing are the pedal and the retention cages utilized to secure the participants foot. A non-functional load cell was created and attached to the left pedal, so that both pedals were the same height.

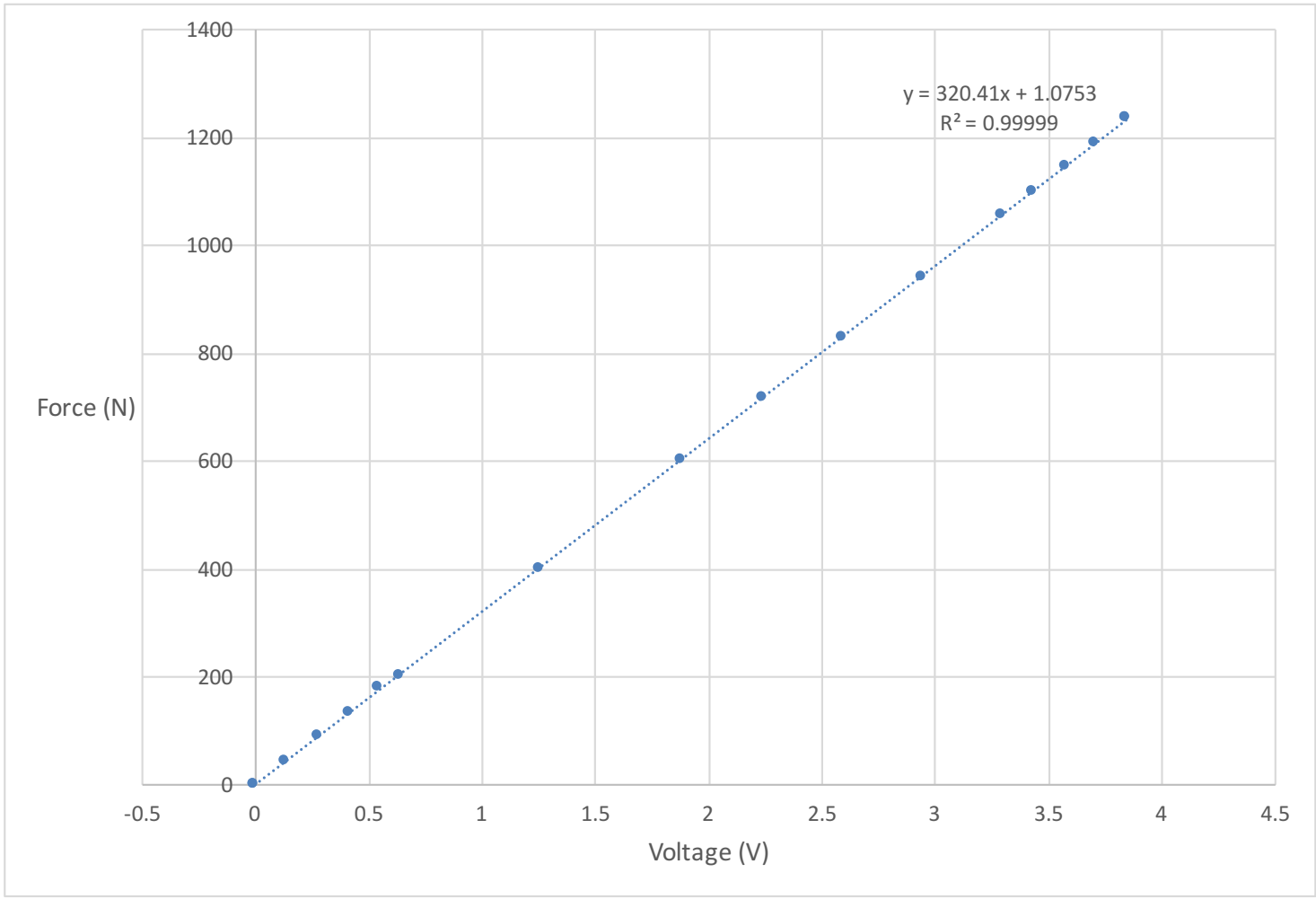


**Figure 4-2.** Calibration of forces applied in the Y direction (superior-inferior) of a load measuring bicycle pedal. Graphed is the voltage output (V) for known masses (N) and the coinciding regression line, regression line equation, and fit of the regression line ($R^2$)

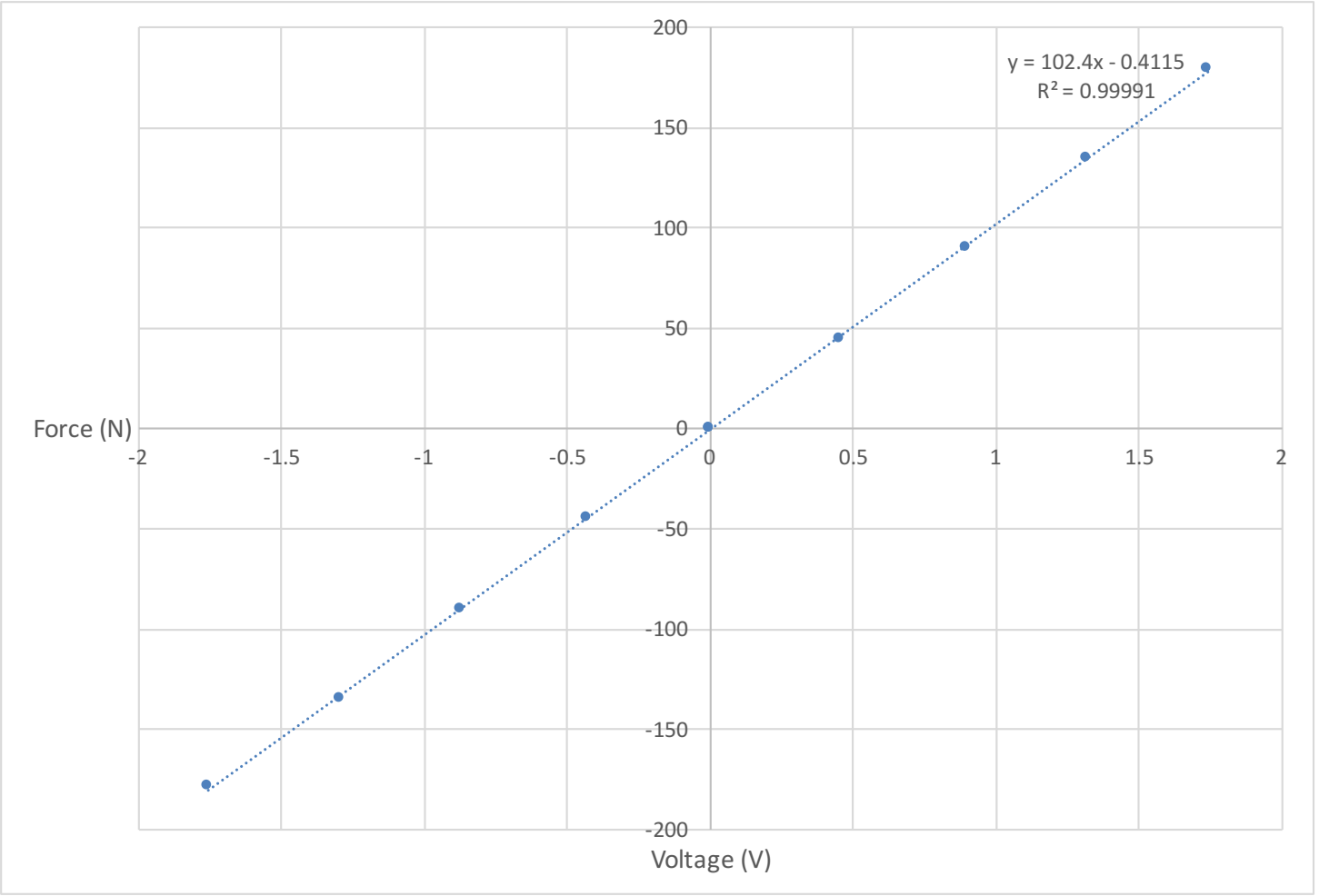


**Figure 4-3.** Calibration of forces applied in the X direction (anterior-posterior) of a load measuring bicycle pedal. Graphed is the voltage output (V) for known masses (N) and the coinciding regression line, regression line equation, and fit of the regression line ($R^2$)

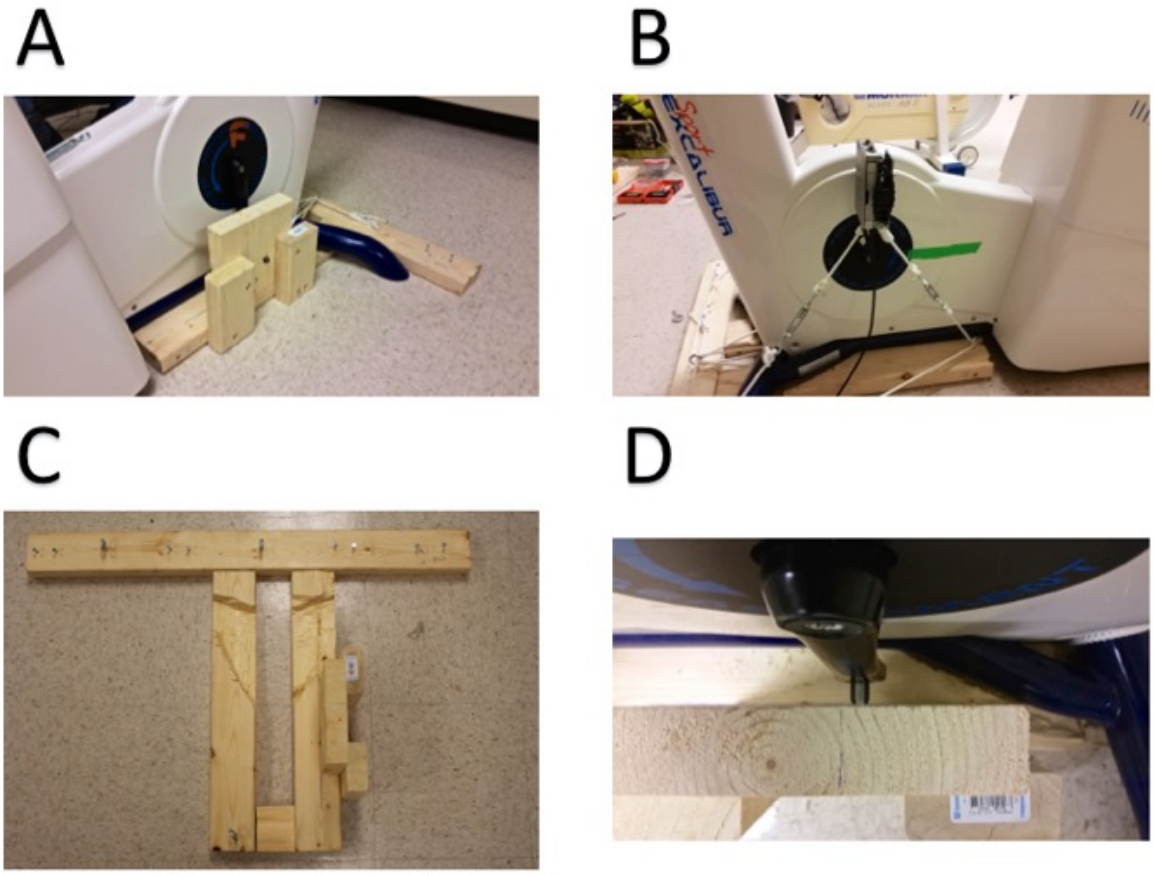


**Figure 4-4.** Displayed is the rig used to calibrate the load measuring bicycle pedal. (A) is an image of the rig attached to the cycle ergometer from the left-side; (B) is an image from the right side; (C) is the rig when not attached to the ergometer; and (D) is an image of how the left crank is attached to the rig to ensure that the crank arms do not rotate.

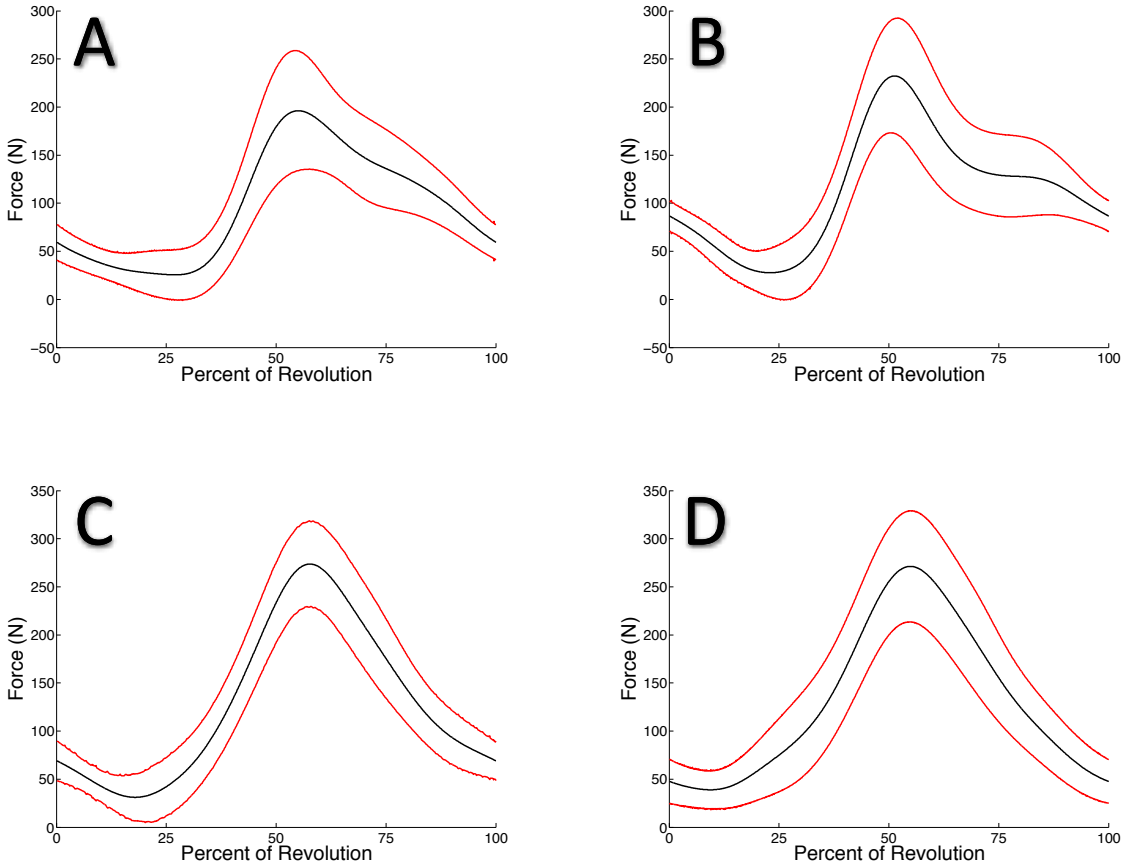


**Figure 4-5.** Examples of the mean (black) vertical pedal reaction force (vPRF) and 95% confidence interval (red) of a time normalized pedal revolution measured in Newtons for participants 1(A), 3(B), 10(C), and 12(D). Mean and 95% confidence intervals are of data collected for the entire bicycling bout at the MRI visit.

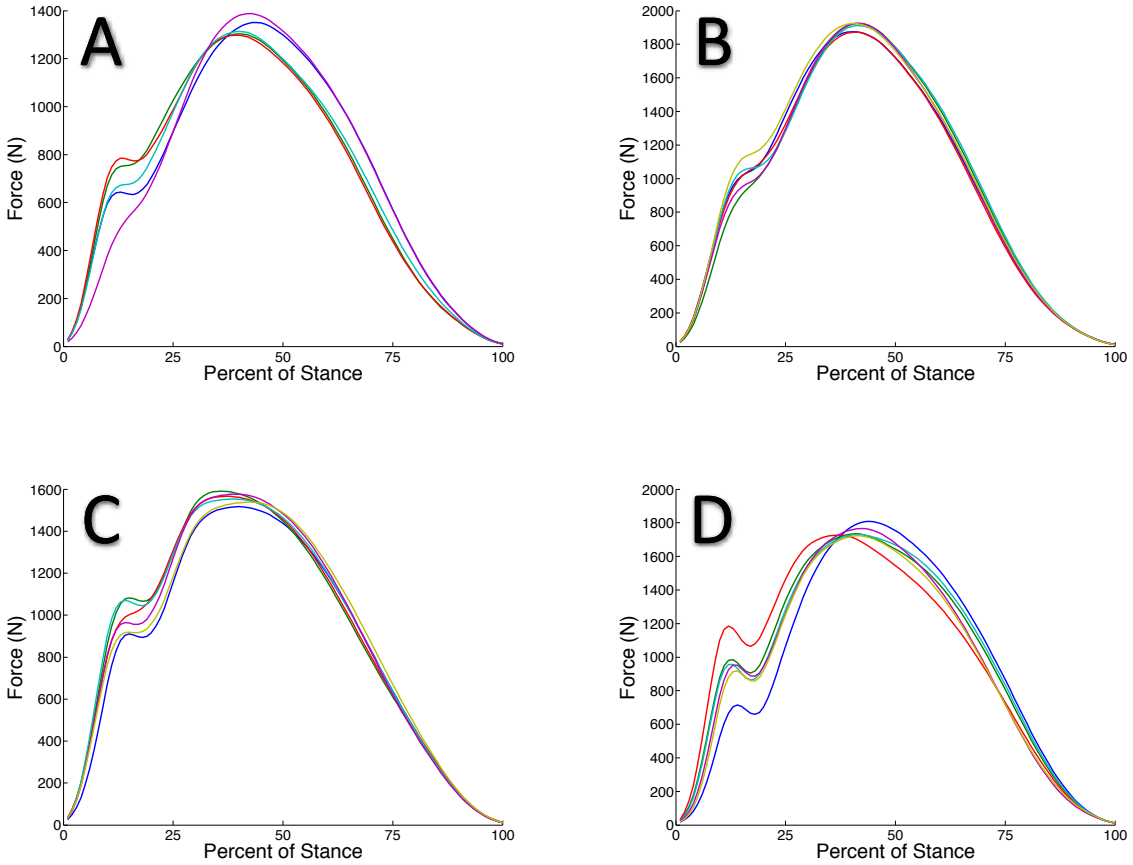


**Figure 4-6.** Examples of the time normalized vertical ground reaction force (vGRF) (N) of the successful trials for participants 1(A), 3(B), 10(C), and 12(D).

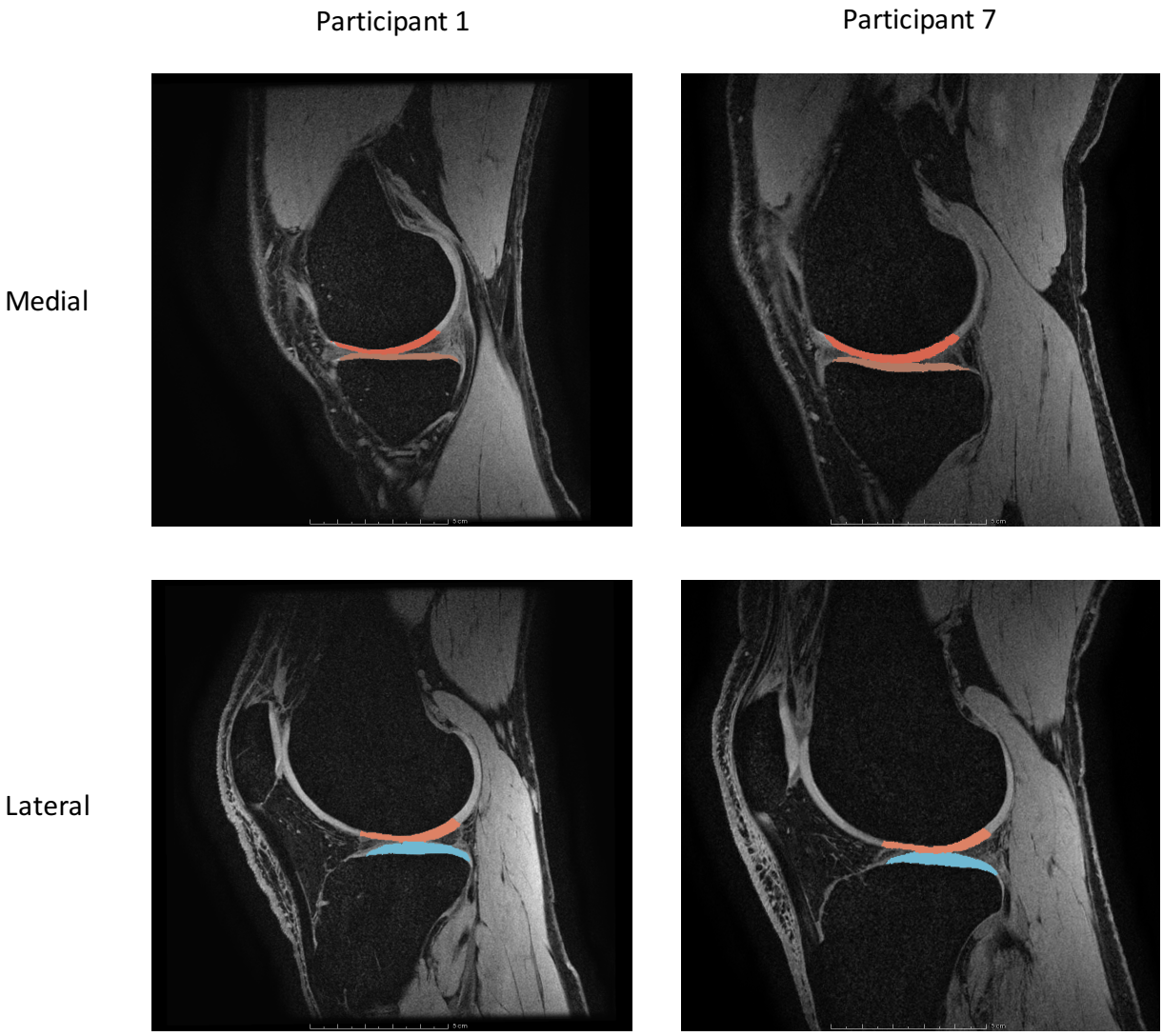


**Figure 4-7** Examples of Fast Spoiled Gradient Recalled Echo (FSPGR) images taken for segmentation purposes. Segmentations of medial (salmon) and lateral (beige) weight-bearing femoral as well as medial (beige) and lateral (blue) tibial cartilage are overlaid on the FSPGR images.

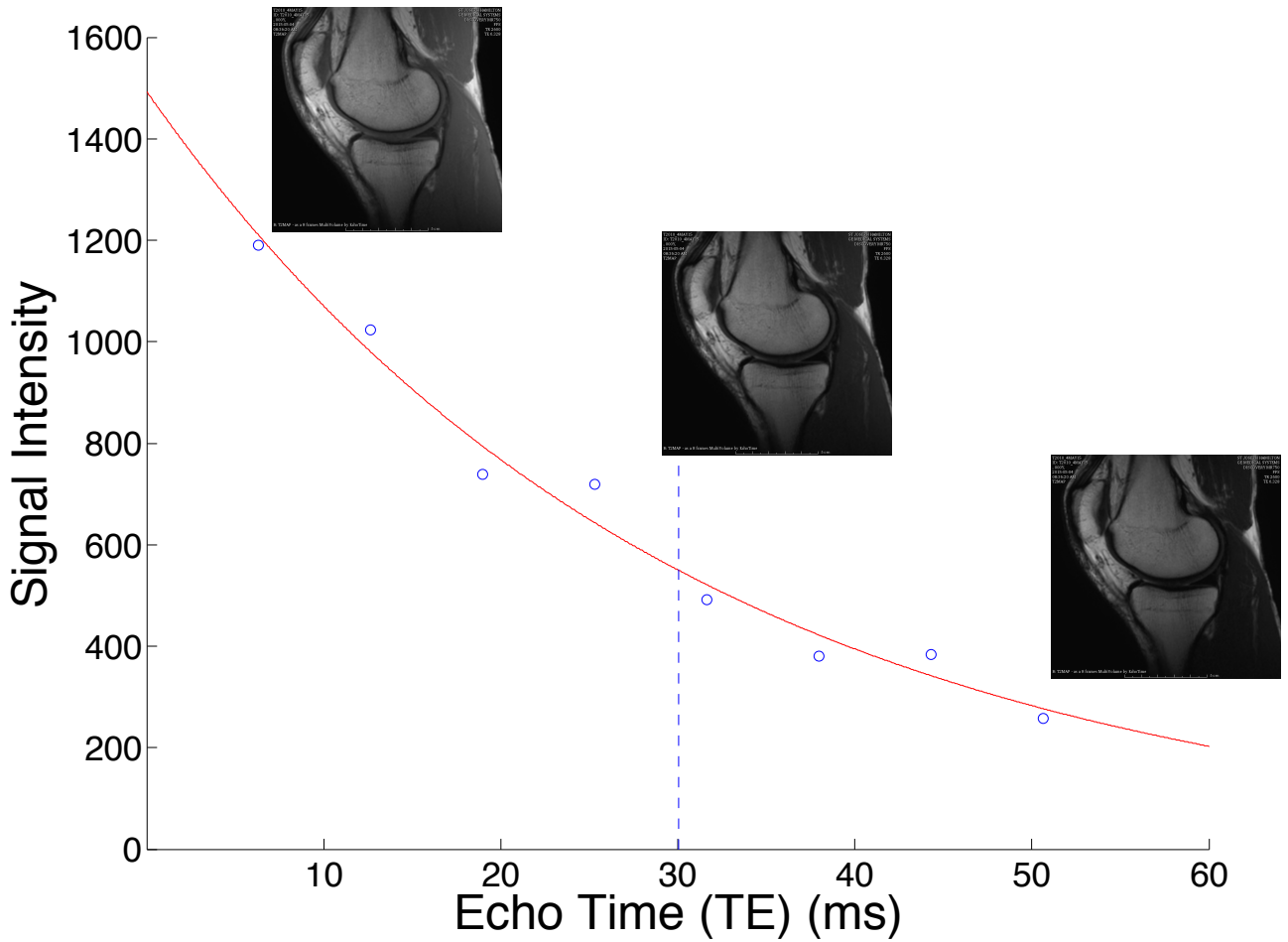


**Figure 4-8.** Displayed is the signal intensity of one pixel taken at 8 time points and the coinciding fit line S(TE)=PD exp(-TE/T2). S(TE) is the signal intensity for a given echo time (TE) and PD is the y-intercept. T2 is a parameter of the fit and coincides with the point at which the signal has decayed to 37% of maximum. The T2 of this pixel was 30.06 ms and is represented by the dashed line. Examples of images of the 1$^{st}$ (6.312ms), 5$^{th}$ (31.560ms), and 8$^{th}$ (50.496ms) echoes are given.

# Imaging Workflow

1. Process T2maps (Matlab)
    1. If T2<0 or T2>100 replace with 0
    2. If $R^{sq}$<0.7 replace with 0

2. Align T2 images to 3D FSPGR images & coinciding segmentation (Slicer)
    1. Save T2 image transformations (Slicer)

3. Apply transformation (2.1) toT2map, aligning T2map to cartilage segmentation (Slicer)

4. Edit segmentations so that if T2map=0 Segmentation Mask = 10 (unique identifying number) (Slicer). This ensures that voxels that were determined to be an error in step 1 are not used in mean T2 calculation.

5. Run Labels Statistics (Slicer), which determines Min/Max/Mean/StdDev of T2 values for each segmented region of interest.

**Figure 4-9.** Imaging analysis necessary to determine mean T2 for each region of interest; FSPGR (Fast Spoiled Gradient Recalled Echo).