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Gait Real-Time Analysis Interactive Lab: Reliability and Validity of Knee Angles and Moments in Patients with Knee Osteoarthritis

Ryan Pinto, *The University of Western Ontario*

Supervisor: Trevor Birmingham, *The University of Western Ontario*
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Abstract

Objectives: 1) Estimate test-retest reliability of knee angles and moments during gait in patients with knee osteoarthritis (OA) using the Gait Real-Time Analysis Interactive Lab (GRAIL); 2) Examine concurrent validity of knee angles and moments using the GRAIL and overground system (gold standard); and 3) Examine known-groups validity of knee angles and moments in patients with knee OA and healthy controls.

Methods: Patients and controls walked using both systems to produce knee angle and moment waveforms during stance, enabling discrete measure comparisons. Patients completed a second session within one week.

Results: Intraclass correlation coefficients ranged from 0.52-to-0.93 for test-retest reliability. Pearson correlations ranged from 0.05-to-0.96 with transverse plane peaks being weakest. Patients had significantly higher first peak knee adduction moments than controls (0.58 %BW*ht).

Conclusion: Preliminary results suggest adequate reliability and validity of knee angles and moments in patients using the GRAIL. Knee transverse plane measures should be interpreted cautiously.

Keywords

Knee osteoarthritis, Gait Analysis, Walking, Kinematics, Kinetics, Test-Retest Reliability, Concurrent Validity, Known-Groups Validity

Co-Authorship Statement

Dr. Trevor Birmingham, Ian Jones, Dr. Rebecca Moyer and Dr. Robert Giffin assisted with the study design. In addition, Ian Jones and Dr. Moyer assisted with data collection. Dr. Birmingham assisted with the thesis preparation.

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List of Abbreviations

ASIS	Anterior Superior Iliac Spine
BMI	Body Mass Index
BW	Body Weight
CI	Confidence Interval
CoR	Coefficient of Repeatability
CSV	Comma Separated Value
CT	Computed Tomography
GOAT	Gait Offline Analysis Tool
GRAIL	Gait Real-Time Analysis Interactive Lab
GRF	Ground Reaction Force
ht	Height
ICC	Intraclass Correlation Coefficient
KAM	Knee Adduction Moment
KFM	Knee Flexion Moment
KL	Kellgren-Lawrence
MAA	Mechanical Axis Angle
MAD	Mechanical Axis Deviation
MDC	Minimal Detectable Change
MDC_{95}	Minimal Detectable Change at the 95% Confidence Level
MSK	Musculoskeletal
OA	Osteoarthritis
PKAM	Peak Knee Adduction Moment

ROM	Range of Motion
SD	Standard Deviation
SEM	Standard Error of Measurement
SkB	Skeleton Builder
VR	Virtual Reality
WBL	Weight-Bearing Line

Chapter 1

1 Introduction: Background and Rationale

Knee osteoarthritis (OA) is a common chronic musculoskeletal (MSK) condition affecting over 240 million people worldwide[1]. Knee OA decreases one's mobility substantially, and is a leading cause of pain, disability and healthcare use[2]. Although improving, relatively little is known about OA disease mechanisms or interventions. Currently, there is no known cure for OA, nor are there treatments proven to alter its progression. Although effective interventions remain elusive, age, obesity, joint trauma and frontal plane malalignment of the lower limb are consistently identified as risk factors for knee OA, and likely act in part by altering dynamic loading of the knee during walking [3–9].

Walking is the most common activity of daily living[10] and is arguably highly germane to the study of knee OA. Walking is often the activity that first triggers pain in patients with knee OA, and is a major contributor to the patient's disability and limitations in participation[11–13]. Perhaps counterintuitively, walking is also often part of treatment regimens shown to improve function and reduce pain for individuals with knee OA[14–16]. Furthermore, various measures of walking are often used as outcome measures to show changes in knee OA status and/or to help judge the effectiveness of proposed treatments[17,18]. Quantitative gait analysis has therefore emerged as an important tool in knee OA research.

A typical quantitative gait analysis occurs in a large open room equipped with motion analysis cameras that track markers located on specific anatomical landmarks as the patient walks through the cameras' field of view and over floor-embedded force plates. Previous studies evaluating the measurement properties of knee joint angles and moments measured using these overground movement analysis systems generally suggest good reliability and validity in patients with knee OA[19]. Specifically, the knee adduction moment (KAM) and impulse both demonstrate excellent reliability in patients with medial compartment knee OA[20,21].

More recently, however, force plate-instrumented treadmills are increasingly being used in gait research as they allow for a larger volume of data to be collected in a shorter time span, use less space and offer a more controlled environment. A harness capable of alleviating a portion of the subject's body weight would allow them to return to weight bearing or gait-retraining earlier in the recovery period. Supplementary measurement devices, such as fluoroscopy machines, are not needed to be completely mobile when used with instrumented treadmills. Far less literature regarding the measurement properties of data collected from these newer treadmill-based movement analysis systems exist, especially in patients with OA, and the reported findings are less consistent[22–33].

The Gait Real-Time Analysis Interactive Lab (GRAIL, Motekforce Link, Amsterdam, NL) is a novel treadmill-based movement analysis system that incorporates a dual belt force plate-instrumented treadmill with optical motion capture cameras and a 180^{o} projection screen with surround sound to create virtual reality (VR) depictions of real-life settings. Although studies in children suggest good agreement between the GRAIL and conventional overground systems for limb kinematics and kinetics,[28,29,34] there is a paucity of research investigating the measurement properties of gait biomechanics data obtained with this new system. If the GRAIL is to be used in knee OA research, then further information about the reliability and validity of its measurements is required. Given the previously reported differences in knee joint angles and moments in patients with medial compartment knee OA compared to healthy controls[35–39], and the frequent use of these parameters to evaluate proposed treatments[17,18], the overall aim of this study was to evaluate the reliability and validity of knee joint angles and moments. Specific objectives are outlined below.

1.1 Objectives

Objectives of the present study were to:

1) Estimate the test-retest reliability of knee joint angles and moments during gait in patients with medial compartment knee OA when tested using the GRAIL;

2) Examine the concurrent validity of the knee joint angles and moments tested using the GRAIL and using a conventional overground movement analysis system (gold standard); and

3) Examine the known-groups validity of knee joint angles and moments, specifically the frontal plane, tested using the GRAIL in patients with knee OA and in healthy age-matched controls.

1.2 Research Hypothesis

We hypothesized that:

1) Knee angles and moments would be highly repeatable on two test occasions with an intraclass correlation coefficient (ICC) >0.85;

2) Knee angles and moments tested on the GRAIL would be highly correlated (r>0.75) to the same measures assessed using the overground system; and

3) Knee angles and moments, specifically frontal plane, would be significantly different between participants with and without knee OA.

Chapter 2

2 Review of the Literature

2.1 Osteoarthritis

Osteoarthritis is a degenerative disease resulting in the loss of articular cartilage within the joints over time. OA, the most common form of arthritis, affects approximately 37% of patients aged 20 and older in Canada diagnosed with the disease[40]. These patients experience OA as their only form of arthritis and report pain in their hip(s) (12%), knee(s) (29%) or both (29%)[40].

Osteoarthritis of the knees and hips combined are the third most prevalent MSK disorder worldwide[41], and this burden is expected to increase largely due to the rise in obesity and an aging population[42]. Individuals who have knee OA can experience stiffness, pain and decreased ROM of the joints and, over time, these symptoms can eventually lead to a loss of functional independence.

Altman and colleagues[43] identify a list of clinical and radiographic criteria for the diagnosis of OA. This list includes knee pain plus radiographic evidence of osteophytes and at least one of the following: age greater than 50 years, stiffness lasting for less than 30 minutes, or crepitus with active motion of the knee[43]. In addition, Kellgren and Lawrence[44] (KL) categorize a rating scale to categorize the severity of knee OA from radiographs based on the presence of osteophytes, joint space width and amount of subchondral sclerosis. In this rating scale, a grade is given from 0 to 4 corresponding to the severity of OA with 0 being none and 4 being severe[44]. This rating scale helps provide a better understanding of patient characteristics.

2.2 Risk Factors Related to Knee Osteoarthritis

Risk factors for OA can fall under systemic factors, local intrinsic joint factors or local extrinsic factors acting on joints with age, obesity and joint trauma being consistently recognized as major risk factors[3-9]. Systemic factors include age, gender, ethnicity, hormonal status, genetic factors, bone density, nutritional factors and inflammation. Local intrinsic factors include previous damage, muscle weakness, joint deformity/alignment and ligament laxity. Local extrinsic factors can include obesity and specific injurious activities such as sport and physical activities or occupation factors[45]. Typically the risk for developing OA presents when one component of the disease becomes abnormal and its interaction with other disease components ultimately leads to cartilage breakdown and progression to clinical OA[46]. Lower limb alignment as well as excessively high loads experienced at the knee are believed to be major contributing factors to the progression and, potentially, development of knee OA[3–8].

2.2.1 Lower Limb Alignment

Lower limb malalignment is a local risk factor that is widely studied for its influence on the development and progression of knee OA[4,8,35,47–49] and is typically measured from the hip to ankle using standing, full-length radiographs. The mechanical axis angle (MAA) is a common measure and refers to the angle formed between lines connecting the centres of the hip, knee and ankle (Figure 2.1a). Another common measure for assessing lower limb alignment is the mechanical axis deviation (MAD) which is the perpendicular distance from the centre of the knee joint to the weight bearing line (WBL). The WBL is represented with a line drawn from the mid-femoral head to mid-ankle (Figure 2.1b)[50]. Persons with neutral lower limb alignment distribute 75% of the knee joint load through the medial tibial plateau during one-legged static stance[51]. In varus alignment, the WBL passes medial to the knee, increasing the MAD which, in turn, increases the force across the medial compartment. In a valgus knee, the WBL passes lateral to the knee and the MAD increases force across the lateral compartment.

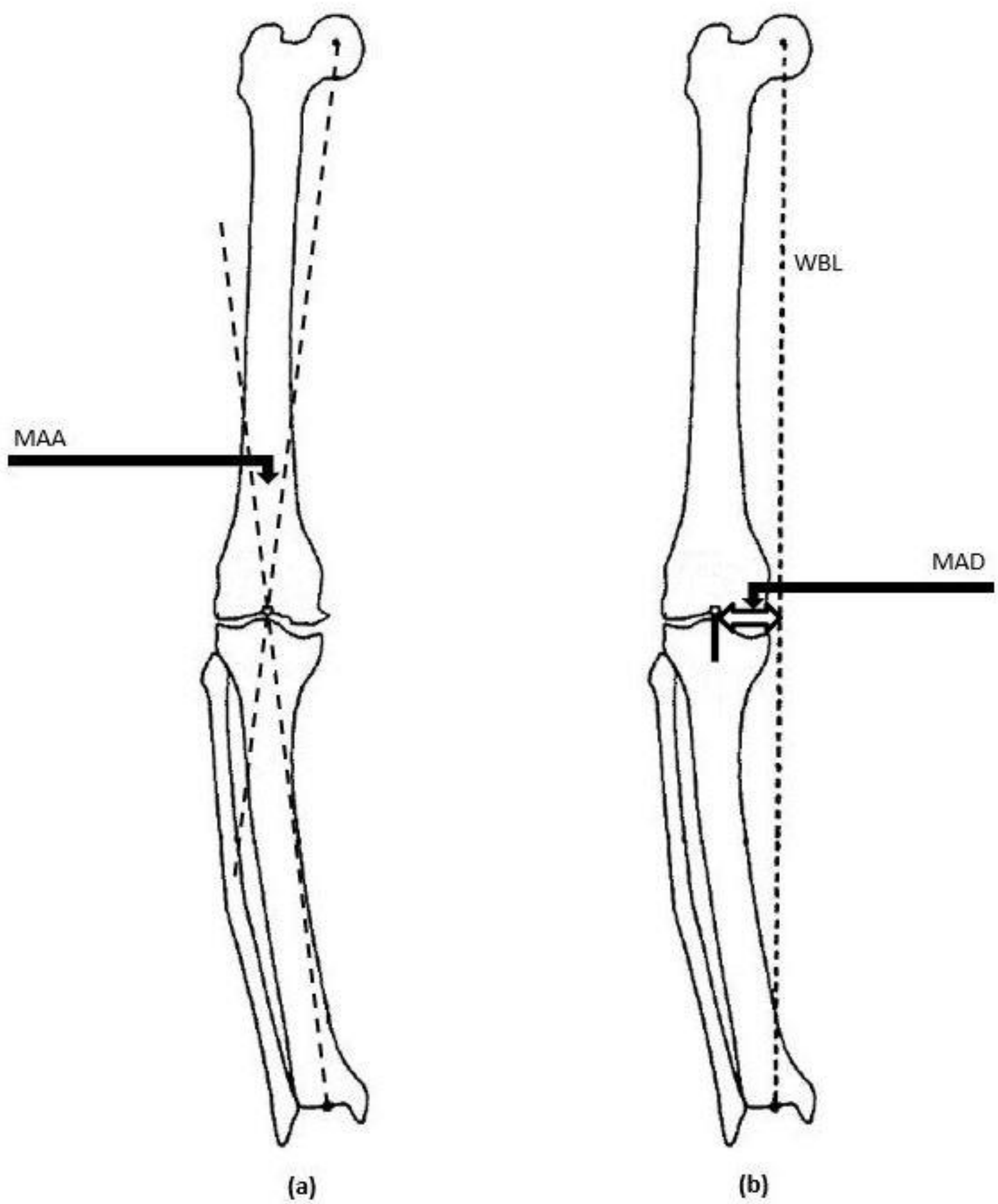


Figure 2.1. The Mechanical axis angle (MAA) of the lower limb (a). The weight bearing line (WBL) and mechanical axis deviation (MAD) of the lower limb (b). Adapted from Tetsworth and Paley, 1994

Malalignment, congenital or acquired, is thought to contribute to articular cartilage deterioration through altering the relative loading within the knee joint leading to a vicious cycle of joint damage (Figure 2.2). In a malaligned joint, the narrowed area is subjected to increased load bearing which leads to increased cartilage damage. In addition to damaged cartilage the underlying bone goes through remodeling and damage, where the cortical bone may remodel and result in increased malalignment. The increased malalignment leads to higher focal stress along the narrowed area, causing more damage and continuing the vicious cycle[8]. Varus alignment at baseline was found to be associated with a 4 fold increase in the risk of medial knee OA progression over an 18 month period[47]. This finding is consistent with the literature that cartilage damage is more prevalent in the medial compartment compared to the lateral and occurs in the presence of varus malalignment[8,35,52,53]. This type of knee OA is commonly referred to as varus gonarthrosis.

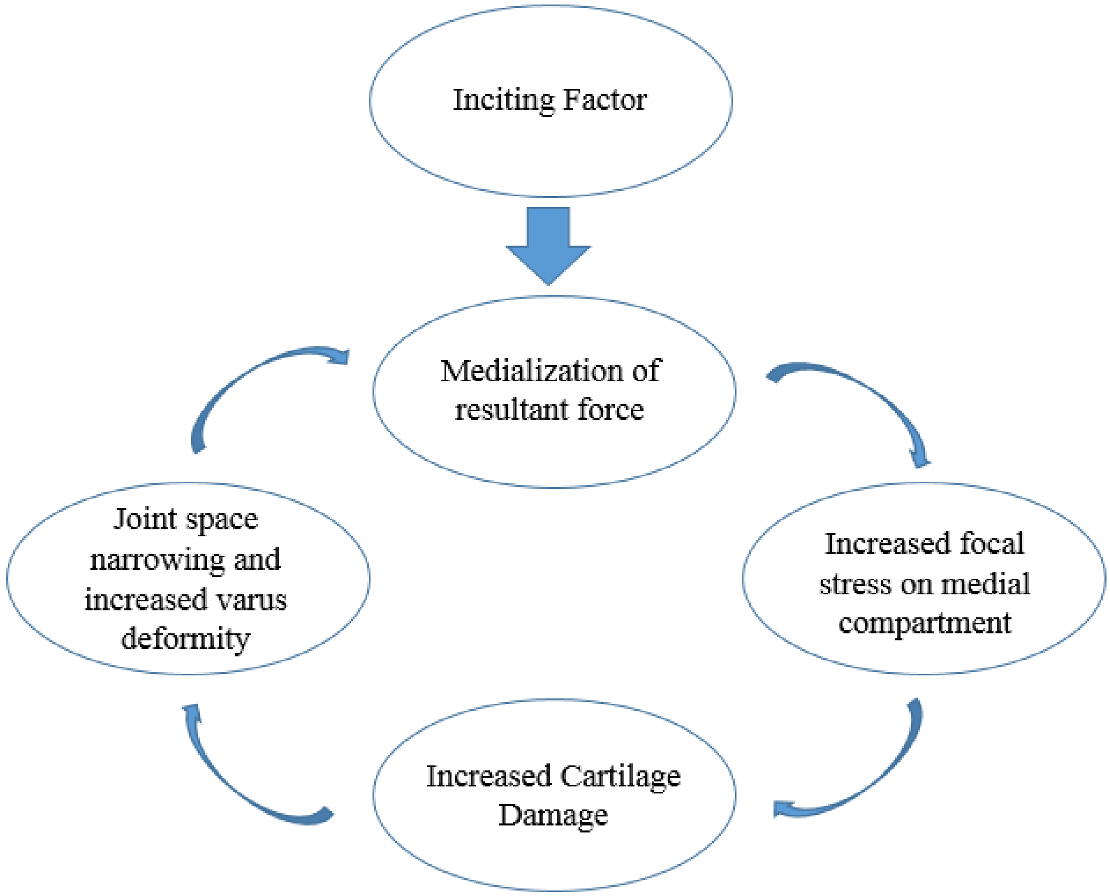


Figure 2.2. The vicious cycle of medial compartment knee osteoarthritis

2.3 Gait Analysis

Kinematics and kinetics about the joints of the lower limb during gait have proven to be important measures for patients with knee OA. Walking is the most common activity of daily living, making analysis of an individual's gait an important aspect of understanding the biomechanics of one's knee joint. Clinical gait analysis can help identify modifiable risk factors, leading to the development of appropriate interventions for these individuals with OA. A typical gait analysis consists of the collection of kinematic and kinetic data regarding joint angles/positions and forces acting on the body respectively. In a typical gait lab, subject preparation utilizes passive reflective markers corresponding to specific anatomical landmarks. From these markers, kinematic data is collected and kinetic data is collected from ground embedded force plates. By combining kinematic and force data, through inverse dynamics, we can quantify external joint loads that are acting on the body. For the purpose of this thesis, I will be focusing on the external joint loads about the knee: adduction/abduction, flexion/extension and internal/external rotation.

2.4 Phases of the Gait Cycle

There are two phases of gait: swing and stance. The stance phase accounts for approximately 65% of the gait cycle with the swing phase occupying the other 35%. The stance phase can be further broken down into 5 main components: initial contact (heel-strike), load response (foot-flat), midstance, terminal stance (heel-raise) and pre-swing (toe-off) (Figure 2.3)[54]. The swing phase can also be broken down further into initial swing (acceleration), midswing and terminal swing (deceleration). During normal gait, the knee is in full extension right before heel-strike, flexing as the heel contacts the floor with the tibia rotating internally. The knee moves from flexion towards extension during the loading response and continues towards extension during midstance and terminal stance. At the toe-off phase the knee moves from near full extension to approximately 40^{o} of flexion with the tibia in slight external rotation[55].

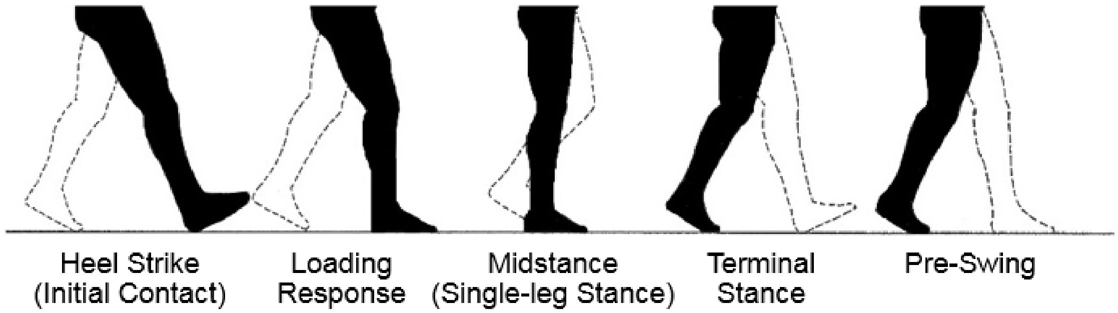


Figure 2.3. The 5 main components of the stance phase. Adapted from Magee (2002)

2.5 External Joint Loads

Knee Adduction Moment

The external KAM is the most common gait analysis outcome measure that is reported in the literature with regards to individuals with knee OA, and has been established as a reliable measure in both healthy subjects as well as patients with medial compartment knee OA[19,20]. In most individuals, the frontal plane component of the ground reaction force (GRF) vector passes medially to the knee joint centre of rotation during the stance phase. This results in a torque, or moment, about the knee. The magnitude of the KAM is dependent on inertial forces, frontal plane GRF and the lever arm, defined as the perpendicular distance between the knee joint centre and the GRF projection (Figure 2.4). This KAM will result in the tibia adducting with respect to the femur, resulting in compression of the medial compartment of the tibiofemoral joint.

Knee Flexion Moment

The knee flexion moment is characterized using the sagittal plane component of the GRF (Figure 2.5). During heel-strike, the GRF vector acts behind the knee joint and causes a flexion moment with the maximum external knee flexion moment occurring by the end of the loading response. At early midstance, the direction of the vector begins to reverse with a progressive decline in the flexion moment. During terminal stance, external reaction forces begin moving anterior to the joint towards an extension moment that gradually increases until the mid-terminal stance. At toe-off, the external reaction forces begin moving posterior to the joint as the knee begins flexing, thus creating another flexion moment[54,55].

Knee Rotation Moment

The knee rotation moment occurs in the transverse plane. The femur is in slight external rotation with respect to the tibia during initial contact. During the loading response phase of gait, the tibia rotates internally and by the end of the loading the knee joint has reached its peak internal rotation[55]. External rotation occurs as the knee extends fully during terminal stance and continues into toe off resulting in an internal rotation moment.

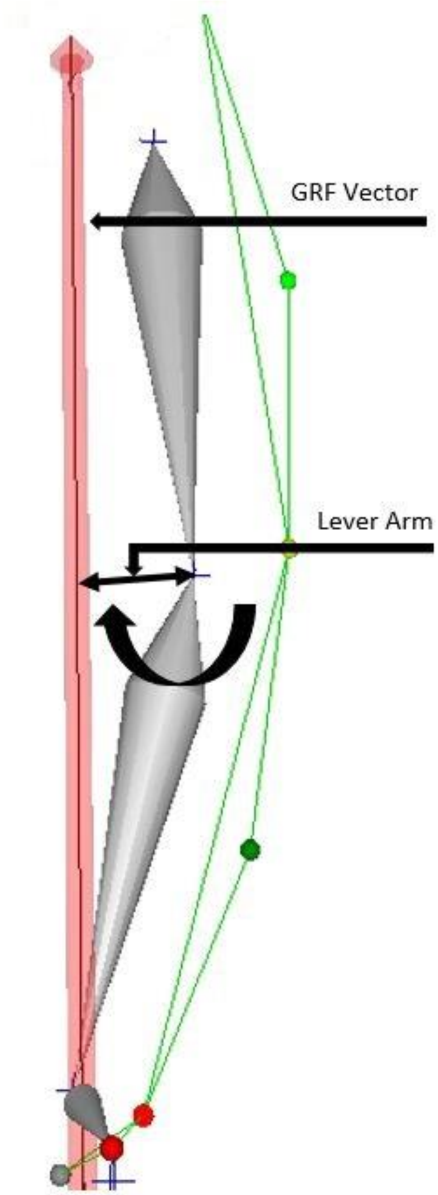


Figure 2.4. The external knee adduction moment is largely the product of the frontal plane ground reaction force (GRF) vector and frontal plane lever arm.

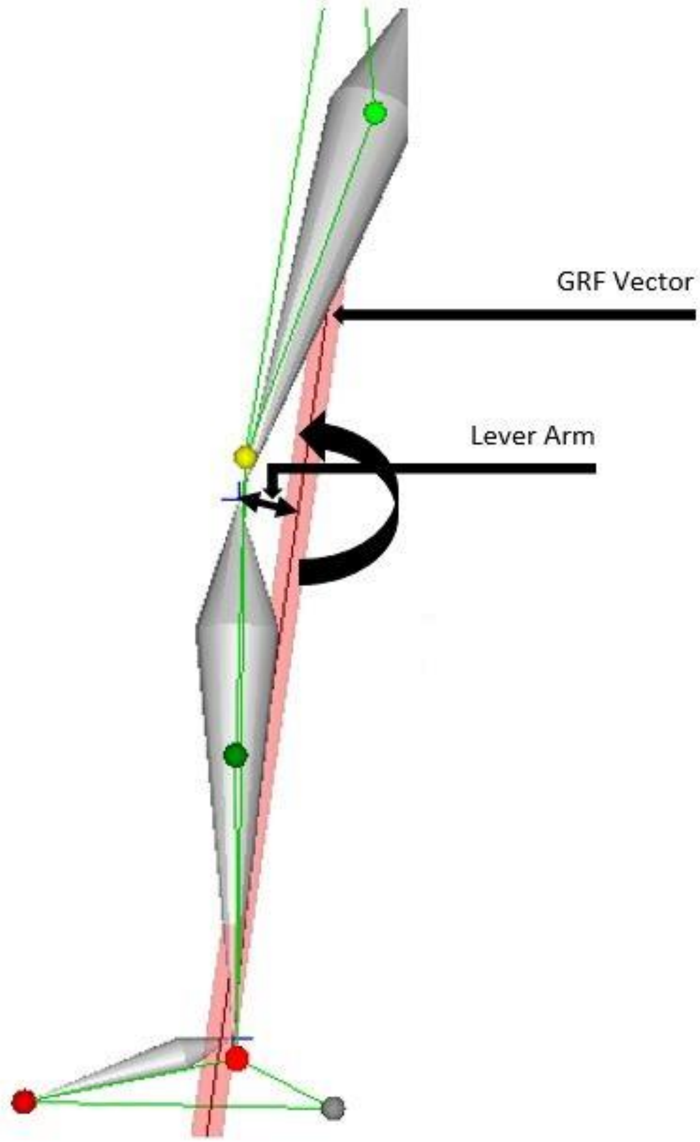


Figure 2.5. The external knee flexion moment is calculated with respect to the sagittal plane components of the ground reaction force (GRF) and lever arm.

2.6 Gait Characteristics of Patients with Medial Compartment Knee OA

Knee Adduction

Several studies suggest individuals with medial compartment knee OA exhibit higher peak magnitudes of the KAM than individuals without OA[35–39]. Static varus alignment of the lower limb contributes to OA progression because of its association with increased joint loads in the medial compartment, typically described as increased KAM during walking[56,57]. There is also evidence to suggest a relationship between the KAM magnitude and measures of disease severity, such as Kellgren and Lawrence grading[20,35,57,58].

Static alignment, measured by the mechanical axis angle, is the best lone predictor of the peak KAM in subjects with mild symptomatic knee OA[56]. A systematic review suggests that the KAM is directly related to varus alignment[57]. Higher KAMs are associated with increased varus alignment and faster OA progression[57] as well as radiographic medial compartment knee OA severity, even when taking into account age, sex and level of pain[58].

Patients with chronic knee pain typically have higher baseline peak KAMs than patients who do not develop pain[5]. In addition, patients who exhibit medial compartment knee OA disease progression have higher baseline KAMs than those without progression over a 6 year follow-up. Medial compartment joint space narrowing during a 6 year follow-up significantly correlates with patient baseline KAM[35]. The KAM significantly correlates with varus alignment and the risk for medial compartment knee OA progression increases 6.46 times with a one percent body weight multiplied by height (%BW*ht) increase in the KAM[35].

A lack of evidence exists to definitively conclude that patients with less severe OA have higher KAMs than age-matched healthy controls[57]. It is important to keep in mind that the differences seen in the KAM are less likely to be the cause for knee OA development but rather the result of changes in the joint such as medial compartment joint space narrowing[59].

Knee Flexion

The knee flexion moment (KFM) has received particular attention in recent years to capture a more complete biomechanical understanding of the changes at the knee during gait that characterize different levels of disease severity in knee OA[36–39,60–63]. Subjects with symptomatic knee OA walk with less sagittal plane excursion[37,38] and lower KFMs in early stance when compared with healthy controls or asymptomatic knees[36,60,61]. Kaufman and colleagues[39] study the gait characteristics of patients with knee OA compared to healthy controls. They note 6^{o} less peak knee motion and significantly lower knee extension in subjects with knee OA. This could be attributed to individuals with a higher body mass index (BMI) having a greater compensation to reduce load at the knee joint by reducing the extension moment[39]. Another study notes similar patterns in patients with knee OA exhibiting approximately 4-6^{o} less flexion than age matched gender control subjects, which could be explained by subjects landing with a slightly flexed knee[64].

Patients with both moderate and severe OA exhibit decreased peak knee flexion and peak knee extension moments in comparison to healthy controls[61]. Changes found only in the severe OA group only include decreased early stance knee extension moments and decreased stance knee flexion angles[61]. Whereas the KAM relates to medial compartment OA progression, a study by Chang and colleagues[63], suggests no definitive association between baseline KFM and outcomes related to medial compartment disease progression after a 2 year follow-up in subjects with mild OA.

Knee Rotation

Nagao and colleagues[65] analyze the rotational angle in osteoarthritic knees during weight-bearing activities. They note significantly lower internal rotation of the tibia, at 20^{o} of knee flexion, in patients with grade 1 knee OA in comparison to healthy controls. This is seen as the first pathological rotational change in OA knees. External rotation at maximum knee extension and the screw-home movement excursion decrease in proportion to medial compartment knee OA progression[65]. Matsui and colleagues[66] evaluate external rotation of the tibia (rotational deformities) in patients with varus alignment using computed tomography (CT). These rotational deformities associate with varus alignment, and the extent of rotational deformity increases in knees with a higher varus deformity[66]. A study by Kaufmann and colleagues[39] suggests no significant difference in the rotation moment during gait between OA patients and healthy controls for both internal and external rotation moments. Other studies also examine rotation moment in subjects with knee OA[37,38]. These studies note that patients with knee OA exhibit a significantly lower ROM for internal-external rotation[37,38]. Patients remain in a relatively neutral position during the stance phase but begin to rotate internally first, then restore the neutral position during the swing phase. This differs from the control group that show more internal rotation during the stance phase and start to rotate externally during the swing phase[37].

2.7 Instrumented Treadmills

Instrumented treadmills are increasingly used in gait research as they allow for a larger volume of data to be collected in a smaller space and in a shorter time span. Various types of instrumented treadmills are used in gait analysis in terms of belt type, force plate placement and mode (i.e., fixed-speed or self-paced). Split-belt treadmills with a force plate underneath each belt offer a more controlled environment with foot strikes independent of each other. Ideally, there should be little noise from the contralateral limb when walking on an instrumented treadmill. It should be noted that when walking on a split belt compared to single belt treadmill, subjects walk with a wider base of gait. As the base of gait widens, the tendency towards knee abduction increases but it does not significantly affect mean frontal plane kinematics[67]. When looking at the literature regarding treadmill gait, it is important to keep in mind the different types of instrumented treadmills that are used.

van Ingen Schenau[68] rationalized that if belt speed is held constant, then the physics of treadmill and overground locomotion should be identical but did make a note that the visual information was important in maintaining balance and stability while walking. During overground walking, the environment moves with respect to the subject, and this is not the case during treadmill walking. van Ingen Schenau[68] proposed that the differences found would most likely be diminished if optical flow during treadmill gait could be aligned with visual information during overground gait. From a subjective perspective, when walking on a treadmill with a virtual reality (VR) environment, compared to without VR, subjects rated walking as more similar to overground walking[69].

2.8 Validity of Treadmill Walking

Temporospatial Parameters

The literature regarding temporospatial parameters comparing treadmill and overground walking is extensive, yet conflicting. Studies find that treadmill walking results in a higher cadence, shorter stance time[32,70,71], shorter swing phase[70], decreased step length[24] and longer double support period [27,70]. One study suggests that treadmill walking results in a 5% increase in the swing phase, 27% decrease in the double support time and a 22% increase in step width[71]. In contrast to this, a later study notes that gait parameters such as stride length, stride time, cadence, single support and double support time are very similar between the two conditions and conclude that treadmill gait is qualitatively and quantitatively similar to overground gait[22]. Other studies also show no differences in cadence, stride length[23,27,33], stance time[33], swing time, step length, stance width[27], step time and double support time[23].

One study suggests that reliable temporal and distance-gait measurements [$ICC_{(2,1)}$ $\geq$0.93], that can be generalized to overground walking, are obtained after 6 minutes of treadmill walking[30]. Consistent with these results, Zeni and colleagues[31] note that incorporating a 5 minute warm-up time into gait studies utilizing a split-belt treadmill will minimize stride and step width variability.

Knee Kinematics

The knee flexion/extension angle is the most common measure reported in the literature for comparisons of treadmill and overground walking. Studies report lower knee flexion angle ROM when walking on a treadmill[22–24,70]. Gates and colleagues[24] note that healthy participants walk on a treadmill with less knee flexion during early stance, late stance and swing when compared with overground walking. Although this finding is statistically significant, the differences are less than 1.2^{o}, which is less than the minimal detectable change (MDC). This finding is in concordance to that of Riley and colleagues[22] who state that it is possible to detect subtle differences in kinematics between the two conditions, but that these differences are generally within the normal variability of gait parameters, i.e., less than marker placement or walking speed variability. Knee kinematics in the transverse and frontal planes are not reported as often when comparing treadmill to overground walking.

Reliable knee joint measurements were found to be obtained after four minutes of treadmill walking with mean knee angle differences less than two degrees and ICCs greater than 0.90[30]. A later study also found no significant changes in the variability of knee flexion at heel-strike after five minutes of treadmill walking. It should be noted that, for the knee, the previous two studies looked at the sagittal plane when determining the effects of accommodation to treadmill walking[31].

Knee Moments

Riley and colleagues[22] utilize the coefficient of repeatability (CoR), 95% confidence interval (CI) for each measured overground gait parameter, to compare between the two modes of walking. They suggest that for data to be meaningful, the treadmill data should lie outside this CI of overground data. Riley and colleagues[22] report non-zero differences in knee flexion/extension, adduction/abduction and internal/external rotation moments, however, they note that the difference in peak knee extension moment is greater than the associated CoR[22]. Similar to this finding, Lee and Hidler[23] suggest that peak knee extensor moments in early and late stance are significantly greater during overground walking than treadmill walking. They also report significantly greater peak flexor moments in late stance and late swing during treadmill walking but do not note any significant differences in the knee adduction moment[23]. One thing to note from the Lee and Hidler[23] study is that overground and treadmill data are collected from the same force plates, by having a raised floor be level with the treadmill. This means that consistent sensors are used between both walking modalities which can help reduce potential error.

2.9 Reliability of Treadmill Walking

A study by Riley and colleagues[22] assessed the repeatability of temporospatial gait parameters over three sessions using an AMTI compound instrumented treadmill consisting of three treadmill force platforms: one large platform in the front and two side-by-side in the back, all synchronized and forming a continuous treadmill surface. Treadmill speed was held constant for all three test sessions, ensuring greater consistency for velocity, cadence and step length than with overground walking. No statistically significant difference for the timing of gait events, and the percentage spent in single and double support were reported[22].

A later study by Faude and colleagues[26] analyzed the within- and between-day reliability of temporospatial gait parameters in healthy seniors using a one-dimensional GRF measuring treadmill (Zebris Medical GmbH FDM-Tsystem, Isny, Germany). Subjects' comfortable walking speed was calculated and used for all the test sessions. Spatial and temporal variability were assessed by calculating the coefficient of variation (standard deviation of analyzed steps divided by the mean) for stride-to-stride length and time, respectively. Faude and colleagues[26] reported high between-day (ICC 0.85-0.96) and within-day (ICC 0.97-0.98) reliability for stride frequency, stride width, stride time, stride length and double stance phase, but temporal and spatial gait variability did show high variability(CoV 16.2-36.1%)[26].

Similar to Faude and colleagues[26], a study by Reed and colleagues[25] assessed within- and between-day reliability of temporospatial gait parameters as well as some kinetic parameters on the Zebris treadmill system (Zebris Medical GmbH, Max-Eyth-Weg 43, D-88316, Isny, Germany). They reported statistically significant differences in 14/16 temporospatial and kinetic gait parameters over the 3 test sessions. For between-day reliability, the minimum change that could be detected with 95% confidence ranges between 3-17%, 14-33% and 4-20% for temporal, spatial and kinetic parameters, respectively. Within-day reliability showed similar results, with temporal and kinetic gait parameters typically being more consistent than spatial parameters. In this study, participants were allowed to select their own comfortable walking speed for each session rather than use a predetermined walking speed. Reed and colleagues[25] described this as allowing them to determine the repeatability of self-selected walking speeds on the treadmill system[25].

2.10 Gait Real-Time Analysis Interactive Lab

The Gait Real-Time Analysis Interactive Lab (GRAIL, Motekforce Link, Amsterdam, NL) is a force plate-instrumented dual-belt treadmill (R-Mill, Motekforce Link, Amsterdam, NL) that is used in conjunction with motion sensing cameras and a 180 degree projection screen and surround sound system allowing the subject to be immersed in VR depictions of real-life settings. Situated under each belt is a force plate (50 x 200 cm) allowing for the collection numerous foot strikes in a much shorter time span compared to overground walking. Computer software (D-Flow) enables the motion analysis system to pass information through to the GRAIL for real time feedback of temporospatial parameters, joint kinematics and joint kinetics.

Recent literature looks to assess the kinematic and kinetic measurement properties of the GRAIL in comparison to overground walking[28,29,34]. van der Krogt and colleagues[28,29] sought to compare kinematic and kinetic data between self-paced treadmill walking and overground walking. Although these studies evaluate 9 children with spastic cerebral palsy, only the results from the 11 typically developing children will be reported. In these studies, subjects walk in a random order beginning either with walking overground or on a self-paced treadmill. van der Krogt and colleagues[28] suggest no significant differences for walking speed and cadence, but did note a 3 cm increase in step width. They report some significant differences in ankle and hip kinematics, but suggest that all are within the range of 1-3^{o} and are considered minor kinematic differences. Significant differences are also seen for peak knee moments with greater abduction and slightly less extension moments during treadmill walking[29]. The increase in abduction moment can be the result of an increase in step width that is associated with split-belt treadmill walking[67].

It is important to note the limited sample size of participants in this study as it can have a potential bias on the results. Subjects also walk at a self-paced speed on the treadmill, which introduces more cautionary gait, potentially caused by decreased positional awareness. Walking at a fixed-speed seems to improved subjects' gait pattern, which likely is better related to overground walking[72]. Another study shows that when walking on the GRAIL, a similar pattern of energy exchange is observed for both fixed speed and self-paced walking, though there is slightly more energy exchanged between the subject and belt during self-paced walking[73].

A review of the literature shows that the studies comparing the GRAIL to overground walking are conducted in typically developing children and in children with cerebral palsy. This data cannot be readily compared to patients with medial compartment knee OA. Therefore, the overall aim of this study was to investigate the measurement properties of gait data assessed using the GRAIL in patients with medial compartment knee OA.

Chapter 3

3 Methodology

3.1 Study Setting and Design

This study was completed in the Wolf Orthopaedic Biomechanics Laboratory (WOBL) and the Fowler Kennedy Sport Medicine Clinic at the University of Western Ontario. To investigate test-retest reliability, patients with knee OA walked using the GRAIL on two test sessions completed at least 24 hours apart and within one week. To investigate concurrent validity and known-groups validity, patients and controls walked using both the GRAIL and overground systems during one test session. Overground test sessions were completed first. Gait speed was calculated (m/s) based on sacral marker position from overground trials and subsequently used to match the treadmill speed for assessments using the GRAIL. All participants provided written informed consent. The study Letters of Information and Ethics Approval Notice are provided in Appendices B and C, respectively.

3.2 Participants

Healthy Controls

Healthy participants were recruited by contacting friends and family members of patients with knee OA who were participants in other studies in the lab, with the goal of obtaining participants of similar age to the patients with knee OA. We included healthy persons between 30-65 years of age, with no complaints of knee pain, no other known musculoskeletal or neurological impairments likely to affect gait, and who answered "NO" to all PAR-Q questions (Appendix A). We excluded persons who had insufficient physical fitness to walk for approximately 20 minutes, were unable to speak/read/print English or provide informed consent.

Knee Osteoarthritis Patients

We recruited participants with medial compartment knee OA from the Fowler Kennedy Sport Medicine Clinic. We included patients who were between 30-65 years of age, had neutral to varus lower limb alignment, had clinical (symptomatic) and radiographic knee OA (as determined by the Altman criteria[43]) that was primarily affecting the medial compartment of the tibiofemoral joint. We excluded patients if they had a previous total joint knee replacement or osteotomy of the symptomatic study limb, major neurological deficit that would affect gait, psychiatric illness that may limit informed consent, inflammatory or infectious arthritis of the knee, insufficient physical fitness to walk for approximately 20 minutes, inability to speak/read/print English or provide informed consent.

3.3 Gait Testing Procedures

3.3.1 Overground Movement Analysis System

The conventional overground movement analysis system consists of a 12-camera motion capture system (Motion Analysis Corporation, Santa Rosa, CA) and a single floor mounted force plate (Advanced Medical Technology, Watertown, MA).

Laboratory Equipment Calibration

The system was calibrated each morning. System calibration consists of both a seed and wand calibration. Seed calibration was completed with an L-frame designed specifically for calibration, where the exact locations of the markers on the frame were known, to define the coordinate system of the data collection area. After this, wand calibration was completed by waving a wand with markers of known distance through the data collection area. Wand calibration was performed to ensure that a direct measurement of an object of known size was made by all of the cameras surrounding the data collection area. Marker positions of the wand were recorded, calculated and then compared with known distances to determine the error associated in tracking. Calibration accuracy was dependent on how closely the known distances were to the measured values. If the standard deviation was greater than 2 mm, or the mean measurement was greater than 2 mm different than the known distances, then calibration was rejected and the entire process was repeated[74].

Subject Preparation

Participants were instructed to wear tight-fitting shorts and a t-shirt for the day of testing to ensure that markers remained as close to anatomical landmarks as possible. Prior to testing, all participants were instructed to remove their shoes and socks to negate the potential effects of variability from footwear. Twenty-two passive reflective markers were placed on each participant based on a modified Helen Hayes marker set[19] (Appendix D).

Static Trials

Two static trials were completed where the participant was asked to stand motionless on the force plate while 3 seconds of data were collected to determine body mass, marker orientation and positions of joint centres of rotation for the ankle and knee. Hip joint centres were defined by first finding the midpoint between markers placed on the left and right ASIS. Percentage offsets (64% lateral, 44% posterior, and 68% inferior) relative to the midpoint position were used to determine the hip joint centre for each side of the body[75]. Participants wore four additional markers during the static trials. These markers were placed bilaterally over the medial knee joint line and medial malleolus to define the positions of joint centers of rotation for both joints. These additional markers were removed prior to the gait trials. These static trials were completed again for the GRAIL.

Walking Trials

Participants were instructed to approach every walking trial at their usual comfortable walking pace. The overground walking trials continued until eight complete foot strikes were obtained. From these trials, the first five clean foot strikes were chosen and used for data processing.

3.3.2 Gait Real-Time Analysis Interactive Lab

The GRAIL consists of a force plate-instrumented dual belt treadmill (R-Mill, Motekforce Link, Amsterdam, NL), 10-camera motion capture system (Raptor-H, Motion Analysis Corporation, Santa Rosa, CA), 180^{o} projection screen with surround sound, and computer software (D-flow, Motekforce Link, Amsterdam, NL). The calibration process, using the seed frame and wand, is identical for both systems.

Subject Preparation

Markers were placed on each participant by trained testers to reduce variability associated with marker placement. For the treadmill trials, markers over the acromion, right scapula, elbow and wrist were removed and additional markers were placed on the participant to meet the criteria for the GRAIL lower limb marker set (Appendix D). A safety harness was worn by all participants and handrails were fitted on either side for extra safety.

Gait Trials

Before the treadmill trial, participants were given adequate rest time until they felt ready to begin walking. Participants completed a 6 minute warm-up to acclimatize to their matched overground walking speed[30]. Participants were monitored constantly throughout the trial and were asked about their walking speed. After 6 minutes, force plate and camera marker data were collected simultaneously with a software program that was consistent with the overground system (Cortex) for 10 gait cycles (i.e. heel strike to heel strike of the same foot).

3.4 Data Reduction

Data processing was done using commercially available software (Presentation Graphs, Cortex, Motion Analysis Corporation, Santa Rosa, CA) and custom post-processing and data reduction methods.

Skeleton Builder (SkB) models (Cortex, Motion Analysis Corporation, Santa Rosa, CA) were used to define anatomical segments for data analysis. In this model, three markers are used in conjunction with each other to define the origin, bone axis, and plane. Anthropometric data were used to estimate inertial properties of each limb where translations and rotations of segments were calculated with respect to marker orientations from the static trial[76].

Force plate data were collected at 600 Hz and 1000 Hz for overground and GRAIL walking, respectively. Correspondingly, camera marker data were collected at 60 Hz and 100 Hz. Each trial was tracked frame-by-frame to ensure that markers corresponded with their respective anatomical landmark. Marker data were filtered with a 4th order Butterworth filter with a 6 Hz cut-off frequency using Excel (Microsoft, Redmond, WA). Knee angles were determined using Euler angles rotated in the following order: flexion/extension (x-axis), ab/adduction (y-axis), internal/external rotation (z-axis). Knee moments were calculated using inverse dynamics (Cortex, Motion Analysis Corporation, Santa Rosa, CA) with a fixed tibia coordinate system[75] and normalized to %BW*ht. Knee joint angles and moments were normalized to 100% of the stance phase, heel-strike to toe-off.

Peak values for knee angles and moments were determined and averaged over 5 trials for the affected limb. All peak values reported were identified using the waveform peaks from each trial analyzed. These peaks were then averaged to give a single value per limb per subject per variable. The peak knee adduction angle was identified as the minimum value during stance. The peak flexion angle was defined as the maximum value in the first half of stance with the peak knee extension angle as the minimum value for the second half of stance. The peak knee internal rotation angle was identified as the minimum value for the first half of stance with the peak external rotation angle as the maximum value in the second half of stance. For the knee adduction moment, the first peak in the waveform was identified as the maximum value during the first half of stance and the second peak as the maximum value in the second half. The peak flexion and external rotation moments were defined as the maximum value in the first half of stance, and the peak extension and internal rotation moments as the minimum value in the second half of stance.

3.5 Statistical Analysis

A sample size of 31 participants is required to be tested on two occasions to detect an ICC of at least 0.85 with a 95% CI width of 0.2[77]. All statistical analyses were performed using MedCalc Version 12.2.1.0 (MedCalc Software, Ostend, Belgium) and IBM SPSS Statistics for Windows Version 24.0 (IBM Corp, Armonk, NY).

To estimate test-retest reliability we calculated an $ICC_{(2,1)}$. Bland and Altman plots were used to visually inspect test and retest data. To assess the absolute reliability we calculated the standard error of measurement (SEM) from the ANOVA used to calculate the ICC. We did this by taking the square root of the error variance term, as described by Stratford and Goldsmith[78]. For interpretation in the discussion, the SEM was then multiplied by 1.96 (i.e. the z value for 95% confidence) to estimate the error in an individual's measurement at any point in time. That value was then multiplied by the square root of 2 to calculate the minimum detectable change (MDC) to estimate the error in an individual's change score[79].

To estimate the concurrent validity we calculated Pearson correlation coefficients (r) to describe the magnitude of the associations between the conventional gait lab and GRAIL measurements. Paired t-tests were run to determine mean differences between overground and GRAIL measurements. Correlation coefficients were interpreted as follows: <0.40 was poor, 0.40-0.75 was good and >0.75 was excellent[80].

To estimate known-groups validity we calculated independent samples t-tests to determine whether the GRAIL could distinguish between patients with knee OA and healthy controls.

Chapter 4

4 Results

To date, 18 patients and 16 controls completed testing. Their demographic and clinical characteristics are reported in Table 4.1. KL grading was completing using static, standing radiographs by a trained tester.

Table 4.1. Demographic and clinical characteristics for Patients with knee OA (N=18) and Controls (N=16). Means ± SD

Subject Characteristic	Knee OA (n=18)	Healthy Controls (n=16)
Age, yr	52.7 ± 8.1	53.2 ± 8.9
Sex, M / F	12 / 6	10 / 6
Height, m	1.76 ± 0.10	1.74 ± 0.11
Weight, kg	93.8 ± 18.8	78.8 ± 16.9
BMI, kg/m^2	30.0 ± 4.4	26.0 ± 4.8
Gait Speed, m/s	1.11 m/s	1.20 m/s
Kellgren Lawrence Grade*	Number of Patients	
2	12	-
3	4	-
4	2	-

*KL Grade Descriptions[44]:
2 – Definite osteophytes, possible joint space narrowing
3 – Moderate multiple osteophytes, definite joint space narrowing, some sclerosis, possible deformity of bone contour
4 – Large osteophytes, marked joint space narrowing, severe sclerosis, definite deformity of bone contour

4.1 Test-Retest Reliability

Summary statistics for reliability of peak knee angles and moments are presented in Table 4.2. Ensemble averages for knee moments of patients with knee OA test and retest sessions are presented in Figures 4.1a-c. Bland and Altman plots of the differences versus the means of the test and retest peak knee angles and moments are displayed in Figures 4.2-4.7.

Visual inspection of the Bland and Altman plots did not reveal any systematic differences between test and retest sessions. A couple outliers were observed for the rotation angles and moments, however data from these subjects were kept in the analysis due to the inherent error associated with measures in the transverse plane.

The knee varus angle showed excellent reliability between test sessions on the GRAIL. The point estimate for the ICC was 0.92 (95% CI 0.80, 0.97). First and second peak KAMs also displayed excellent reliability with ICCs of 0.87 (95% CI 0.70, 0.95) and 0.93 (95% CI 0.83, 0.97), respectively.

Knee flexion and extension angles showed good reliability with ICCs ranging from 0.62-0.70 (95% CI 0.31, 0.87). The knee flexion moment displayed fair reliability with ICCs of 0.52 (95% CI 0.10, 0.79) with the extension moment showing excellent reliability with measures of 0.77 (95% CI 0.48, 0.91).

Knee internal and external rotation angles showed good reliability with ICCs ranging from 0.52-0.66 (95% CI 0.10, 0.86). The knee internal rotation moment showed excellent reliability with ICCs of 0.76 (95% CI 0.45, 0.90) while the knee external rotation moment showed good reliability with ICCs of 0.63 (95% CI 0.24, 0.85).

Table 4.2. Point estimates and 95% confidence intervals (CI) for Intraclass Correlation Coefficients ($ICC_{2,1}$) and Standard Errors of Measurement (SEM) for peak knee angles and moments (n=18)

Gait Variable	ICC (95% CI)	$\pm$ SEM
Knee Angle		
Varus	0.92 (0.80, 0.97)	1.50
Flexion	0.62 (0.24, 0.84)	3.66
Extension	0.70 (0.37, 0.87)	3.21
Internal Rotation	0.66 (0.31, 0.86)	3.99
External Rotation	0.52 (0.10, 0.78)	4.95
Knee Moments		
Adduction (1^{st} Peak)	0.87 (0.70, 0.95)	0.31
Adduction (2^{nd} Peak)	0.93 (0.83, 0.97)	0.32
Flexion	0.52 (0.10, 0.79)	0.59
Extension	0.77 (0.48, 0.91)	0.52
Internal Rotation	0.76 (0.45, 0.90)	0.61
External Rotation	0.63 (0.24, 0.85)	1.00

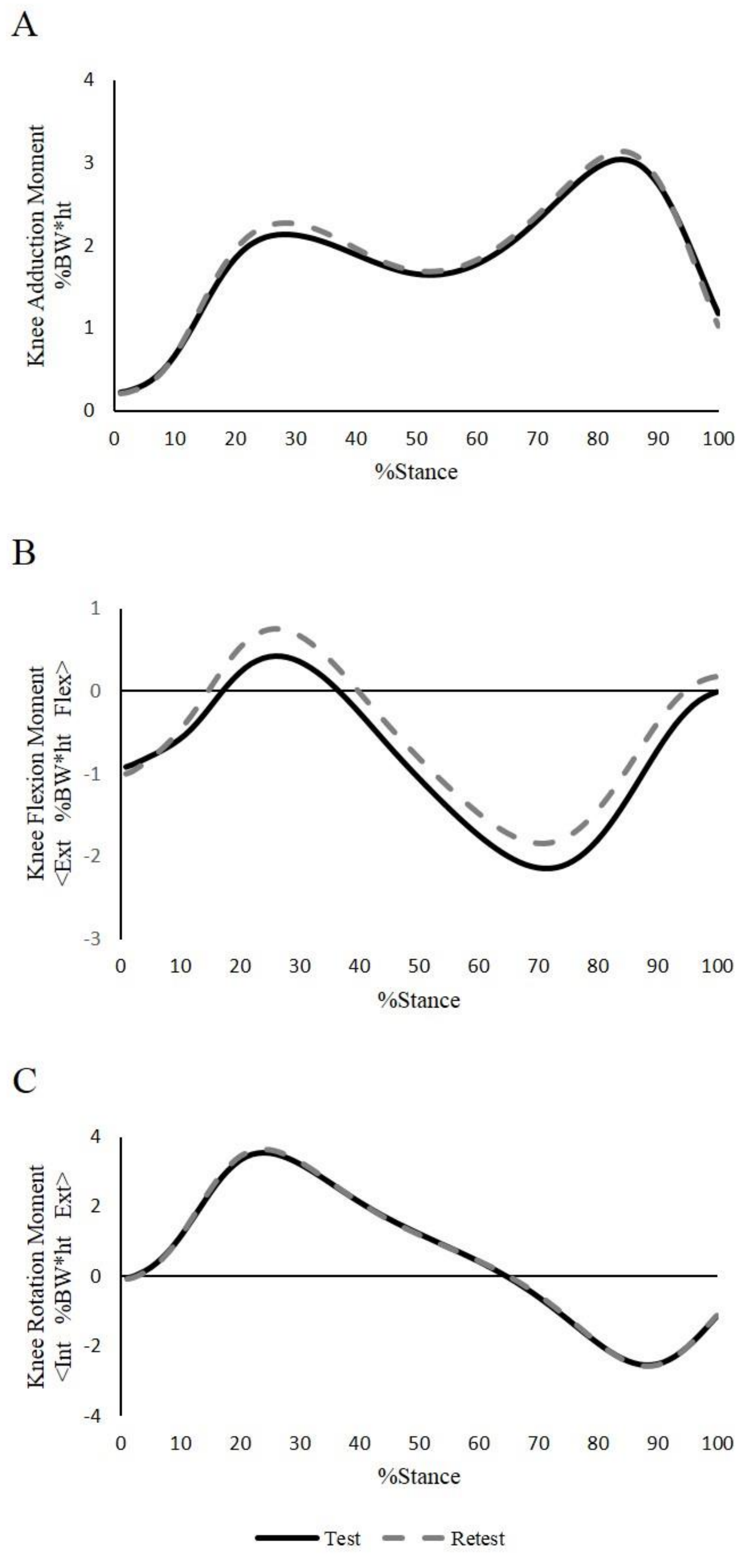


Figure 4.1. GRAIL test (solid line) and retest (dotted line) ensemble averages (n=18) for knee (a) adduction moment, (b) flexion moment and (c) rotation moment for patients with knee OA. BW = body weight, ht = height.

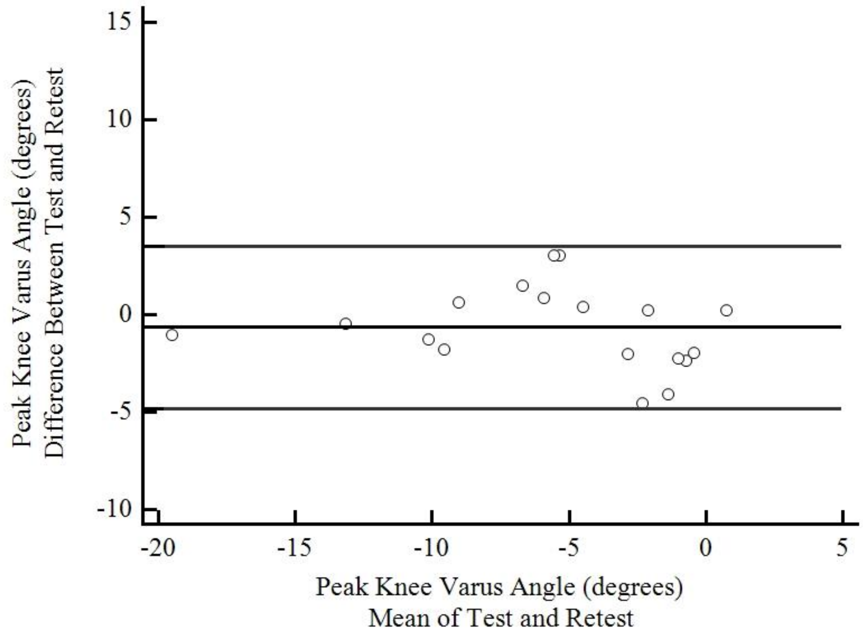


Figure 4.2. Bland and Altman plot of the differences versus the means for the test and retest peak knee varus angle. Solid lines represent the mean $\pm$ 1.96 standard deviations. BW = body weight, ht = height.

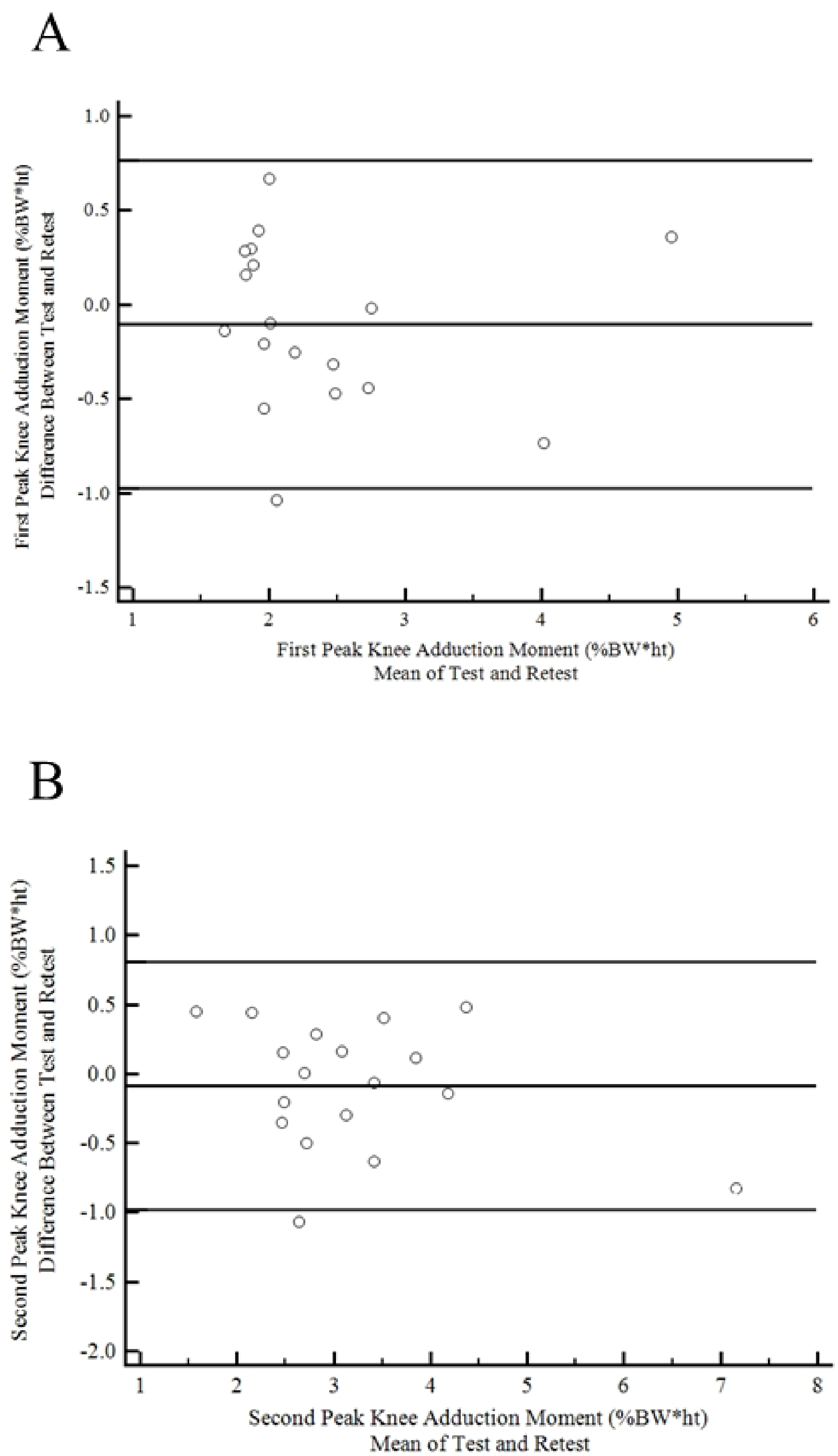
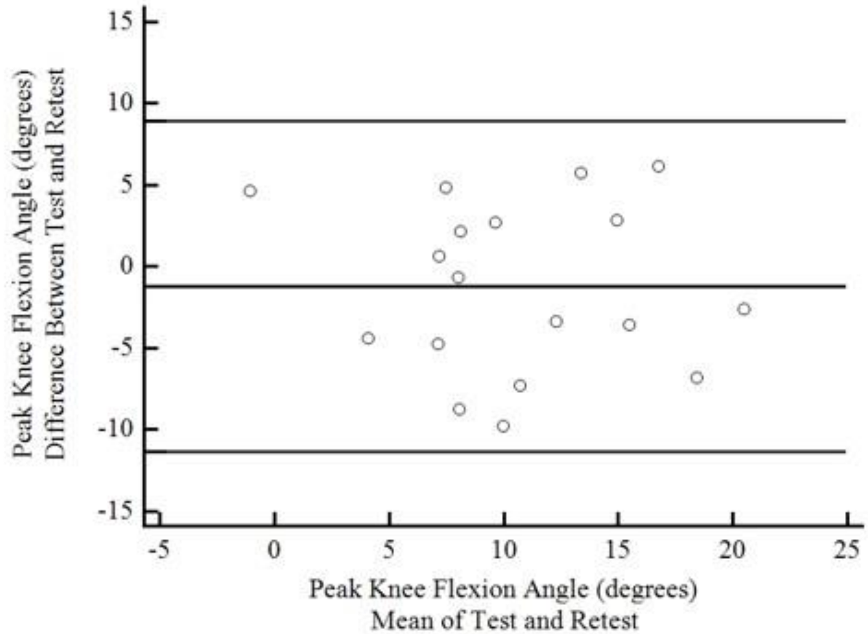


Figure 4.3 Bland and Altman plots of the differences versus the means for the test and retest peak knee adduction moments. (A) first peak knee adduction moment, (B) second peak knee adduction moment. Solid lines represent the mean $\pm$ 1.96 standard deviations. BW = body weight, ht = height.

A



B

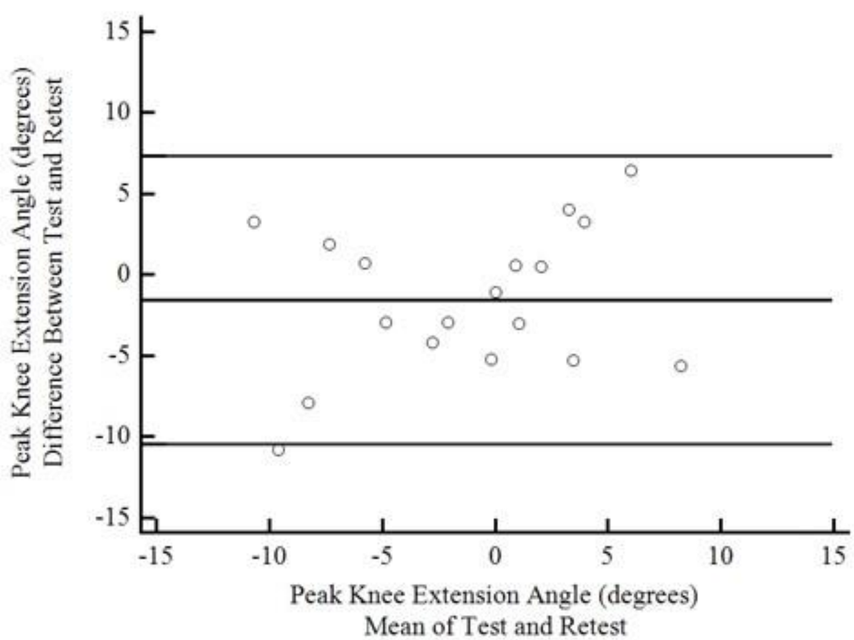


Figure 4.4 Bland and Altman plots of the differences versus the means for the test and retest peak knee sagittal angles. (A) peak knee flexion angle, (B) peak knee extension angle. Solid lines represent the mean ± 1.96 standard deviations. BW = body weight, ht = height.

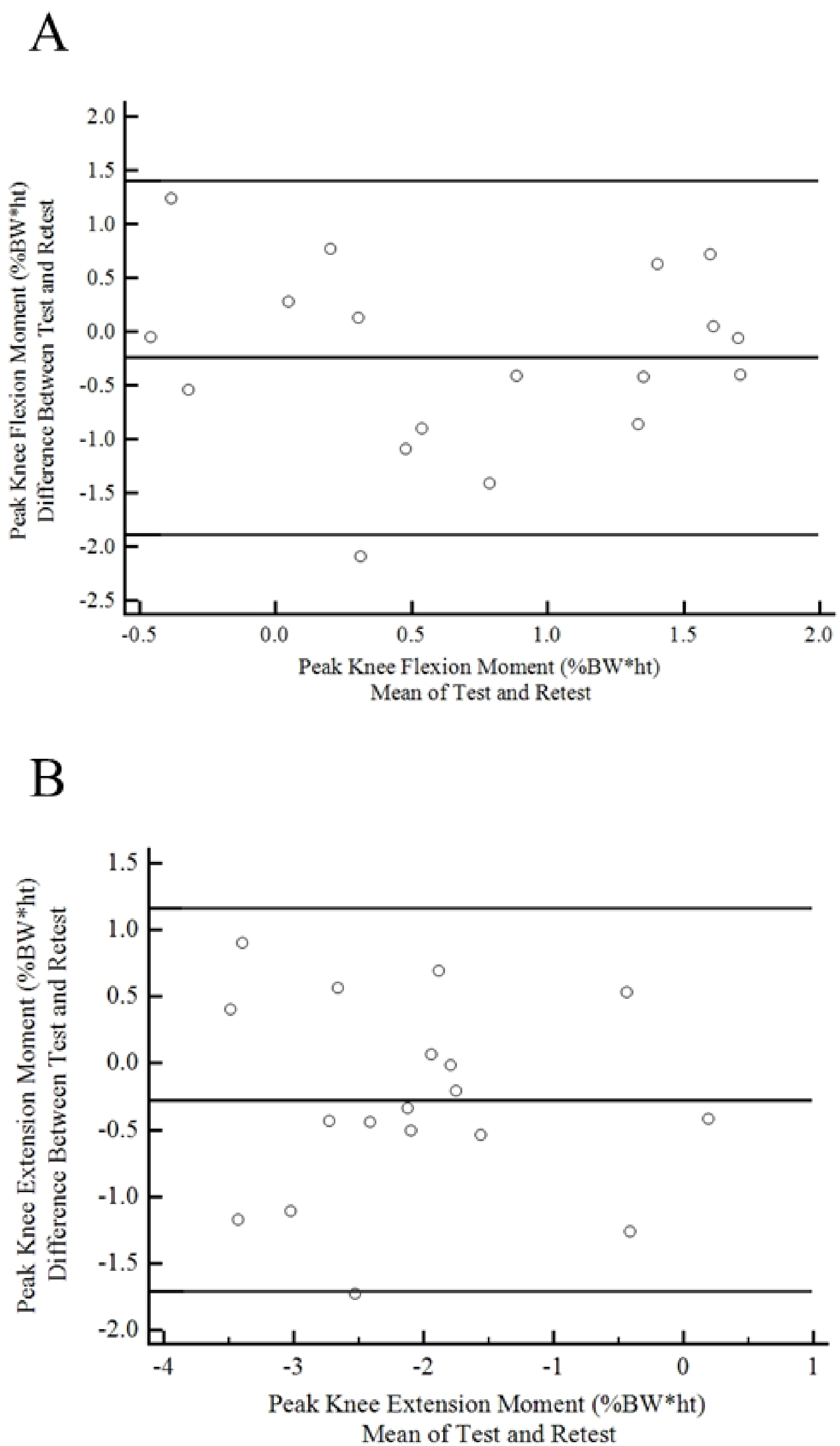
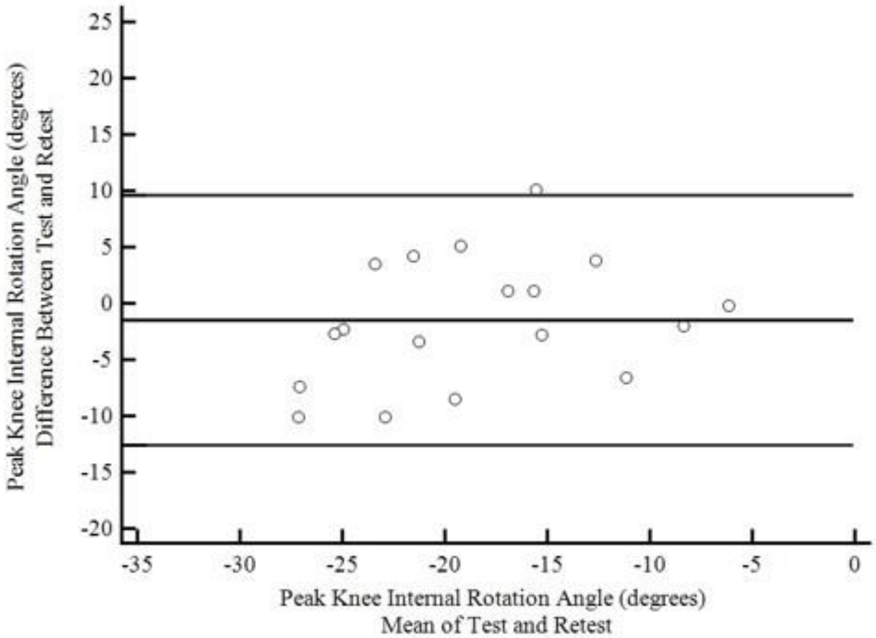


Figure 4.5 Bland and Altman plots of the differences versus the means for the test and retest peak knee sagittal moments. (A) peak knee flexion moment, (B) peak knee extension moment. Solid lines represent the mean ± 1.96 standard deviations. BW = body weight, ht = height.

A



B

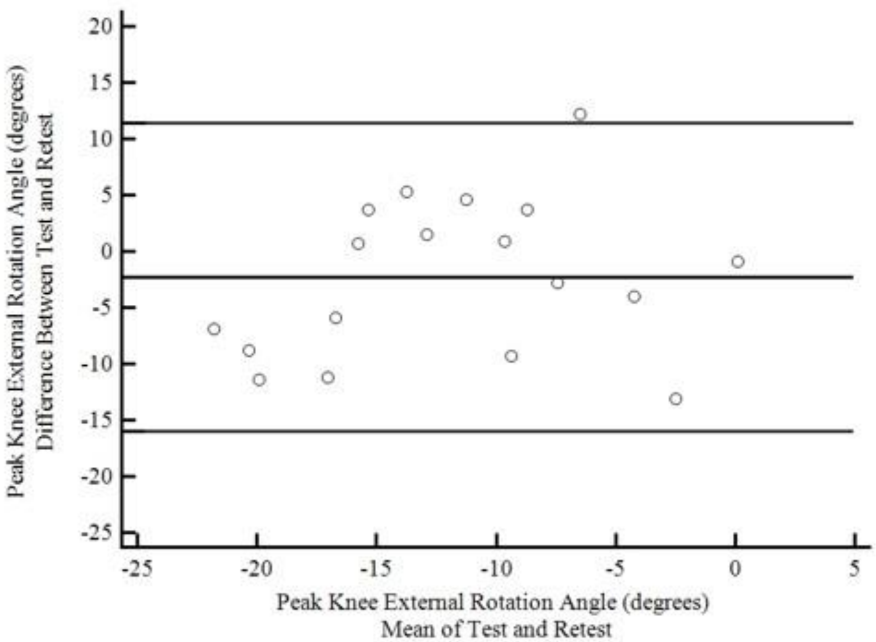


Figure 4.6 Bland and Altman plots of the differences versus the means for the test and retest peak knee transverse angles. (A) peak knee internal rotation angle, (B) peak knee external rotation angle. Solid lines represent the mean ± 1.96 standard deviations. BW = body weight, ht = height.

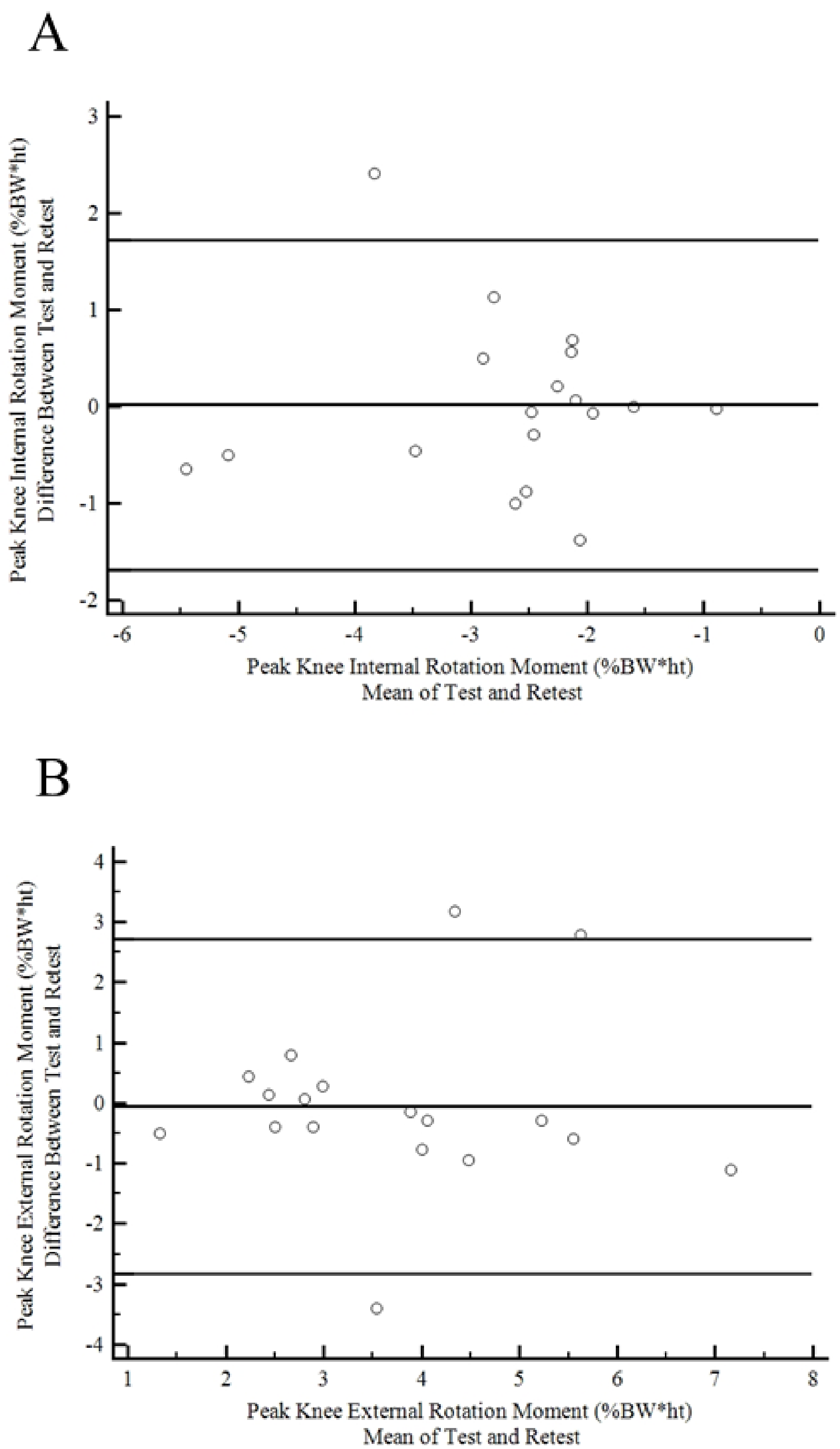


Figure 4.7 Bland and Altman plots of the differences versus the means for the test and retest peak knee transverse moments. (A) peak knee internal rotation moment, (B) peak knee external rotation moment. Solid lines represent the mean $\pm$ 1.96 standard deviations. BW = body weight, ht = height.

4.2 Concurrent Validity

Pearson correlation coefficients (r) describing the association between the GRAIL and overground walking are presented in Table 4.3. Mean differences between GRAIL and overground walking are presented in Table 4.4. Scatterplots of peak knee angles and moments collected on the GRAIL versus overground walking are presented in Figures 4.8-4.13.

Visual inspection of scatterplot data does not suggest a systematic shift for frontal and sagittal plane measures. Transverse moments appear to be larger when walking on the GRAIL compared to overground walking.

Knee angles had good-to-excellent correlations ranging from 0.69-0.96 (95% CI 0.46, 0.98). Knee adduction and flexion/extension moments also had good-to-excellent correlations ranging from 0.74-0.87 (95% CI 0.54, 0.93), while the rotation moments had very poor correlations ranging from 0.05-0.12 (95% CI -0.29, 0.44).

Table 4.3. Point estimates and 95% confidence intervals (CI) for Pearson correlation coefficients (r) for peak knee angles and moments assessed using the GRAIL and overground systems (n=34)

Gait Variable	Pearson's r (95% CI)
Knee Angle	
Varus	0.96 (0.91, 0.98)
Flexion	0.91 (0.82, 0.95)
Extension	0.89 (0.79, 0.94)
Internal Rotation	0.78 (0.59, 0.88)
External Rotation	0.69 (0.46, 0.83)
Knee Moments	
Adduction (1^{st} Peak)	0.87 (0.74, 0.93)
Adduction (2^{nd} Peak)	0.74 (0.54, 0.86)
Flexion	0.76 (0.58, 0.88)
Extension	0.82 (0.66, 0.91)
Internal Rotation	0.05 (-0.29, 0.38)
External Rotation	0.12 (-0.23, 0.44)

Table 4.4 Means and mean differences for peak knee angles and moments assessed using the GRAIL and overground systems (n=34)

*Significant difference ($p < 0.05$)

Gait Variable	GRAIL Mean (± SD)	Overground Mean (± SD)	Mean Difference (95% CI)
Knee Angles			
Varus	-4.99 (4.65)	-6.25 (4.37)	-1.26 (-1.73, -0.79)*
Flexion	11.09 (6.55)	10.69 (7.21)	-0.40 (-1.46, 0.66)
Extension	-2.14 (5.90)	-1.57 (5.52)	0.57 (-0.37, 1.50)
Internal Rotation	-18.22 (7.91)	-19.39 (7.64)	-1.18 (-3.00, 0.64)
External Rotation	-12.77 (7.91)	-11.06 (7.17)	1.71 (-0.38, 3.80)
Knee Moments			
Adduction 1st Peak	2.05 (0.83)	2.28 (0.83)	0.23 (0.08, 0.39)*
Adduction 2nd Peak	2.94 (1.03)	2.18 (0.79)	-0.76 (-1.00, -0.52)*
Flexion	0.69 (0.90)	0.92 (0.98)	0.23 (0.00, 0.46)*
Extension	-2.11 (1.06)	-1.72 (0.81)	0.38 (0.17, 0.60)*
Internal Rotation	-2.67 (1.12)	-0.88 (0.29)	1.79 (1.39, 2.19)*
External Rotation	3.69 (1.44)	0.04 (0.04)	-3.65 (-4.15, -3.15)*

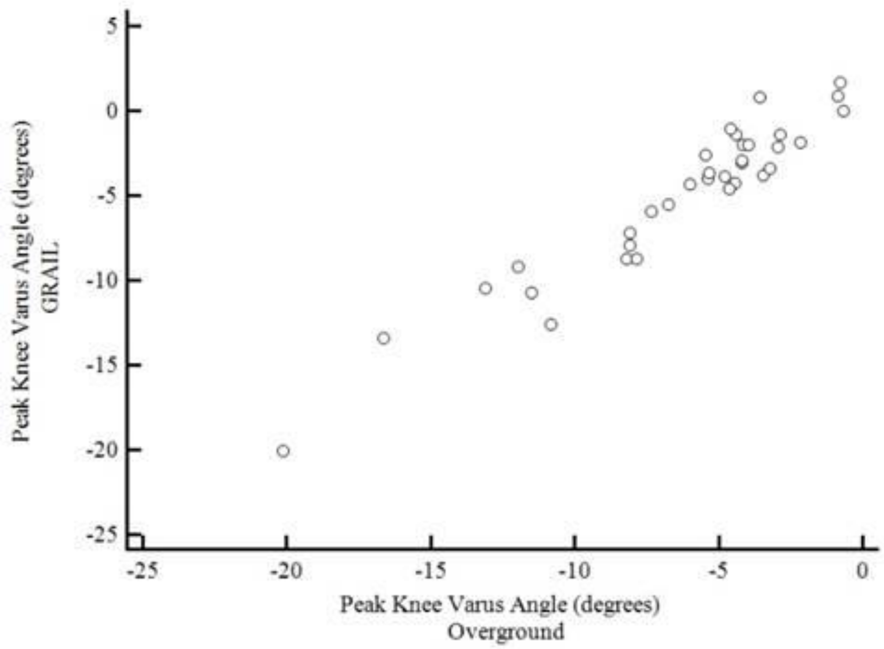
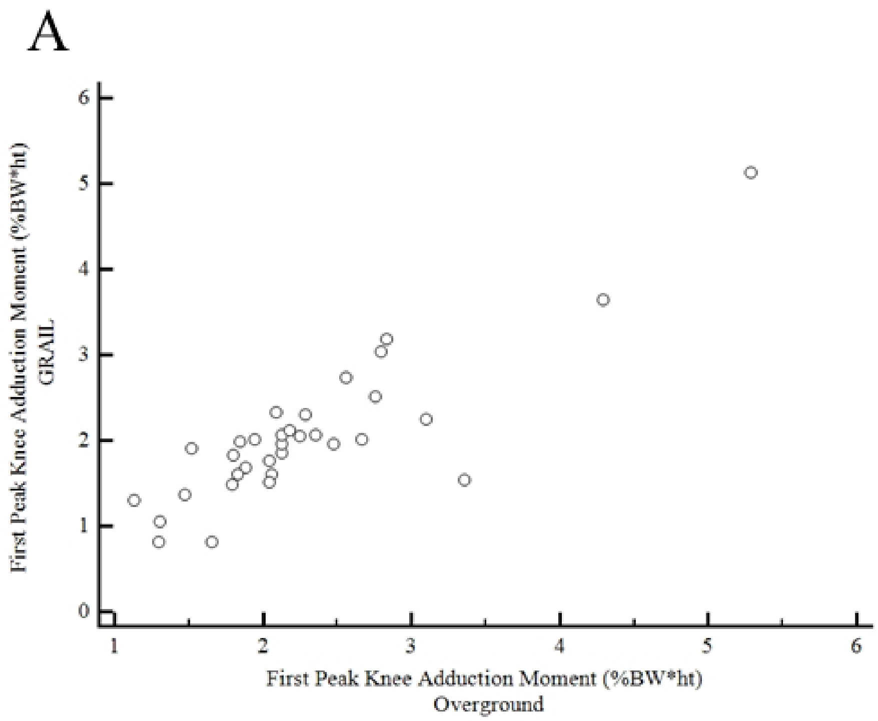


Figure 4.8. Scatterplot of the frontal plane peak knee angle collected on the GRAIL versus overground walking. BW = body weight, ht = height.



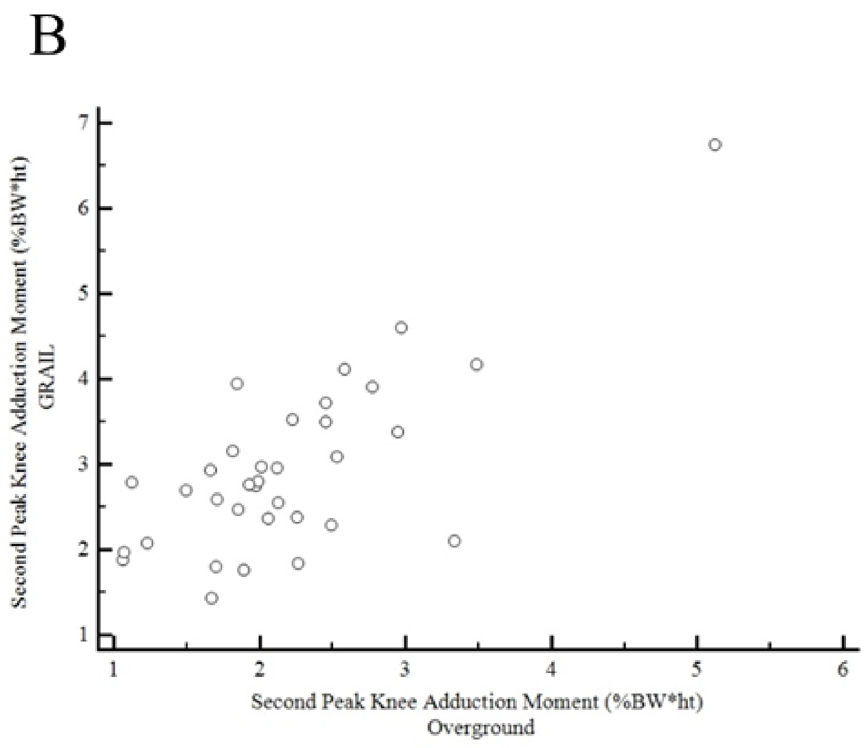


Figure 4.9. Scatterplot of frontal plane peak knee moments collected on the GRAIL versus overground walking. (A) first peak knee adduction moment, (B) second peak knee adduction moment. BW = body weight, ht = height.

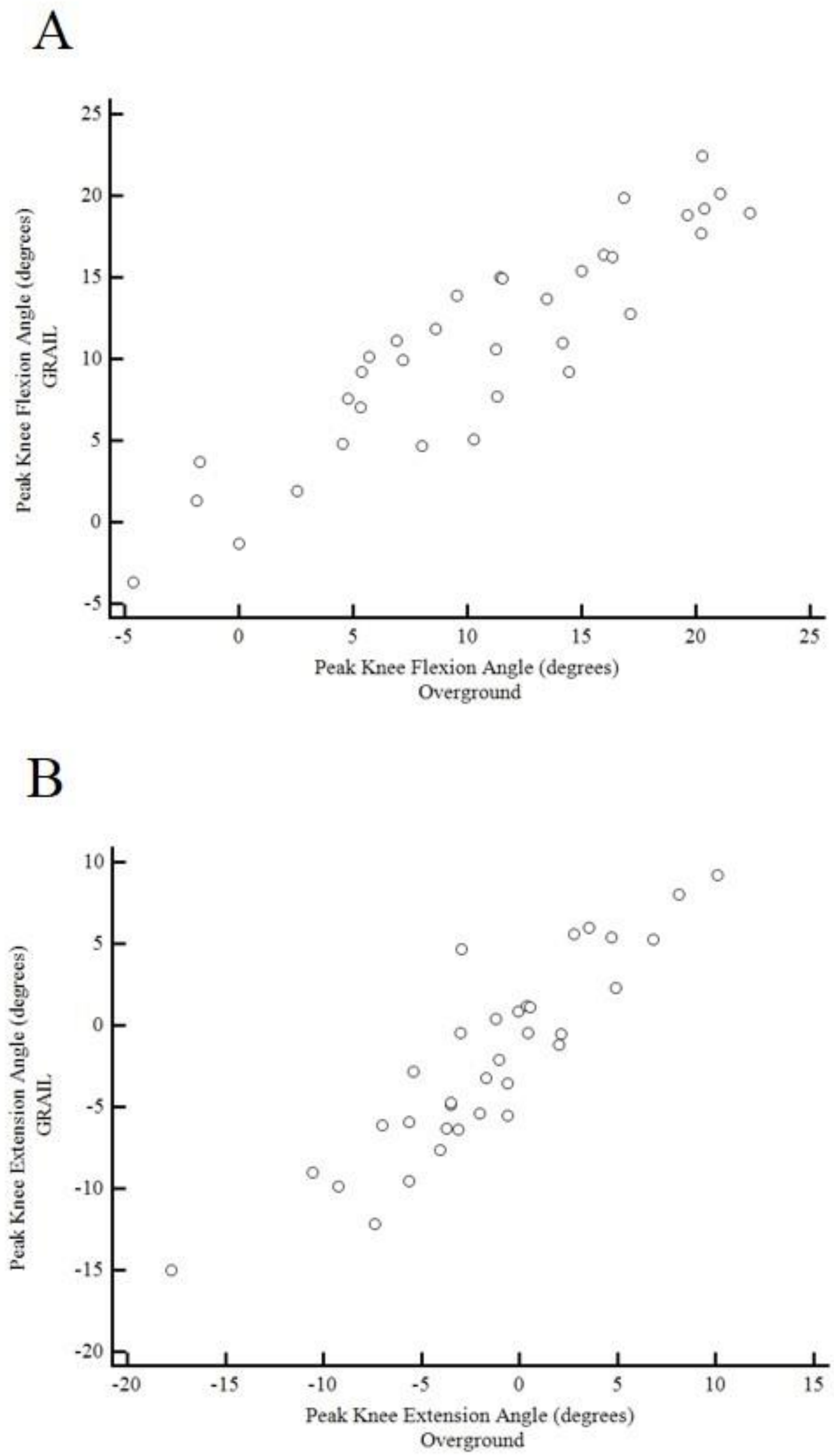


Figure 4.10. Scatterplot of sagittal plane peak knee angles collected on the GRAIL versus overground walking. (A) peak knee flexion angle, (B) peak knee extension angle. BW = body weight, ht = height.

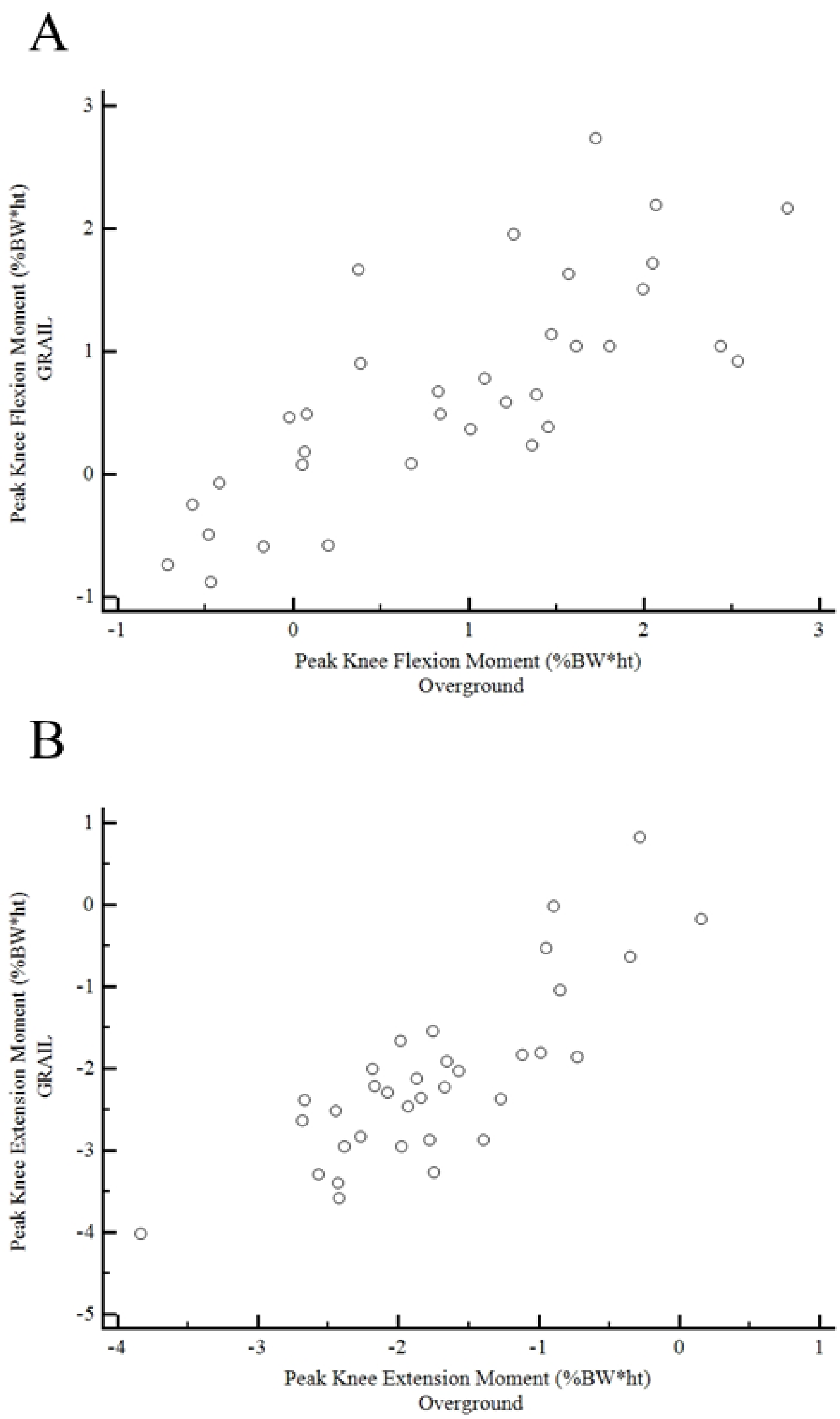
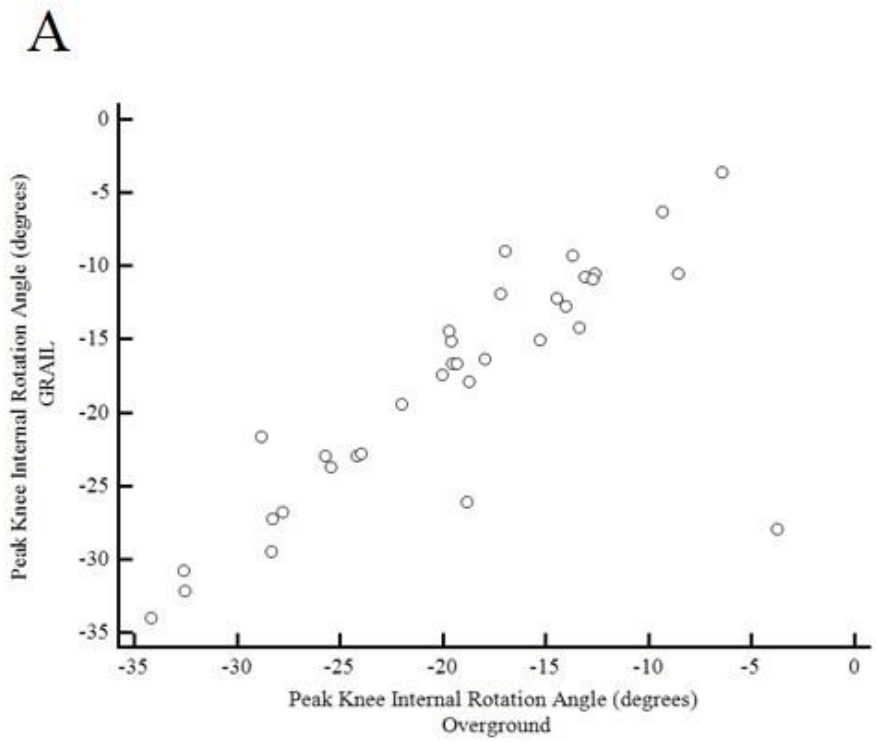


Figure 4.11. Scatterplot of sagittal plane peak knee moments collected on the GRAIL versus overground walking. (A) peak knee flexion moment, (B) peak knee extension moment. BW = body weight, ht = height.



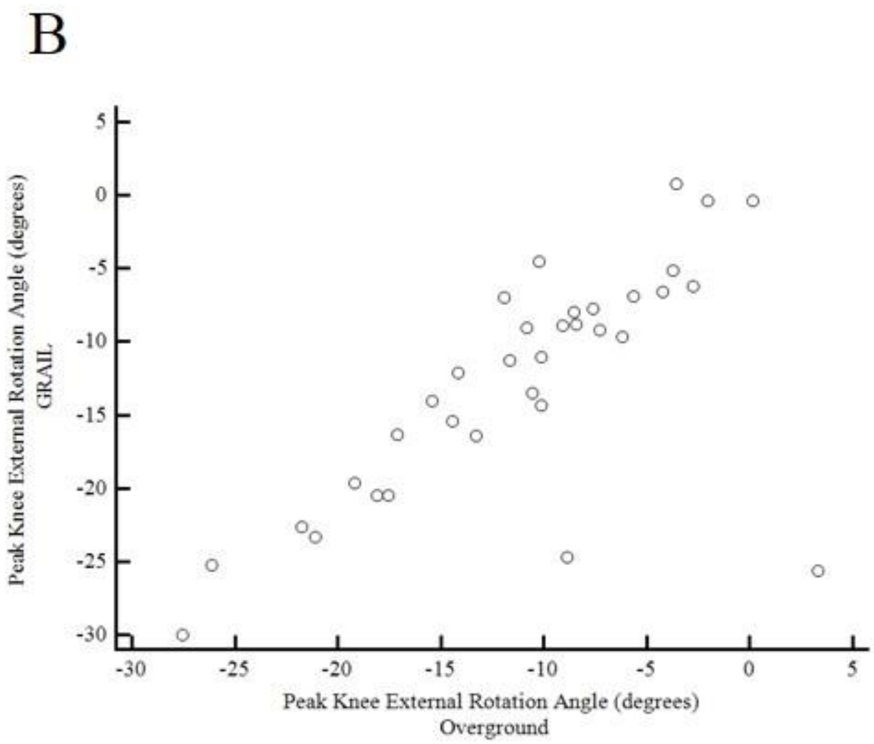


Figure 4.12. Scatterplot of transverse plane peak knee angles collected on the GRAIL versus overground walking. (A) peak knee internal rotation angle, (B) peak knee external rotation angle. BW = body weight, ht = height.

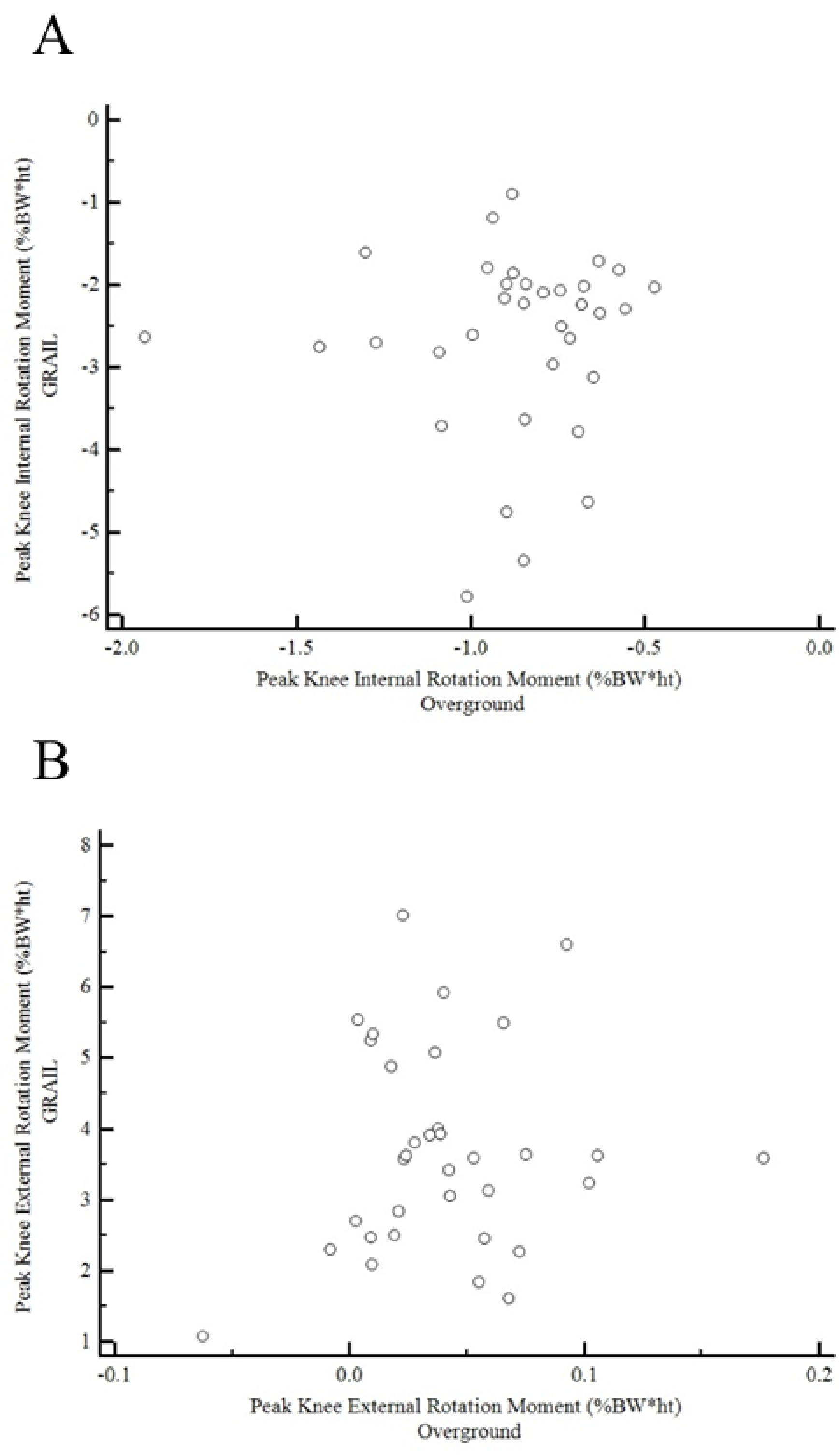


Figure 4.13. Scatterplot of transverse plane peak knee moments collected on the GRAIL versus overground walking. (A) peak knee internal rotation moment, (B) peak knee external rotation moment. BW = body weight, ht = height.

4.3 Known-Groups Validity

Ensemble averages for knee moments in patients with knee OA and healthy controls are displayed in Figures 4.14a-c. Results from the independent t-tests comparing peak knee angles and moments in patients and controls are reported in Table 4.4. Patients with medial compartment knee OA had a significantly higher first peak KAM than healthy controls ($p < 0.05$). There were no significant differences observed.

Table 4.5. Peak knee angles and moments for patients with knee OA (n=18) and healthy controls (n=16).

*Significant difference ($p < 0.05$)

Gait Variable	Knee OA Mean (± SD)	Healthy Control Mean (± SD)	Mean Difference (95% CI)
Knee Angle			
Varus	-5.86 (5.10)	-4.01 (4.03)	-1.85 (-5.09, 1.39)
Flexion	10.00 (5.72)	12.31 (7.37)	-2.31 (-6.88, 2.28)
Extension	-2.03 (6.49)	-2.26 (5.36)	0.23 (-3.96, 4.42)
Internal Rotation	-19.32 (7.65)	-16.98 (8.25)	-2.34 (-7.89, 3.22)
External Rotation	-12.99 (7.91)	-12.52 (8.15)	-0.47 (-6.09, 5.14)
Knee Moments			
Adduction (Peak 1)	**2.31 (0.85)**	**1.73 (0.69)**	**0.58 (0.03, 1.14)***
Adduction (Peak 2)	3.18 (1.16)	2.67 (0.81)	0.51 (-0.19, 1.22)
Flexion	0.60 (0.85)	0.79 (0.97)	-0.19 (-0.82, 0.44)
Extension	-2.22 (1.09)	-1.98 (1.05)	-0.24 (-0.99, 0.52)
Internal Rotation	-2.70 (1.22)	-2.62 (1.04)	-0.08 (-0.88, 0.72)
External Rotation	3.73 (1.66)	3.65 (1.20)	0.08 (-0.94, 1.11)

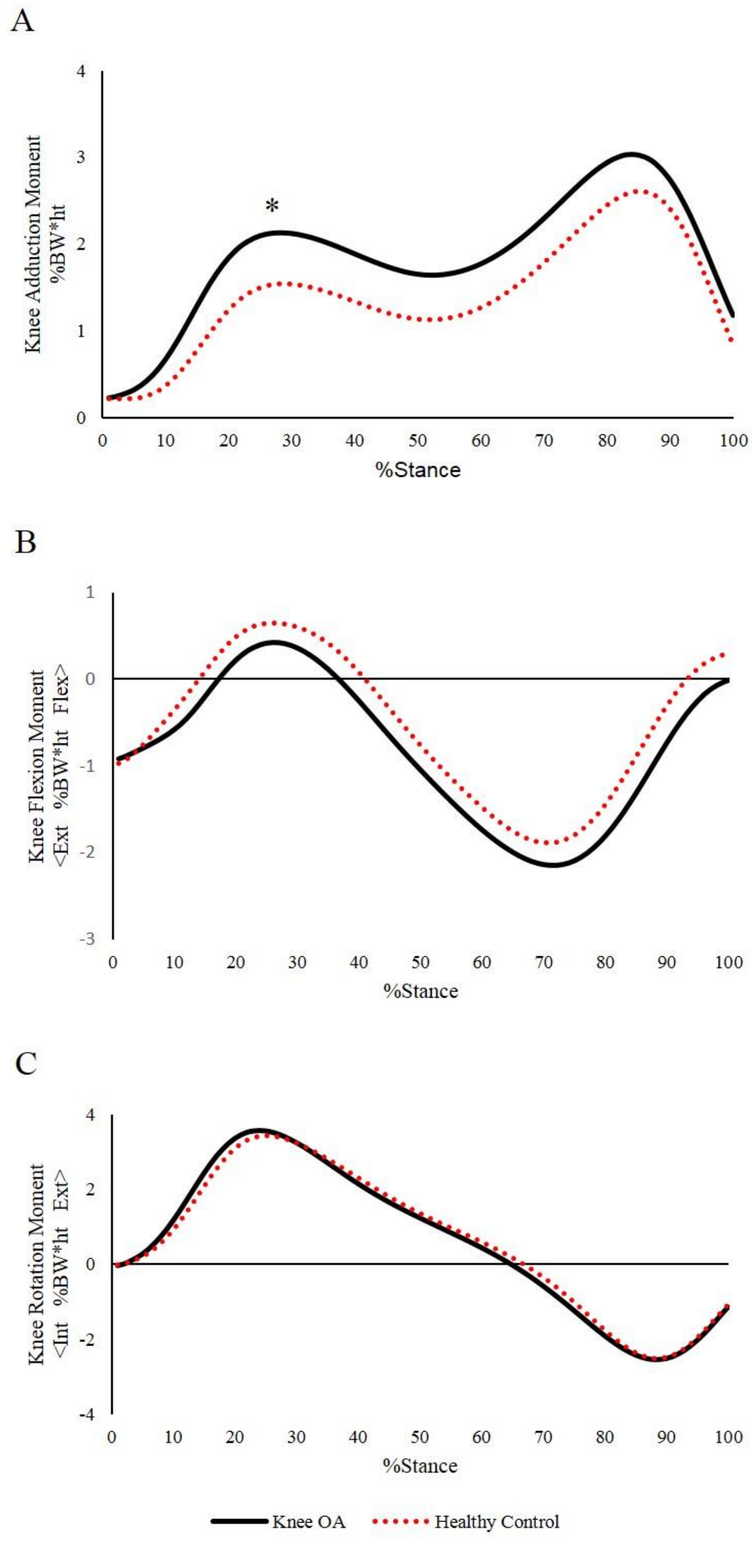


Figure 4.14. GRAIL ensemble averages for knee (a) adduction moment, (b) flexion moment and (c) rotation moment for patients with knee OA (solid line) and healthy controls (dotted line). BW = body weight, ht = height. *Significant difference between groups ($p < 0.05$)

Chapter 5

5 Discussion

5.1 Test-Retest Reliability

The present results suggest excellent test-retest reliability for knee varus angle and KAM peaks during gait in patients with medial compartment knee OA assessed using the GRAIL. It is particularly important that these specific gait parameter can be assessed reliably in this patient population because they are most commonly linked to medial compartment loading and to OA progression[20,35,57,58].

Good reliability was observed for knee flexion and extension angles, although it should be noted that the confidence intervals around the ICCs for those measures were quite wide, and we therefore cannot rule out poor reliability. For example, the knee flexion and extension angles had CIs with lower ends of 0.24 and 0.37, respectively. Similarly, the test-retest reliability of knee flexion and extension moments could be classified as good-to-excellent, but had CIs with lower ends of 0.10 and 0.48, respectively. It is unclear why these sagittal plane data were less reliable than the frontal plane data. Specifically, we do not know if there were measurement errors related to data collection and processing, or if patients' true sagittal plane values are more variable from day to day.

Internal and external rotation angles and moments can be described as having good-to-excellent reliability with wide CIs, with lower ends being classified as poor-to-good (0.10-0.45). Based on these preliminary results, internal/external rotation angles and moments should be interpreted with extreme caution.

While the ICC provides a measure of relative reliability (i.e. it can be used to described group performance as it represents the ratio of the between-subject variability to the total variability), the SEM provides a measure of absolute reliability (i.e. it can be used to describe an individual's performance). Perhaps with the exception of the frontal plane measures, all of the variables investigated in the present thesis had relatively large SEM values (Table 4.1). Accordingly, with the exception of the knee varus angle and the knee adduction moment, there was considerable error in an individual's measure at one time, and relatively large changes in an individual's change score would be needed to confidently know a true change had occurred.

For example, based on the present SEM for the first peak KAM (0.31), we can be 95% confident that a patient's value of 2.5 %BW*ht can vary from 1.89 to 3.11 %BW*ht (i.e. SEM x 1.96 = $\pm$ 0.61) simply due to measurement error. Furthermore, the calculated minimum detectable change (MDC_{95}) of $\pm$ 0.87 %BW*ht (i.e. SEM x 1.96 x $\sqrt{2}$ = $\pm$ 0.87) suggests that 95% of stable patients' KAM would change by less than 0.87 %BW*ht upon repeated testing. Therefore, if we observe a change in an individual patient's KAM $\geq$ 0.87 %BW*ht, for example following an intervention intended to decrease medial compartment loading, we can be confident that a true change in the KAM has occurred.

Results from studies investigating the test-retest reliability of gait data from other treadmill-based systems are inconsistent. Some authors report poor reliability in 14 of 16 temporospatial and kinetic gait parameters over three test sessions in healthy young adults[25], while other authors report no significant differences for the timing of gait events or the percentage spent in single and double limb support[22]. Moreover, another study suggests good test-rest reliability for temporospatial gait parameters, but lower reliability for stride time and length variability mearures[26]. We are unaware of previous studies evaluating the test-retest reliability of knee angles and moments from treadmill-based movement analysis systems, or for patients with knee OA. Previous studies used heterogeneous instrumentation, testing procedures, and sample populations[22,25,26]. Therefore, the generalizability of these studies to patients with medial compartment knee OA is limited.

By assessing the test-retest reliability, SEM and MDC of the GRAIL, we will be able to confidently use it as a measurement tool to assess change in patients' gait measures. Since we work primarily with patients with knee OA, it is crucial to understand the MDC values to confidently know if a true change has occurred in patients' gait parameters following various interventions.

5.2 Concurrent Validity

The present results suggest excellent associations between GRAIL and overground measurements for knee adduction and flexion/extension angles and moments. Although highly correlated to overground walking, the knee adduction angle was significantly lower on the GRAIL; however, these observed differences were less than 1.3° and would generally fall within the normal variability of gait parameters. Consistent with results reported by Riley et al.[22], we observed systematic differences ($<1.5^{\circ}$) between treadmill and overground measures for peak knee flexion and extension angles (Table 4.4), although differences did not reach statistical significance. The mean differences in the internal rotation angle (1.18°) and external rotation angle (1.71°) were also consistent, but small and not statistically significant (Table 4.4).

When walking on the GRAIL, subjects exhibited a smaller first peak KAM and larger second peak KAM with differences of 0.23 and 0.76 %BW*ht, respectively. The differences observed for the first peak KAM are similar to those described by van der Krogt and colleagues[29], who reported significantly lower knee adduction moments when walking on the GRAIL. The lower first peak KAM could potentially be attributed to a wider step width associated with walking on a split belt treadmill[67].

Previous investigators comparing gait data collected from the same participants using overground and treadmill movement analysis systems also report conflicting results. Some investigators report significant differences in the temporospatial aspects between the two walking modalities[70,71], while others report that the two modalities provide similar values[22,30]. When tested in healthy participants, some authors report the knee flexion angle range of motion (ROM) is lower when walking on a treadmill[22–24,70], while other authors suggest knee joint measurements are similar to overground values if a familiarization period of 5 minutes of treadmill walking is provided[30,31].

Opposite to previously reported findings comparing treadmill and overground walking [22,23,29], the present knee extension moments were statistically significantly higher when walking on the GRAIL. This difference might be attributed to either the differences in participants, or differences in testing procedures. All subjects in the present study ranged between 30-65 years of age and were required to walk overground first to determine a comfortable self-selected walking speed to be used for treadmill trials. van der Krogt and colleagues[29] tested nine children with spastic cerebral palsy and 11 typically developing children on the GRAIL, all ranging from ages 8-15. Children were randomized to either walk first on the GRAIL at a self-selected speed or overground in their own shoes. Also, in the present study, five clean force plate strikes were averaged for each patient and healthy control which differed from 2-5 (cerebral palsy) and 4-5 (typically developing) force plate strikes used in the van der Krogt and colleagues[29] study.

We observed excellent correlations for the internal rotation angle (r=0.78) and good correlations for the external rotation angle (r=0.69). Correlations between overground walking and the GRAIL measurements of internal and external rotation moments were the lowest (r=0.05-0.12). Moments in the transverse plane displayed the largest discrepancies between systems with significantly greater moments of 1.79 and 3.65 %BW*ht for the internal and external rotation moments, respectively (Table 4.4). These results suggest that data collected using the GRAIL cannot be readily compared with overground walking for transverse plane kinematics and kinetics.

5.3 Known-Groups Validity

The present results suggest that the GRAIL is able to distinguish between subjects with medial compartment knee OA and healthy controls based on the first peak KAM. Patients with knee OA had significantly higher first peak KAMs than healthy controls. Although the second peak KAM was 0.51 %BW*ht higher than healthy controls, the difference did not reach statistical significance. No other significant differences were observed between groups for other knee angles and moments.

This finding is consistent with the literature in that subjects with medial compartment knee OA demonstrate significantly higher peak KAMs than healthy controls[19,20,36]. Although there was not a significant difference seen in the second peak KAM, this could be due to the relatively small sample size, or to the fact that both patients and controls consistently displayed a higher second peak KAM on the treadmill when compared with overground walking.

Although not found to be significantly different, subjects with knee OA did exhibit less sagittal plane ROM on the treadmill when compared with the healthy group. This difference was seen to be only 1^{o} compared with previously reported values of 4-6^{o} during overground walking[39,64]. Patients with knee OA also exhibited a slightly lower KFM and slightly greater knee extension moment on the GRAIL when compared with healthy controls, though they were not found to be significantly different. Although not significant, the decreases observed in peak KFMs are consistent with previous reports showing that patients with medial compartment knee OA display a slightly lower flexion moment than healthy controls[36,61].

5.4 Limitations

The present results should be considered preliminary, as data collection is continuing. While the present point estimates are likely reasonably accurate, we anticipate they will change somewhat with a greater sample size, and importantly, the confidence intervals around the estimates will decrease. Another limitation in the present study is the variability in marker placement between test sessions. This was limited by having proper training for palpation of correct anatomical landmarks, and having one tester apply all markers on both test session. All subjects were instructed to wear tight fitting clothing to try to minimize potential marker artefacts caused by excess clothing movement. Variability across test sessions associated with re-calibrating the camera system is also possible. It should be noted, however, that errors associated with maker placement, soft tissue artefacts and re-calibration are all inherent in testing gait in patients with knee OA and should be considered when estimating reliability.

Between-day gait variability was reduced as much as possible by having all subjects come in within one week from their initial test session. We did this to minimize the chance that a true change occurred in their gait. In the first test session the subject completed an overground walking trial followed by a treadmill walking trial. They were allowed adequate rest until they felt comfortable to begin walking on the treadmill. The second test session consisted of only treadmill walking. Although it should not have a substantial effect on walking, fatigue may have played a role in the assessment of test-retest reliability of the GRAIL. To try to minimize the effects of fatigue, all subjects were given at least 5 minutes of rest between overground and treadmill trials and were then asked if they were ready to proceed. If not, then more rest was allotted until they felt ready to begin walking on the treadmill.

It should also be noted that there is a high number of patients with KL grade 2 knee OA. This could potentially contribute to a similar gait pattern between groups for some of the sagittal plane angles and moments. Future recruitment will focus on enrolling more patients with KL grade 3 and 4 knee OA to ensure a more even distribution of OA patients.

Chapter 6

6 Conclusion

Frontal and sagittal plane knee joint angles and moments during gait in patients with medial compartment knee OA can be assessed reliably using the GRAIL. Consistent with previous studies evaluating test-retest reliability of gait data assessed with conventional overground movement analysis systems, frontal and sagittal plane knee joint angles and moments can distinguish among groups of patients, and therefore are well-suited for use in studies evaluating gait in samples of patients with knee OA; however, individual performances can vary considerably and observed differences in a single patient's should be interpreted carefully. Measures of frontal and sagittal plane knee joint angles and moments assessed using the GRAIL and conventional overground movement analysis systems show good-to-excellent correlation. The transverse plane rotation angles and moments should be interpreted with greater caution as they show greater variance between test sessions and between movement analysis systems. The GRAIL is able to distinguish between patients with medial compartment knee OA and age-matched healthy controls based on the first peak KAM. Overall, these findings support our hypotheses and suggest adequate reliability, concurrent validity and know-groups validity.

References

1. Vos T, Barber RM, Bell B, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990-2013: A systematic analysis for the Global Burden of Disease Study 2013. *Lancet*. 2015;386(9995):743-800.

2. Cross M, Smith E, Hoy D, et al. The global burden of hip and knee osteoarthritis: estimates from the Global Burden of Disease 2010 study. *Ann Rheum Dis*. 2014;73(7):1323-1330.

3. Schipplein OD, Andriacchi TP. Interaction between active and passive knee stabilizers during level walking. *J Orthop Res*. 1991;9:113-119.

4. Cooper C, Snow S, McAlindon TE, et al. Risk factors for the incidence and progression of radiographic knee osteoarthritis. *Arthritis Rheum*. 2000;43(5):995-1000.

5. Amin S, Luepongsak N, McGibbon C a, LaValley MP, Krebs DE, Felson DT. Knee adduction moment and development of chronic knee pain in elders. *Arthritis Rheum*. 2004;51(3):371-376.

6. Creaby MW, Wang Y, Bennell KL, et al. Dynamic knee loading is related to cartilage defects and tibial plateau bone area in medial knee osteoarthritis. *Osteoarthr Cartil*. 2010;18:1380-1385.

7. Raynauld J-P, Martel-Pelletier J, Berthiaume M-J, et al. Long term evaluation of disease progression through the quantitative magnetic resonance imaging of symptomatic knee osteoarthritis patients: correlation with clinical symptoms and radiographic changes. *Arthritis Res Ther*. 2006;8(1):R21.

8. Felson DT. Osteoarthritis as a Disease of Mechanics. *Osteoarthr Cartil*. 2013;21:10-15.

9. Moyer RF, Birmingham TB, Chesworth BM, Kean CO, Giffin JR. Alignment, body mass and their interaction on dynamic knee joint load in patients with knee osteoarthritis. *Osteoarthr Cartil*. 2010;18(7):888-893.

10. Tudor-Locke C, Bassett DR. How Many Steps/Day Are Enough? Preliminary Pedometer Indices for Public Health. *Sport Med*. 2004;34(1):1-8.

11. Neogi T. The Epidermiology and Impact of Pain in Osteoarthritis. *Osteoarthr Res Soc*. 2013;21(9):1145-1153.

12. Creamer P, Lethbridge-Cejku M, Hochberg MC. Factors associated with functional impairment in symptomatic knee osteoarthritis. *Rheumatology (Oxford)*. 2000;39(5):490-496.

13. Thomas E, Peat G, Mallen C, et al. Predicting the course of functional limitation among older adults with knee pain: do local signs, symptoms and radiographs add anything to general indicators? *Ann Rheum Dis*. 2008;67(10):1390-1398.

14. Kovar PA, Allegrante JP, MacKenzie CR, Peterson MGE, Gutin B, Charlson ME. Supervised fitness walking in patients with osteoarthritis of the knee: A randomized, controlled trial. *Ann Intern Med*. 1992;116:529-534.

15. Bieler T, Siersma V, Magnusson SP, Kjaer M, Christensen HE, Beyer N. In hip osteoarthritis, Nordic Walking is superior to strength training and home-based exercise for improving function. *Scand J Med Sci Sports*. 2016:1-14.

16. Evcik D, Sonel B. Effectiveness of a home-based exercise therapy and walking program on osteoarthritis of the knee. *Rheumatol Int*. 2002;22:103-106.

17. Moyer RF, Birmingham TB, Dombroski CE, et al. Combined effects of a valgus knee brace and lateral wedge foot orthotic on the external knee adduction moment in patients with varus gonarthrosis. *Arch Phys Med Rehabil*. 2013;94(1):103-112.

18. Birmingham TB, Giffin JR, Chesworth BM, et al. Medial opening wedge high tibial osteotomy: A prospective cohort study of gait, radiographic, and patient-reported outcomes. *Arthritis Care Res*. 2009;61(5):648-657.

19. Kadaba MP, Ramakrishnan HK, Wootten ME, Gainey J, Gorton G, Cochran G V. Repeatability of kinematic, kinetic, and electromyographic data in normal adult gait. *J Orthop Res*. 1989;7:849-860.

20. Birmingham TB, Hunt M a., Jones IC, Jenkyn TR, Giffin JR. Test-retest reliability of the peak knee adduction moment during walking in patients with medial compartment knee osteoarthritis. *Arthritis Care Res*. 2007;57(6):1012-1017.

21. Robbins SMK, Birmingham TB, Jones GR, Callaghan JP, Maly MR. Developing an estimate of daily cumulative loading for the knee: Examining test-retest reliability. *Gait Posture*. 2009;30(4):497-501.

22. Riley PO, Paolini G, Croce U Della, Paylo KW, Kerrigan DC, a. Kinematic and Kinetic Comparison of Overground and Treadmill Walking in Healthy Subjects. *Gait Posture*. 2007;26:17-24.

23. Lee SJ, Hidler J. Biomechanics of overground vs. treadmill walking in healthy individuals. *J Appl Physiol*. 2008;104:747-755.

24. Gates DH, Darter BJ, Dingwell JB, Wilken JM. Comparison of walking overground and in a Computer Assisted Rehabilitation Environment (CAREN) in individuals with and without transtibial amputation. *J Neuroeng Rehabil*. 2012;9(1):81.

25. Reed LF, Urry SR, Wearing SC. Reliability of spatiotemporal and kinetic gait parameters determined by a new instrumented treadmill system. *BMC Musculoskelet Disord*. 2013;14(1):249-260.

26. Faude O, Donath L, Roth R, Fricker L, Zahner L. Reliability of gait parameters during treadmill walking in community-dwelling healthy seniors. *Gait Posture*. 2012;36(3):444-448.

27. Parvataneni K. Ploeg L. Olney S.J. Brouwer B. Kinematic, kinetic and metabolic parameters of treadmill versus overground walking in healthy older adults. *Clin Biomech*. 2009:95-100.

28. van der Krogt M, Sloot L, Hoekstra T, Kraan L, Harlaar J. Kinematic evaluation of walking on the “GRAIL” versus overground. *Gait Posture*. 2014;39(2014):S50-S51.

29. van der Krogt MM, Sloot LH, Buizer AI, Harlaar J. Kinetic comparison of walking on a treadmill versus over ground in children with cerebral palsy. *J Biomech*. 2015;48:3586-3592.

30. Matsas A. Knee joint kinematics from familiarised treadmill walking can be generalised to overground walking in young unimpaired subjects. *Gait Posture*. 2000;11(1):46-53.

31. Zeni J a., Higginson JS. Gait parameters and stride-to-stride variability during familiarization to walking on a split-belt treadmill. *Clin Biomech*. 2010;25(4):383-386.

32. Alton F, Baldey L, Caplan S, Morrissey MC. A kinematic comparison of overground and treadmill walking. *Clin Biomech*. 1998;13:434-440.

33. Hollman JH, Watkins MK, Imhoff AC, Braun CE, Akervik K a., Ness DK. A comparison of variability in spatiotemporal gait parameters between treadmill and overground walking conditions. *Gait Posture*. 2016;43:204-209.

34. van der Krogt MM, Sloot LH, Harlaar J. Overground versus self-paced treadmill walking in a virtual environment in children with cerebral palsy. *Gait Posture*. 2014;40(4):587-593.

35. Miyazaki T, Wada M, Kawahara H, Sato M, Baba H, Shimada S. Dynamic load at baseline can predict radiographic disease progression in medial compartment knee osteoarthritis. *Ann Rheum Dis*. 2002;61:617-622.

36. Baliunas a. J, Hurwitz DE, Ryals a. B, et al. Increased knee joint loads during walking are present in subjects with knee osteoarthritis. *Osteoarthr Cartil*. 2002;10:573-579.

37. Bytyqi D, Shabani B, Lustig S, Cheze L, Karahoda Gjurgjeala N, Neyret P. Gait knee kinematic alterations in medial osteoarthritis: Three dimensional assessment. *Int Orthop*. 2014;38:1191-1198.

38. Nagano Y, Naito K, Saho Y, et al. Association between in vivo knee kinematics during gait and the severity of knee osteoarthritis. *Knee*. 2012;19:628-632.

39. Kaufman KR, Hughes C, Morrey BF, Morrey M, An KN. Gait characteristics of patients with knee osteoarthritis. *J Biomech*. 2001;34:907-915.

40. Macdonald K V, Sanmartin C, Langlois K, Marshall D a. Symptom onset, diagnosis and management of osteoarthritis. *Stat Canada*. 2014;25:10-17.

41. Vos T, Flaxman AD, Naghavi M, et al. Years lived with disability for 1160 sequelae of 289 diseases and injuries 1990-2010: A systematic analysis for the Global Burden of Disease Study 2010. *Lancet*. 2012;380:2163-2196.

42. Borkhoff CM, Wieland ML, Myasoedova E, et al. Reaching those most in need: a scoping review of interventions to improve health care quality for disadvantaged populations with osteoarthritis. *Arthritis Care Res (Hoboken)*. 2011;63(1):39-52.

43. Altman R, Asch E, Bloch D, et al. Development of criteria for the classification and reporting of osteoarthritis. Classification of osteoarthritis of the knee. Diagnostic and Therapeutic Criteria Committee of the American Rheumatism Association. *Arthritis Rheum*. 1986;29:1039-1049.

44. Kellgren JH, Lawrence JS. Radiological Assessment of Osteo-Arthrosis. *Ann Rheum Dis*. 1957;16(3):494-502.

45. Arden N, Blanco F, Cooper C, et al. Atlas of Osteoarthritis. 2015:90.

46. Andriacchi TP, Favre J, Erhart-Hledik JC, Chu CR. A Systems View of Risk Factors for Knee Osteoarthritis Reveals Insights into the Pathogenesis of the Disease. *Ann Biomed Eng*. 2015;43(2):376-387.

47. Sharma L, Song J, Felson DT, Cahue S, Shamiyeh E, Dunlop DD. The role of knee alignment in disease progression and functional decline in knee osteoarthritis. *JAMA*. 2001;286(2):188-195.

48. Sharma L. Local factors in osteoarthritis. *Curr Opin Rheumatol*. 2001;13:441-446.

49. Cerejo R, Dunlop DD, Cahue S, Channin D, Song J, Sharma L. The influence of alignment on risk of knee osteoarthritis progression according to baseline stage of disease. *Arthritis Rheum*. 2002;46(10):2632-2636.

50. Tetsworth K, Paley D. Malalignment and degenerative arthropathy. *Orthop Clin North Am*. 1994;25:367-377.

51. Hsu R, S H, Mb C, Ey C. Normal axial alignment of the lower extremity and load-bearing distribution at the knee. *Clin Orthop Relat Res*. 1990:215-227.

52. Andriacchi TP, Mundermann A, Smith RL, Alexander EJ, Dyrby CO, Koo S. A framework for the in vivo pathomechanics of osteoarthritis at the knee. *Ann Biomed Eng*. 2004;32(3):447-457.

53. Heidari B. Knee osteoarthritis prevalence, risk factors, pathogenesis and features: Part I. *Casp J Intern Med*. 2011;2:206-212.

54. Magee DJ. *Orthopedic Physical Assessment*.; 2002.

55. Perry J. *Gait Analysis - Normal and Pathological Function*.; 1992.

56. Hurwitz DE, Ryals a R, Karar A, Case JP, Andriacchi TP. Static Alignment is a Better Indicator of the Dynamic Knee Joint Loads During Gait in Subjects with Knee Osteoarthritis Than Radiographic Disease Severity, Toe Out Angle and Pain. *Orthop Res Soc*. 2002;20:101-107.

57. Foroughi N, Smith R, Vanwanseele B. The association of external knee adduction moment with biomechanical variables in osteoarthritis: A systematic review. *Knee*. 2009;16:303-309.

58. Sharma L, Hurwitz DE, Thonar EJM a, et al. Knee adduction moment, serum hyaluronan level, and disease severity in medial tibiofemoral osteoarthritis. *Arthritis Rheum*. 1998;41:1233-1240.

59. Andriacchi TP, Mündermann A. The role of ambulatory mechanics in the initiation and progression of knee osteoarthritis. *Curr Opin Rheumatol*. 2006;18:514-518.

60. Hurwitz DE, Ryals a R, Block J a, Sharma L, Schnitzer TJ, Andriacchi TP. Knee pain and joint loading in subjects with osteoarthritis of the knee. *J Orthop Res*. 2000;18:572-579.

61. Astephen JL, Deluzio KJ, Caldwell GE, Dunbar MJ. Biomechanical changes at the hip, knee, and ankle joints during gait are associated with knee osteoarthritis severity. *J Orthop Res*. 2008;26:332-341.

62. Walter JP, D’Lima DD, Colwell CW, Fregly BJ. Decreased knee adduction moment does not guarantee decreased medial contact force during gait. *J Orthop Res*. 2010;28:1348-1354.

63. Chang a. H, Moisio KC, Chmiel JS, et al. External knee adduction and flexion moments during gait and medial tibiofemoral disease progression in knee osteoarthritis. *Osteoarthr Cartil*. 2014;23:1099-1106.

64. Childs JD, Sparto PJ, Fitzgerald GK, Bizzini M, Irrgang JJ. Alterations in lower extremity movement and muscle activation patterns in individuals with knee osteoarthritis. *Clin Biomech*. 2004;19:44-49.

65. Nagao N, Tachibana T, Mizuno K. The rotational angle in osteoarthritic knees. *Int Orthop*. 1998;22:282-287.

66. Matsui Y, Kadoya Y, Uehara K, Kobayashi A, Takaoka K. Rotational deformity in varus osteoarthritis of the knee: analysis with computed tomography. *Clin Orthop Relat Res*. 2005;(433):147-151.

67. Altman AR, Reisman DS, Higginson JS, Davis IS. Kinematic comparison of split-belt and single-belt treadmill walking and the effects of accommodation. *Gait Posture*. 2012;35:287-291.

68. Van Ingen Schenau G. Some fundamental aspects of the biomechanics of overground versus treadmill locomotion. *Med Sci Sport Exerc*. 1980;12:257.

69. Harlaar J. Sloot L. Van Der Krogt M. Effects of a virtual reality environment in self-paced treadmill walking. *Gait Posture*. 2013:S109-S110.

70. Murray MP, Spurr GB, Sepic SB, Gardner GM, Mollinger L a. Treadmill vs. floor walking: kinematics, electromyogram, and heart rate. *J Appl Physiol*. 1985;59(5):87-91.

71. Stolze H, Kuhtz-Buschbeck JP, Mondwurf C, et al. Gait analysis during treadmill and overground locomotion in children and adults. *Electroencephalogr Clin Neurophysiol - Electromyogr Mot Control*. 1997;105:490-497.

72. Sloot LH, van der Krogt MM, Harlaar J. The biomechanical effect of virtual reality depends on treadmill mode. *Gait Posture*. 2014;39(2014):S49-S50.

73. Sloot LH, van der Krogt MM, Harlaar J. Energy exchange between subject and belt during treadmill walking. *J Biomech*. 2014;47(6):1510-1513.

74. *CORTEX Version 5.0 Reference Manual*. Santa Rosa, CA: Motion Analysis Corporation; 2013.

75. *KinTools RT*. Santa Rosa, CA: Motion Analysis Corporation; 2010.

76. de Lava P. Adjustments to Zatsiorsky-Seluyanov's segment inertia parameters. *Medicine (Baltimore)*. 1998;24(7):1065-1068.

77. Bonett DG. Sample size requirements for estimating intraclass correlations with desired precision. *Stat Med*. 2002;21(May 2002):1331-1335.

78. Stratford PW, Goldsmith CH. Use of the standard error as a reliability index of interest: an applied example using elbow flexor strength data. *Phys Ther*. 1997;77:745-750.

79. Stratford PW, Binkley J, Solomon P, et al. Defining the Minimum Level of Detectable Change for the Roland- Morris Questionnaire. 1996;76(4):359-365.

80. Fleiss JL. *Design and Analysis of Clinical Experiments*. New York: Wiley & Sons; 1986.

Appendix A

Par-Q Form

Physical Activity Readiness
Questionnaire - PAR-Q
(revised 2002)

PAR-Q & YOU

(A Questionnaire for People Aged 15 to 69)

Regular physical activity is fun and healthy, and increasingly more people are starting to become more active every day. Being more active is very safe for most people. However, some people should check with their doctor before they start becoming much more physically active.

If you are planning to become much more physically active than you are now, start by answering the seven questions in the box below. If you are between the ages of 15 and 69, the PAR-Q will tell you if you should check with your doctor before you start. If you are over 69 years of age, and you are not used to being very active, check with your doctor.

Common sense is your best guide when you answer these questions. Please read the questions carefully and answer each one honestly: check YES or NO.

YES	NO	
☐	☐	**1. Has your doctor ever said that you have a heart condition and that you should only do physical activity recommended by a doctor?**
☐	☐	**2. Do you feel pain in your chest when you do physical activity?**
☐	☐	**3. In the past month, have you had chest pain when you were not doing physical activity?**
☐	☐	**4. Do you lose your balance because of dizziness or do you ever lose consciousness?**
☐	☐	**5. Do you have a bone or joint problem (for example, back, knee or hip) that could be made worse by a change in your physical activity?**
☐	☐	**6. Is your doctor currently prescribing drugs (for example, water pills) for your blood pressure or heart condition?**
☐	☐	**7. Do you know of any other reason why you should not do physical activity?**

If you answered

YES to one or more questions

Talk with your doctor by phone or in person BEFORE you start becoming much more physically active or BEFORE you have a fitness appraisal. Tell your doctor about the PAR-Q and which questions you answered YES.

- You may be able to do any activity you want — as long as you start slowly and build up gradually. Or, you may need to restrict your activities to those which are safe for you. Talk with your doctor about the kinds of activities you wish to participate in and follow his/her advice.
- Find out which community programs are safe and helpful for you.

NO to all questions

If you answered NO honestly to all PAR-Q questions, you can be reasonably sure that you can:

- start becoming much more physically active – begin slowly and build up gradually. This is the safest and easiest way to go.
- take part in a fitness appraisal – this is an excellent way to determine your basic fitness so that you can plan the best way for you to live actively. It is also highly recommended that you have your blood pressure evaluated. If your reading is over 144/94, talk with your doctor before you start becoming much more physically active.

DELAY BECOMING MUCH MORE ACTIVE:

- if you are not feeling well because of a temporary illness such as a cold or a fever – wait until you feel better; or
- if you are or may be pregnant – talk to your doctor before you start becoming more active.

PLEASE NOTE: If your health changes so that you then answer YES to any of the above questions, tell your fitness or health professional. Ask whether you should change your physical activity plan.

Informed Use of the PAR-Q: The Canadian Society for Exercise Physiology, Health Canada, and their agents assume no liability for persons who undertake physical activity, and if in doubt after completing this questionnaire, consult your doctor prior to physical activity.

No changes permitted. You are encouraged to photocopy the PAR-Q but only if you use the entire form.

NOTE: If the PAR-Q is being given to a person before he or she participates in a physical activity program or a fitness appraisal, this section may be used for legal or administrative purposes.

"I have read, understood and completed this questionnaire. Any questions I had were answered to my full satisfaction."

NAME ________________________________

SIGNATURE ________________________________ DATE ________________________

SIGNATURE OF PARENT ________________________________ WITNESS ________________________
or GUARDIAN (for participants under the age of majority)

Note: This physical activity clearance is valid for a maximum of 12 months from the date it is completed and becomes invalid if your condition changes so that you would answer YES to any of the seven questions.

Appendix B

Letters of Information and Consent Forms for patients with knee OA and healthy controls

LETTER OF EXPLANATION FOR THE STUDY
Primary Investigator: Trevor Birmingham PhD
Co-Investigators: Ryan Pinto, MSc Candidate, Robert Giffin MD

Project Title: **Gait Real-Time Analysis Interactive Lab: Reliability and Validity of Knee Joint Angles and Moments**

What is the purpose and what are the potential benefits of the study?
The purpose of this letter is to provide you with the information you require to make an informed decision about participating in this study. The study in which you are asked to participate is designed to investigate the measurement properties (test-retest reliability and validity) of the Gait Real-Time Analysis Interactive Lab (GRAIL). The GRAIL consists of a treadmill that measures the forces placed on it, motion sensing cameras that can follow your joints, and projectors that create virtual reality (VR) depictions of real-life settings. This testing will add to our capability of investigating gait biomechanics with newer technology in a realistic environment. Individuals are invited to voluntarily participate in this study.

What are the criteria for participating in the study?
You are invited to participate in this study because you meet the eligibility criteria for the knee osteoarthritis (OA) group. For the knee OA group, you must have knee OA as determined by x-ray and physician diagnosis. There will be a total of 35 participants recruited for the knee OA group as well as 35 participants for a separate healthy control group.

What is the procedure?
You will be asked to perform several walking trials in the Wolf Orthopaedic Biomechanics Lab, Fowler Kennedy Sport Medicine Clinic in the 3M Centre at the University of Western Ontario. You will be asked to walk through the laboratory ten to fifteen times over a ten metre runway, and approximately ten minutes walking on a treadmill. We encourage you to approach all walking tasks as you would in a normal, everyday setting. While you are walking, you will wear positional markers which are placed over your toes, heels, ankles, knees, thighs, pelvis, scapula, shoulders, elbows, and wrists allowing monitoring of your movements and your muscles during walking. The positional markers only detect activity, they do not send electricity to you and are not painful. Motion sensing cameras will only pick up marker position and will not capture your identity. A safety harness will be made available to you during treadmill walking.

How long and how many visits does the testing involve?
The testing will be completed in two laboratory sessions within one week yet separated by at least 24 hours. We anticipate 1 hour of time to allow for warm-up and completion of the test.

Are there any discomforts or risks associated with testing?
There are no identified risks in participating in this study beyond the normal risk of injury related to performing regular walking and treadmill walking. A safety harness will be available for the treadmill portion of the study.

Will the results be kept confidential?
Your individual results will be held in strict confidence. No person other than the investigators will be given access to your records without your expressed permission. When the results are reported, individual records will be coded or reported as group data. Computer files of data collected will be stored on a password protected hard drive in the Wolf Orthopedic Biomechanics Lab located behind secure-locking doors. Written records will be secured in a locked cabinet at the Wolf Orthopedic Biomechanics Lab. The information collected will be retained for a period of 15 years, as per the guidelines for research records

Is your participation voluntary?

Participation in the study is voluntary. You may refuse to participate, withdraw consent or/and withdraw your data from the study at any time with no effect on you. You may decline being contacted for further research that may continue from this project. Participation in this study does not prevent you from participating in other research studies at the present time or in the future. There will be no direct compensation to you for participation in this study.

Who should you contact with any questions?

Please contact us at the address below, or by phone, to ask any questions you may have about the study.
Trevor Birmingham PhD
Professor
[redacted]

Ryan Pinto BSc
MSc Graduate Student
[redacted]

Representatives of Western University's Health Sciences Research Ethics Board may contact you or require access to your study-related records to monitor the conduct of the research. If you have any questions about your rights as a research participant or the conduct of the study you may contact, Director of the Office of Research Ethics [redacted]

Please keep this information letter for future reference.

Thank you.

[redacted]

Trevor Birmingham

CONSENT FORM

Gait Real-Time Analysis Interactive Lab: Reliability and Validity of Knee Joint Angles and Moments

I have read the Letter of Information, have had the nature of the study explained to me and I agree to participate. All questions have been answered to my satisfaction.

_________________________ _________________________ _______________

Print Name Signature Date

Preferred Method of Contact: Email ___ Phone ___

Contact Information ____

Signature of Person Obtaining Consent

_________________________ _________________________ _______________

Print Name Signature Date

Possibility of future research

There may be future opportunities for you to participate in ongoing research. If you are interested in being contacted, please check the appropriate box below. If contacted, you will be asked to read a new letter of information and sign a new consent form.

□ Please do not keep my name and contact information. I do not wish to be contacted in the future.

□ Please keep my name and contact information so that I may be contacted to learn about future research opportunities or have access to my data in the future.

By signing this consent form I acknowledge that I do not waive my legal rights

LETTER OF EXPLANATION FOR THE STUDY
Primary Investigator: Trevor Birmingham PhD
Co-Investigators: Ryan Pinto, MSc Candidate, Robert Giffin MD

Project Title: **Gait Real-Time Analysis Interactive Lab: Reliability and Validity of Knee Joint Angles and Moments**

What is the purpose and what are the potential benefits of the study?

The purpose of this letter is to provide you with the information you require to make an informed decision about participating in this study. The study in which you are asked to participate is designed to investigate the measurement properties (test-retest reliability and validity) of the Gait Real-Time Analysis Interactive Lab (GRAIL). The GRAIL consists of a treadmill that measures the forces placed on it, motion sensing cameras that can follow your joints, and projectors that create virtual reality (VR) depictions of real-life settings. This testing will add to our capability of investigating gait biomechanics with newer technology in a realistic environment. Individuals are invited to voluntarily participate in this study.

What are the criteria for participating in the study?

You are invited to participate in this study because you meet the eligibility criteria for the healthy group. For the healthy group, you must have no pre-existing injuries or disabilities that would affect your walking ability. There will be a total of 35 participants recruited for the healthy group as well as 35 participants for a separate knee osteoarthritis group.

What is the procedure?

You will be asked to perform several walking trials in the Wolf Orthopaedic Biomechanics Lab, Fowler Kennedy Sport Medicine Clinic in the 3M Centre at the University of Western Ontario. You will be asked to walk through the laboratory ten to fifteen times over a ten metre runway, and approximately ten minutes walking on a treadmill. We encourage you to approach all walking tasks as you would in a normal, everyday setting. While you are walking, you will wear positional markers which are placed over your toes, heels, ankles, knees, thighs, pelvis, scapula, shoulders, elbows, and wrists allowing monitoring of your movements and your muscles during walking. The positional markers only detect activity, they do not send electricity to you and are not painful. Motion sensing cameras will only pick up marker position and will not capture your identity. A safety harness will be made available to you during treadmill walking.

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Will the results be kept confidential?

Your individual results will be held in strict confidence. No person other than the investigators will be given access to your records without your expressed permission. When the results are reported, individual records will be coded or reported as group data. Computer files of data collected will be stored on a password protected hard drive in the Wolf Orthopedic Biomechanics Lab located behind secure-locking doors. Written records will be secured in a locked cabinet at the Wolf Orthopedic Biomechanics Lab. The information collected will be retained for a period of 15 years, as per the guidelines for research records

Is your participation voluntary?

Participation in the study is voluntary. You may refuse to participate, withdraw consent or/and withdraw your data from the study at any time with no effect on you. You may decline being contacted for further research that may continue from this project. Participation in this study does not prevent you from participating in other research studies at the present time or in the future. There will be no direct compensation to you for participation in this study.

Who should you contact with any questions?

Please contact us at the address below, or by phone, to ask any questions you may have about the study.

Trevor Birmingham PhD
Professor
[redacted]

Ryan Pinto BSc
MSc Graduate Student
[redacted]

Representatives of Western University's Health Sciences Research Ethics Board may contact you or require access to your study-related records to monitor the conduct of the research. If you have any questions about your rights as a research participant or the conduct of the study you may contact, Director of the Office of Research Ethics [redacted]

Please keep this information letter for future reference.

Thank you.

[redacted]

Trevor Birmingham

CONSENT FORM

Gait Real-Time Analysis Interactive Lab: Reliability and Validity of Knee Joint Angles and Moments

I have read the Letter of Information, have had the nature of the study explained to me and I agree to participate. All questions have been answered to my satisfaction.

__________________________ ________________________ ________________

Print Name Signature Date

Preferred Method of Contact: Email ___ Phone ___

Contact Information ____

Signature of Person Obtaining Consent

_________________________ ________________________ _______________

Print Name Signature Date

Possibility of future research

There may be future opportunities for you to participate in ongoing research. If you are interested in being contacted, please check the appropriate box below. If contacted, you will be asked to read a new letter of information and sign a new consent form.

□ Please do not keep my name and contact information. I do not wish to be contacted in the future.

□ Please keep my name and contact information so that I may be contacted to learn about future research opportunities or have access to my data in the future.

By signing this consent form I acknowledge that I do not waive my legal rights

Appendix C

Ethics Approval Notice

Western Research

Research Ethics

Western University Health Science Research Ethics Board
HSREB Delegated Initial Approval Notice

Principal Investigator: Dr. Trevor Birmingham
Department & Institution: Health Sciences\Physical Therapy,Western University

Review Type: Delegated
HSREB File Number: 107146
Study Title: Gait Real-Time Analysis Interactive Lab: Reliability and Validity of Lower Limb Kinematics and Kinetics
Sponsor:

HSREB Initial Approval Date: November 05, 2015
HSREB Expiry Date: November 05, 2016

Documents Approved and/or Received for Information:

Document Name	Comments	Version Date
Instruments	PAR-Q Form (Received 6Oct15)	
Western University Protocol	Revised Western Protocol Clean Version	2015/09/25
Letter of Information & Consent	Knee OA Group LOI and Consent Clean Version	2015/09/25
Letter of Information & Consent	Healthy Group LOI and Consent Clean Version	2015/09/25

The Western University Health Science Research Ethics Board (HSREB) has reviewed and approved the above named study, as of the HSREB Initial Approval Date noted above.

HSREB approval for this study remains valid until the HSREB Expiry Date noted above, conditional to timely submission and acceptance of HSREB Continuing Ethics Review.

The Western University HSREB operates in compliance with the Tri-Council Policy Statement Ethical Conduct for Research Involving Humans (TCPS2), the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use Guideline for Good Clinical Practice Practices (ICH E6 R1), the Ontario Personal Health Information Protection Act (PHIPA, 2004), Part 4 of the Natural Health Product Regulations, Health Canada Medical Device Regulations and Part C, Division 5, of the Food and Drug Regulations of Health Canada.

Members of the HSREB who are named as Investigators in research studies do not participate in discussions related to, nor vote on such studies when they are presented to the REB.

The HSREB is registered with the U.S. Department of Health & Human Services under the IRB registration number IRB 00000940.

[redacted]

Ethics Officer, on behalf of Dr. Joseph Gilbert, HSREB Chair

[redacted]

This is an official document. Please retain the original in your files

Western University, Research, Support Services Bldg., Rm. 5150
London, ON, Canada N6G 1G9 t. 519.661.3036 f. 519.850.2466 www.uwo.ca/research/ethics

Appendix D

Marker Sets

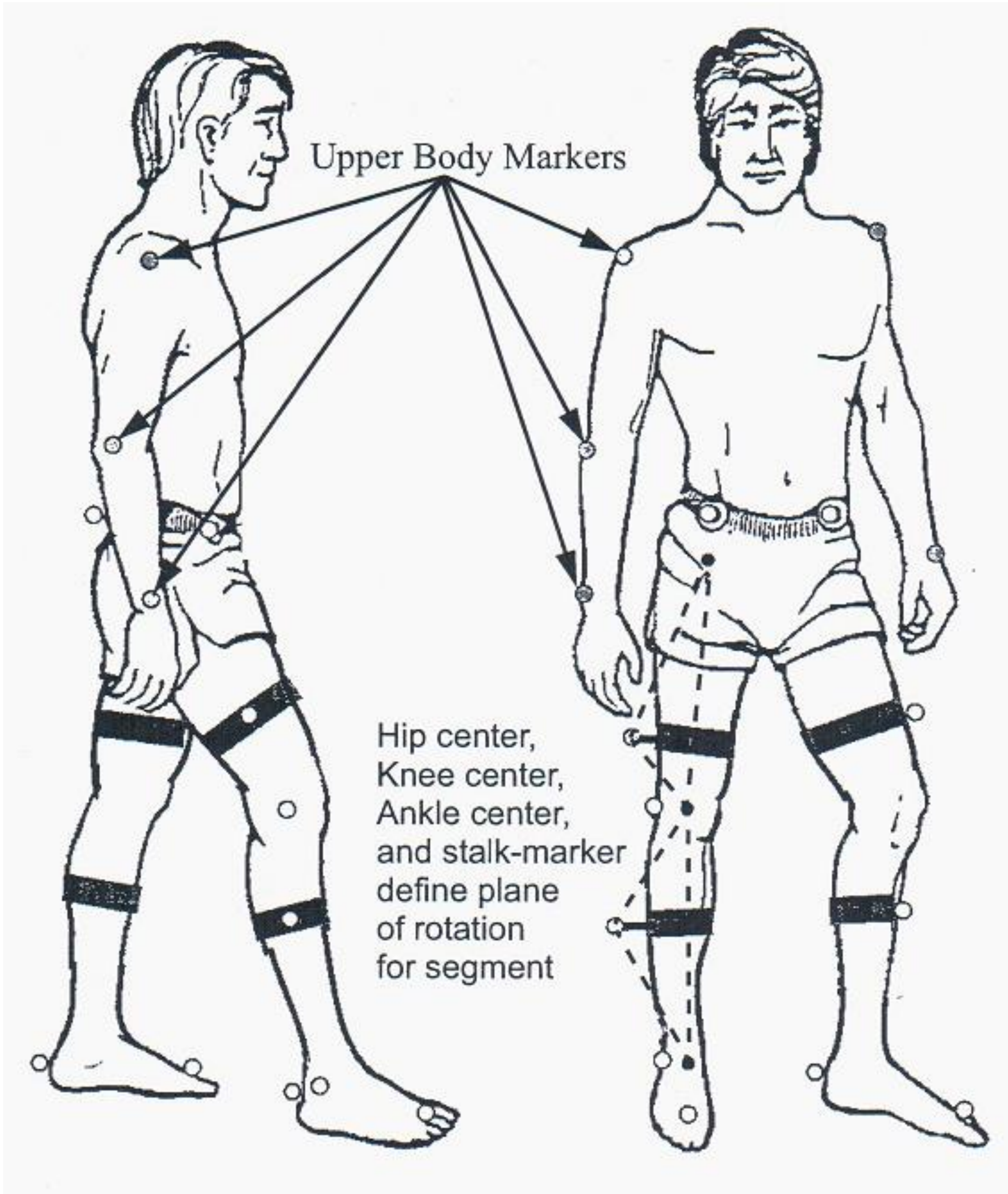

Figure D.1. Helen Hayes marker set placement. Reproduced from Motion Analysis Corporation[1].

Table D.1. Helen Hayes marker placement descriptions. Adapted from Motion Analysis Corporation[1].

Name	Static	Lower Body	Full Body	Placement
Left Lateral Knee Right Lateral Knee	+	+	+	Along flexion/extension axis on lateral femoral condyle
Left Medial Knee Right Medial Knee	+			Along flexion/extension axis on medial femoral condyle
Left Lateral Ankle Right Lateral Ankle	+	+	+	Over the lateral malleolus of the ankle
Left Medial Ankle Right Medial Ankle	+			Over the medial malleolus of the ankle
Left Thigh Right Thigh	+	+	+	Just below the mid-point of the thigh
Left Shank Right Shank	+	+	+	On the mid-point of the lower shank
Left Toe Right Toe	+	+	+	Centre of foot between 2nd and 3rd metatarsals
Left Heel Right Heel	+	+	+	Posterior calcaneus at same height as the toe marker
Left ASIS Right ASIS	+	+	+	Anterior superior iliac spine
Sacrum	+	+	+	Superior aspect of the L5-sacral joint
Left Shoulder Right Shoulder			+	Tip of acromion process
Left Elbow Right Elbow			+	Lateral epicondyle of the humerus
Left Wrist Right Wrist			+	Centred between the styloid processes of the radius and ulna

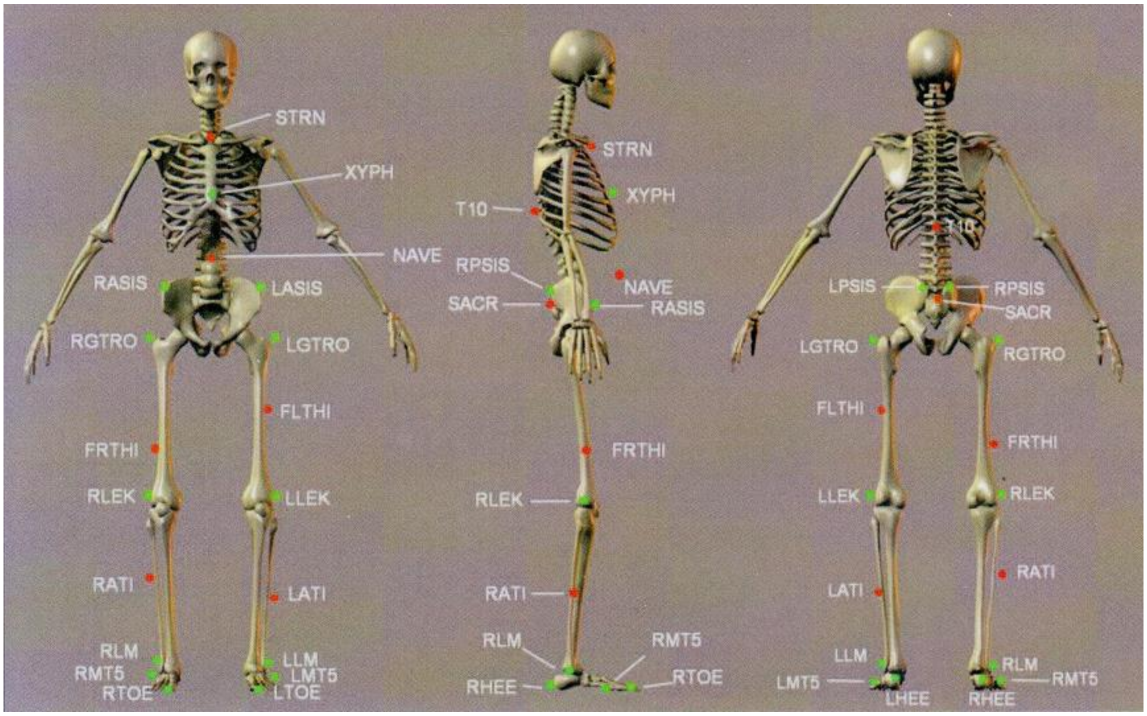

Figure D.2. GRAIL Lower Limb marker set. Reproduced from Motek Medical[2].

Table D.2. GRAIL Lower Limb marker set placement. Reproduced from Motek Medical[2].

Name	Position	Placement
T10	T10	10^{th} thoracic vertebrae
SACR	Sacrum bone	Sacral bone
NAVE	Navel	Navel
XYPH	Xyphoid process	Xyphoid process of the sternum
STRN	Sternum	Jugular notch of the sternum
LASIS	Front left pelvic bone	Left anterior superior iliac spine
RASIS	Front right pelvic bone	Right anterior superior iliac spine
LPSIS	Back left pelvic bone	Left posterior superior iliac spine
RPSIS	Back right pelvic bone	Right posterior superior iliac spine
LGTRO	Left femur greater trochanter	Centre of the greater trochanter
FLTHI	Left thigh	1/3 of the distance from the LGTRO to the LLEK
LLEK	Left lateral epicondyle of the knee	Lateral side of the joint line
LATI	Left tibia	2/3 of the distance from the LLEK to the LLM
LLM	Left lateral malleolus of the ankle	Centre of the left lateral malleolus
LHEE	Left heel	Centre of the heel at the same height as the toe marker
LTOE	Left toe	Centre of the foot between the 2^{nd} and 3^{rd} metatarsals
LMT5	Left 5^{th} metatarsal	Base of the 5^{th} metatarsal bone on the joint line
RGTRO	Right femur greater trochanter	Centre of the greater trochanter

FRTHI	Right thigh	1/3 of the distance from the RGTRO to the RLEK
RLEK	Right lateral epicondyle of the knee	Lateral side of the joint line
RATI	Right tibia	2/3 of the distance from the RLEK to the RLM
RLM	Right lateral malleolus of the ankle	Centre of the right lateral malleolus
RHEE	Right heel	Centre of the heel at the same height as the toe marker
RTOE	Right toe	Centre of the foot between the 2nd and 3rd metatarsals
RMT5	Right 5th metatarsal	Base of the 5th metatarsal bone on the joint line

References

1. *OrthoTrak 5.2 Gait Analysis Software Reference Manual*: Motion Analysis Corporation, Santa Rosa, CA; 2001.

2. *HBM Human Body Model Reference Manual*: Motek Medical, Amsterdam, NL; 2014.

RYAN PINTO

EDUCATION & TRAINING

Master of Science (M.Sc.), Health & Rehabilitation Sciences (Candidate) 2014 – Present
Specialization: Physical Therapy Science
Western University – London, Ontario

- Thesis: Gait Real-Time Analysis Interactive Lab (GRAIL): Concurrent Validity and Reliability of Knee Angles and Moments

CSEP-CEP Certification 2013
University of Waterloo – Waterloo, Ontario

Bachelor of Science (B.Sc.), Kinesiology, Honours, Co-operative Program 2008 – 2013
Minor: Human Nutrition
University of Waterloo – Waterloo, Ontario

CONFERENCES & PRESENTATIONS

Oral Presentations

Gait Real-Time Analysis Lab: Concurrent Validity and Reliability of Lower Limb Kinematics and Kinetics.
Ryan Pinto, Ian Jones, Rebecca Moyer, J. Robert Giffin, Trevor Birmingham (2015).

- *2015:* Bodies of Knowledge Graduate Research Conference, University of Toronto – Toronto, Ontario
- *2015:* The Saltin International Graduate Course in Clinical & Exercise Physiology – Toronto, Ontario

Poster Presentations

Known-Groups Validity and Test-Retest Reliability of the Total Moment of the Knee During Gait. Kendal Marriott, Trevor Birmingham, Rebecca Moyer, Ryan Pinto, J. Robert Giffin (2016).

- *2016:* Osteoarthritis Research Society International (OARSI) World Congress – Amsterdam, Netherlands

Gait Real-Time Analysis Lab: Concurrent Validity and Reliability of Knee Angles and Moments.
Ryan Pinto, Ian Jones, Rebecca Moyer, J. Robert Giffin, Trevor Birmingham (2015).

- *2016:* Canadian Bone & Joint National Conference – London, Ontario *(Award Winner)*
- *2015:* Faculty of Health Sciences Research Day, Western University – London, Ontario
- *2015:* Health & Rehabilitation Science Graduate Research Conference, Western University – London, Ontario *(Award Winner)*

WORK EXPERIENCE

Laboratory Support/Research Assistant 2014 – Present
Wolf Orthopaedic Biomechanics Laboratory (WOBL), Western University – London, Ontario

Teaching Assistant 2015 – 2016
Western University – London, Ontario

Course Co-Supervisor 2015 – 2016
Western University – London, Ontario

Personal Trainer 2015 – 2016
Western Student Recreation Centre – London, Ontario

Assistant Kinesiologist 2012
CGI – Markham, Ontario

Kinesiology Assistant 2011
The Village of Riverside Glen – Guelph, Ontario

VOLUNTEER EXPERIENCE

Volunteer 2013
UW Well-Fit, University of Waterloo – Waterloo, Ontario

Physiotherapist Assistant 2010
KidsAbility – Waterloo, Ontario

AWARDS & ACHEVIEMENTS

Innovations in Musculoskeletal Research Award 2016
Canadian Bone & Joint National Conference – London, Ontario
Best Master of Science (M.Sc.) Poster Award 2015
Western University – London, Ontario
Co-op Student of the Year Award Nominee 2012
University of Waterloo – Waterloo, Ontario
Merit Scholarship 2008
University of Waterloo – Waterloo, Ontario
Queen Elizabeth Aiming for the Top Scholarship 2008
Erin Branch Royal Canadian Legion Award 2008
Hardo Shulwitz Memorial Health & Physical Education Award 2008